Assessment of Long-term Occupational Pesticide Exposure and its Application to an Epidemiological Study on Ill-health among UK Farmers

A thesis submitted to the University of Manchester for the degree of Doctor of Philosophy in the Faculty of Medical and Human Sciences

2013

Haytham Alhamwi

School of Medicine
Centre for Occupational and Environmental Health
List of Contents

List of Figures ................................................................................................................................. 8
List of Tables ....................................................................................................................................... 10
Abstract ............................................................................................................................................... 14
Declaration ........................................................................................................................................ 15
Copyright Statement ........................................................................................................................ 15
Acknowledgments ............................................................................................................................ 16
Dedication ........................................................................................................................................... 16
List of Abbreviations ........................................................................................................................ 17

Chapter 1: Introduction .................................................................................................................. 19

1.1 Rationale of this PhD project ..................................................................................................... 19
1.2 Main aim and specific objectives of this PhD project ............................................................... 21
1.3 Assessment of long-term occupational exposure to pesticides ............................................... 22
  1.3.1 Pesticides ............................................................................................................................... 22
  1.3.2 Main categories of pesticides ............................................................................................... 23
  1.3.2.1 Insecticides ....................................................................................................................... 23
  1.3.2.1.1 Organophosphates ........................................................................................................ 23
  1.3.2.1.2 Carbamates .................................................................................................................... 28
  1.3.2.1.3 Organochlorines ............................................................................................................ 30
  1.3.2.1.4 Synthetic pyrethroids ................................................................................................... 32
  1.3.2.1.5 Avermectins .................................................................................................................. 34
  1.3.2.2 Herbicides .......................................................................................................................... 35
  1.3.2.3 Fungicides .......................................................................................................................... 38
  1.3.3 Pesticide exposure in sheep farming and other farming sectors ......................................... 40
  1.3.3.1 Sheep farming .................................................................................................................... 40
  1.3.3.2 Cattle and other livestock farming ..................................................................................... 43
  1.3.3.3 Crops and grains ............................................................................................................... 45
  1.3.4 Techniques used to assess long-term exposure ................................................................... 46
  1.3.4.1 Self-reported exposure ..................................................................................................... 47
  1.3.4.2 Exposure measurement ..................................................................................................... 49
  1.3.4.3 Biological markers ............................................................................................................ 49
  1.3.4.4 Expert assessment ............................................................................................................. 50
  1.3.4.5 Job exposure matrix ......................................................................................................... 51
  1.3.4.6 Exposure intensity algorithm ............................................................................................. 53
  1.3.4.6.1 Sheep dipping model ...................................................................................................... 56
  1.3.4.6.2 Pesticide applicator model ............................................................................................. 58
  1.3.5 Routes of occupational exposure to pesticides ..................................................................... 61
  1.3.5.1 Dermal ............................................................................................................................... 61
  1.3.5.2 Inhalation ............................................................................................................................ 62
Chapter 4: Evaluation of the new sheep dipping model..................134
  4.1 Introduction ................................................................. 134
  4.2 Materials and methods........................................................ 135
  4.2.1 Analysis of OP urinary metabolites...................................... 135
  4.2.2 Exposure estimates ......................................................... 136
  4.2.3 Statistical analysis ......................................................... 137
  4.3 Results .............................................................................. 137
  4.3.1 Descriptive analysis ......................................................... 137
  4.3.2 Association between exposure estimates and diazinon urinary metabolites .140
  4.4 Discussion........................................................................ 143

Chapter 5: Probabilistic model for pesticide exposure through sheep dipping.........................................................148
  5.1 Introduction ........................................................................ 148
  5.2 Development of the probabilistic model .................................... 149
  5.2.1 Development steps............................................................. 149
  5.2.2 Modification of the conceptual algorithm .................................. 150
  5.2.3 Distribution of model variables ............................................. 152
  5.3 Results of probabilistic model.................................................. 156
  5.4 Application of probabilistic models to different exposure scenarios ..160
  5.4.1 Illustration of differences between probabilistic and deterministic approaches for three dipping tasks in the same dipping session ............... 161
  5.4.2 Illustration of differences between probabilistic and deterministic approaches for farmers in the SHAW study.............................................. 162
  5.5 Discussion........................................................................ 164

Chapter 6: Occupational pesticide exposure in the SHAW study ........168
  6.1 Introduction ....................................................................... 168
  6.2 Materials and methods.......................................................... 168
Chapter 7: Validation of self-reporting exposure among farmers

7.1 Introduction .................................................................216
7.2 Materials and Methods ..................................................216
7.2.1 June Survey of Agriculture and Horticulture (JSAH) ..........216
7.2.2 Collection of JSAH data of SHAW farmers ......................217
7.2.3 Data handling ............................................................217
7.2.4 Statistical methods .....................................................218
Appendix 3: A letter to the farmers asking for their permission to observe a sheep

Appendix 2: SHAW Phase 2 Occupational and Exposure Questionnaire

Appendix 1: SHAW Phase 1 Health and Work History Questionnaire

References

Chapter 9: General discussion

Appendices

Appendix 1: SHAW Phase 1 Health and Work History Questionnaire

Appendix 2: SHAW Phase 2 Occupational and Exposure Questionnaire

Appendix 3: A letter to the farmers asking for their permission to observe a sheep dipping session
Appendix 4: Exposure scores for all variables of sheep dipping exposure algorithm assigned by experts........................................................................................................338
Appendix 5: Assumptions for the missing information in the HSDS used for the validation study ..........................................................................................................................345
Appendix 6: Abstracts of studies used to obtain the distributions of variables used in the probabilistic model..................................................................................................................346
Appendix 7: Distributions of the conceptual algorithm variables used in the probabilistic model..............................................................................................................................355
Appendix 8: Telephone Questionnaire: Using pesticides in cattle farming..................370
Appendix 9: Rules used for data handling of occupational pesticide exposure.............371
Appendix 10: Deterministic values of REST variables in the SHAW algorithm.............374
Appendix 11: Details of exposure assessment model in the SHAPE study....................375
Appendix 12: Rules for applying SHAPE models for the SHAW study.......................377
Appendix 13: Rules for applying TASK models for the SHAW study........................378
Appendix 14: Assumptions to determine OP probability in livestock sectors ...............379
Appendix 15: OPPROB for different types of crops ....................................................381
Appendix 16: Consent form for CPH number ...............................................................383
Appendix 17: Comparisons of age and memory between farmers who had the same answers in SHAW and JSAH and those who had different answers ........384
Appendix 18: Distributions of screen-identified neuropsychiatric illnesses among farmers whose answers in SHAW study were same as the JSAH and among farmers whose answers were different .................................................................386
Appendix 19: Association between neuropsychiatric illnesses and pesticide exposure in different farming sectors .................................................................390

Word count: 77,791
List of Figures

Figure 1-1: General structure of OP pesticides .......................................................... 23
Figure 1-2: Structure of diazinon ............................................................................. 24
Figure 1-3: The amounts of OPs (in tonnes) applied to crops in Great Britain (1965-
1997) ..................................................................................................................... 25
Figure 1-4: Reaction between OPs and acetylcholinesterase .............................. 25
Figure 1-5: Metabolic pathways of diazinon .......................................................... 27
Figure 1-6: Structure of carbaryl, carbofuran and aldicarb ................................. 29
Figure 1-7: The total annual usage of carbamate (in tonnes) applied to all crops in
Great Britain (1990-2010) .................................................................................. 29
Figure 1-8: Structure of DDT, lindane and aldrin .................................................. 30
Figure 1-9: The total annual usage of organochlorines (in tonnes) applied to all crops
in Great Britain (1990-2010) ............................................................................. 31
Figure 1-10: Structure of pyrethrin, permethrin, cypermethrin and deltamethrin ....33
Figure 1-11: The total annual usage of synthetic pyrethroids (in tonnes) applied to
all crops in Great Britain (1990-2010) ................................................................. 33
Figure 1-12: General structure of avermectins ...................................................... 34
Figure 1-13: Structure of 2,4-D, MCBA, paraquat and glyphosate ....................... 37
Figure 1-14: The total annual usage of herbicides (in tonnes) applied to all crops in
Great Britain (1990-2010) .................................................................................. 37
Figure 1-15: The total annual usage of fungicides (in tonnes) applied to all crops in
Great Britain (1990-2010) .................................................................................. 39
Figure 1-16: Sheep ectoparasites .......................................................................... 41
Figure 1-17: Sheep treatment methods ................................................................. 42
Figure 1-18: The total number of cattle, pigs and poultry in the UK (1970-2010).....43
Figure 1-19: Warble fly ......................................................................................... 44
Figure 1-20: Applying pesticides to crops and grains ........................................... 46
Figure 1-21: Evolution of exposure measures to assess occupational pesticide
exposure through sheep dipping ............................................................................. 47
Figure 1-22: Assessing exposure to OPs among farm workers with a JEM .......... 52
Figure 1-23: Total sales of OP sheep dip products in the UK and annual numbers of
human Suspected Adverse Reactions to sheep dips by year of onset of the adverse reaction ................................................................. 68
Figure 3-1: Handling the concentrate ................................................................... 96
Figure 3-2: Dipping bath ....................................................................................... 97
Figure 3-3: Clothes of the dippers at the end of the session ................................. 98
Figure 3-4: Development of the conceptual model and the assessment algorithm ....99
Figure 3-5: Conceptual model for pesticide exposure from each source in sheep dipping including routes, transport processes and modifying factors

Figure 4-1: Number of days between sampling and first dipping day and last dipping day

Figure 4-2: Distribution of TOTAL exposure scores

Figure 4-3: Distribution of detectable diazinon urinary metabolite levels

Figure 5-1: Methodology for developing the probabilistic exposure model of sheep dipping

Figure 5-2: Methodology for obtaining the distribution of each variable used in the probabilistic model

Figure 5-3: Distribution of exposure scores from CON and DIP sources

Figure 5-4: Distribution of exposure scores from DIS, AFT and INC sources

Figure 5-5: Distribution of exposure scores from each source and total exposure

Figure 5-6: Ratio of pesticide exposure from each source to the total exposure

Figure 5-7: Exposure estimates of three different dipping tasks in the same session

Figure 5-8: Exposure estimates of four farmers in the SHAW study

Figure 6-1: Estimation of pesticide exposure in sheep and other farming sectors

Figure 6-2: Number of subjects who had ever been farmers in each farming sector between 1942-2005 and those who applied pesticides in that sector

Figure 6-3: Number of sheep farmers using different treating methods by year

Figure 6-4: Annual number of treating days in sheep sector

Figure 6-5: Percentage of farmers who used different types of PPE during handling the concentrate to treat sheep

Figure 6-6: Sheep dipping exposure model scores after excluding zero results

Figure 6-7: Cattle farming exposure model scores after excluding zero results

Figure 6-8: Crops farming exposure model scores after excluding zero results

Figure 6-9: Associations between scores of general pesticide exposure models and scores of OP exposure models in sheep dipping

Figure 6-10: Associations between scores of general pesticide exposure models and scores of OP exposure models in different sectors

Figure 7-1: Number of accessible SHAW farmers’ records

Figure 7-2: Agreements between SHAW Phase 1 data and JSAH data over time

Figure 7-3: Agreements between SHAW Phase 2 data and JSAH data over time

Figure 7-4: Distributions of PERdiff in different farm types over time
List of Tables

Table 1-1: Classification of herbicides .......................................................... 36
Table 1-2: Chemical classification of non-systemic and systemic fungicides .......... 39
Table 1-3: Summaries of pesticide exposure algorithms used in different farming sectors .................................................................................................................. 54
Table 1-4: Determinants used in assessment metrics of pesticide exposure ............ 63
Table 1-5: DSM-IV Criteria for major depressive episode .................................... 69
Table 1-6: UK Parkinson’s Disease Society Brain Bank clinical diagnostic criteria of PD .................................................................................................................................. 76
Table 1-7: Neuropsychological test batteries used in the study of Stephens et al. ....... 81
Table 2-1: SHAW Phase 1 ill-health definitions ..................................................... 88
Table 2-2: Demographics and farming variables of SHAW phase 1 population .......... 89
Table 2-3: Demographics and farming variables of SHAW phase 2 population .......... 92
Table 3-1: Modifying factors in handling the concentrate ...................................... 106
Table 3-2: Modifying factors in dipping sheep in the diluted pesticide .................. 107
Table 3-3: Modifying factors in handling dipped sheep ......................................... 108
Table 3-4: Modifying factors in the disposal of sheep dip ..................................... 109
Table 3-5: Modifying factors in incidental exposure (falling in the bath and spilling the concentrate on the body) ................................................................. 109
Table 3-6: Scores of dipper’s task ....................................................................... 116
Table 3-7: Ratio of body parts covered with single or combinations of PPE .......... 116
Table 3-8: Effectiveness of the PPE in sheep dipping activities ............................. 117
Table 3-9: Skin area (m²) that could be contaminated during each activity and as a proportion of the whole body .......................................................... 118
Table 3-10: Exposure scores for variables of handling the concentrate assigned by experts .................................................................................................................. 121
Table 3-11: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts ................................................................. 123
Table 3-12: Exposure scores for variables of the disposal of sheep dip assigned by experts .................................................................................................................. 126
Table 3-13: Exposure scores for variables of incidental exposure assigned by experts 127
Table 3-14: Weights of exposure routes for each exposure source in sheep dipping ... 128
Table 3-15: Weights of pesticide exposure sources in sheep dipping .................... 129
Table 4-1: Pesticide exposure estimates .............................................................. 138
Table 4-2: Detected urinary diazinon metabolite levels ........................................ 140
Table 4-3: Correlations between exposure estimates and diazinon metabolites ....... 140
Table 4-4: Associations between exposure estimates and detecting diazinon metabolites .................................................................................................................. 140
Table 4-5: Association between exposure estimates and urinary diazinon metabolites

Table 4-6: Inter-rater agreement between exposure estimates of sampling day and total urinary diazinon metabolites

Table 4-7: Geometric means of diazinon urinary metabolites by three exposure intensities

Table 5-1: Summary of distributions used in the probabilistic model

Table 5-2: Exposure data of four dippers interviewed in the SHAW study

Table 6-1: Simple surrogates of pesticide exposure from sheep dipping

Table 6-2: Parameters and scores of the exposure model variables

Table 6-3: Simple surrogates of pesticide exposure from other farming sectors

Table 6-4: Number of farmers who had ever applied pesticides in different farming sectors

Table 6-5: Treating methods used by sheep farmers

Table 6-6: Cumulative number of flock size, treating years and treating days in sheep sector

Table 6-7: PPE use by sheep farmers when using pesticides

Table 6-8: Dipping Task

Table 6-9: Description of dipping bath

Table 6-10: Cattle treatments applied by the SHAW farmers

Table 6-11: PPE used by cattle farmers when using pesticides

Table 6-12: Other livestock treatments applied by the SHAW farmers

Table 6-13: PPE used by other livestock farmers when using pesticides

Table 6-14: Type of crops and grains treated

Table 6-15: Pesticide application methods in the crops sector

Table 6-16: Pesticide exposure surrogates in sheep farming

Table 6-17: Pesticide exposure surrogates in cattle and other livestock sectors

Table 6-18: Pesticide exposure surrogates in crops farming

Table 6-19: Correlations between scores of general pesticide exposure models and surrogates of sheep dipping

Table 6-20: Correlations between scores of OP pesticide exposure models and surrogates of sheep dipping

Table 6-21: Correlations between scores of exposure models and surrogates of pesticide exposure in all farming sectors (EXP and YR)

Table 7-1: Matching between SHAW phase 1 data and JSAH data

Table 7-2: Number of farmers included in the analysis of phase 1 and phase 2 data

Table 7-3: Agreements between SHAW Phase 1 data and JSAH data over time

Table 7-4: Correlations between figures of the SHAW and the JSAH over time

Table 7-5: Agreements between SHAW Phase 2 data and JSAH data over time
Table 7-6: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1983 .................................................................226
Table 7-7: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1983 .........................226
Table 7-8: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983 .........................226
Table 7-9: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983 .........................227
Table 7-10: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983 .........................227
Table 7-11: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983 .........................227
Table 7-12: Correlation between age and PERdiff over time ........................................228
Table 7-13: Correlation between memory scores and PERdiff over time .......................228
Table 8-1: Number of screen-positive and screen-negative subjects for each illness according to SHAW phase 1 and phase 2 definitions ...........................................235
Table 8-2: Definitions of pesticide exposure surrogates and models in the sheep farming sector ...........................................................................................................236
Table 8-3: Definitions of pesticide exposure surrogates and models in other farming sectors ............................................................................................................237
Table 8-4: Memory scores of screen-positive and screen-negative farmers in each illness according to different definitions ..............................................239
Table 8-5: Association between memory and pesticide exposure surrogates in different farming sectors ..................................................................................240
Table 8-6: Association between memory and pesticide exposure estimated by exposure models in different farming sectors ........................................241
Table 8-7: Association between depression and pesticide exposure surrogates in different farming sectors ...........................................................................242
Table 8-8: Association between depression and pesticide exposure estimated by exposure models in the sheep sector .........................................................243
Table 8-9: Association between depression and pesticide exposure estimated by exposure models in other farming sectors ........................................244
Table 8-10: Association between neuropathy and pesticide exposure surrogates in different farming sectors .................................................................246
Table 8-11: Association between neuropathy and pesticide exposure estimated by exposure models in the sheep sector ..............................................247
Table 8-12: Association between neuropathy and pesticide exposure estimated by exposure models in other farming sectors ........................................248
Table 8-13: Association between Parkinsonism and pesticide exposure surrogates in different farming sectors .................................................................249
Table 8-14: Association between Parkinsonism and pesticide exposure estimated by exposure models in the sheep sector .................................................................250
Table 8-15: Association between Parkinsonism and pesticide exposure estimated by exposure models in other farming sectors .............................................251
Table 8-16: Association between dementia and pesticide exposure surrogates in different farming sectors .................................................................253
Table 8-17: Association between dementia and pesticide exposure estimated by exposure models in the sheep sector ...............................................254
Table 8-18: Association between dementia and pesticide exposure estimated by exposure models in other farming sectors ........................................255
Abstract

In the UK, dipping sheep with pesticides for treating ectoparasites has been one of the main pesticide applications and it was compulsory between 1984 and 1991 when organophosphates (OPs) were the main ingredients of sheep dips. As a result many current elderly sheep farmers have been exposed to OPs. The acute health effects of many pesticides especially OPs are very well documented, while the effects of long-term exposure are still unclear. Difficulties in assessing past pesticide exposure have been suggested to be one of the main reasons for this uncertainty. The overall aim of this PhD was to develop long-term occupational pesticide exposure models for UK farmers, specifically for OP exposure among sheep dippers, and to apply them to the Study of Health in Agricultural Work (SHAW) in order to examine the associations between long-term pesticide exposure and neuropsychiatric ill-health. A comprehensive conceptual exposure model to assess pesticide exposure during sheep dipping was developed and included five sources of pesticide exposure; handling the concentrate, dipping sheep in the bath, handling sheep after dipping, disposal of sheep dip, and any incidental exposure. Dermal, ingestion and inhalation routes were described for each source and different modifying factors for each route were identified. A semi-quantitative exposure algorithm was developed and all sources, routes and modifying factors were assigned scores and weights by assessment of the literature and expert judgment. The new model was evaluated by comparing its estimates of diazinon exposure among dippers who participated in the Health and Sheep Dipping Survey (HSDS) with diazinon urinary metabolite levels in spot urines collected after the dipping session. The model estimates generally did not correlate well with metabolite levels though there was evidence of an association between total metabolites and ordinal categories of exposure intensity. The uncontrolled conditions of the HSDS and the lack of 24 hr urine collections may have contributed to these results. A probabilistic model was also developed from the conceptual model and indicated that although handling the concentrate and dipping sheep are the most important exposure sources, other sources like handling dipped sheep and disposal of sheep dip should not be neglected. This probabilistic model was applied to different scenarios: probabilistic estimates may give a more comprehensive description of exposures than deterministic estimates as they take into account all conceptual variables. Occupational pesticide exposure among UK farmers in the SHAW study was then estimated using simple surrogates and more sophisticated models. The validity of self-reported exposure history among SHAW farmers was investigated by making comparison with data collected contemporaneously by the June Census. Farmers recall was generally reliable especially for a specific type of livestock or crop rather than the number of livestock or acreage. Associations between screen-identified ill-health and pesticide exposure were only demonstrated by using more developed metrics. Exposure to pesticides but not specifically OPs in sheep farming was associated with neuropathy and Parkinsonism. Exposure to OPs in sheep dipping was associated with a decrease risk of dementia. Depression was not associated with any exposure. In conclusion, this thesis developed a comprehensive model for pesticide exposure from sheep dipping and simpler exposure models for other farming sectors. The application of these models to the SHAW study suggests that long term pesticide exposure among farmers mainly via sheep dipping may result in ill-health; however the associations between exposure and outcomes may only be revealed by the use of more sophisticated exposure models rather than simple exposure surrogates. The study also indicates that even the use of well-derived deterministic estimates might lead to exposure misclassification. This misclassification may be investigated by using probabilistic approaches.
Declaration

I declare that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Copyright Statement

1. The author of this thesis (including any appendices and/or schedules to this thesis) owns certain copyright or related rights in it (the “Copyright”) and he has given The University of Manchester certain rights to use such Copyright, including for administrative purposes.

2. Copies of this thesis, either in full or in extracts and whether in hard or electronic copy, may be made only in accordance with the Copyright, Designs and Patents Act 1988 (as amended) and regulations issued under it or, where appropriate, in accordance with licensing agreements which the University has from time to time. This page must form part of any such copies made.

3. The ownership of certain Copyright, patents, designs, trade marks and other intellectual property (the “Intellectual Property”) and any reproductions of copyright works in the thesis, for example graphs and tables (“Reproductions”), which may be described in this thesis, may not be owned by the author and may be owned by third parties. Such Intellectual Property and Reproductions cannot and must not be made available for use without the prior written permission of the owner(s) of the relevant Intellectual Property and/or Reproductions.

4. Further information on the conditions under which disclosure, publication and commercialisation of this thesis, the Copyright and any Intellectual Property and/or Reproductions described in it may take place is available in the University IP Policy (see http://www.campus.manchester.ac.uk/medialibrary/policies/intellectualproperty.pdf), in any relevant Thesis restriction declarations deposited in the University Library, The University Library’s regulations (see http://www.manchester.ac.uk/library/aboutus/regulations) and in The University’s policy on presentation of Theses.
Acknowledgments

Firstly, my full gratitude is to the one and the only almighty God who helped me to complete my PhD through those most difficult times in the history of Syria, my beloved country.

I would like to thank my supervisors Dr. Andy Povey and Dr. Frank de Vocht who have been always approachable, very helpful and without whose guidance, this thesis would have not been achieved. Thank you for being so kind and supportive. I would like also to thank Dr. Jill Stocks, my co-supervisor, who was generous with her time to appraise my work and to discuss other important issues such as politics and religions!

This work would have not been performed without the help of many people. I am grateful to Dr. Igor Burstyn, Dr. John Cherrie, and my advisor Dr. Adrian Hirst who agreed to be part of the expert panel to assign weighting factors for the exposure assessment model. My sincere thanks to the farmers who gave me the opportunity to visit their farm and watch a sheep dipping session.

I would like to express my gratitude also to all my colleagues at the Centre for Occupational & Environmental Health. My sincere thanks to Professor Raymond Agius and Miss Eileen Woodhouse for their support and their warm feelings. The memories of the kindness and support I was surrounded with by my officemates, Getahun Bero Bedad, Anna Molter, Chom Supapvanich and Abimbola Adebooye, will never fade.

My warmest thanks to my Syrian and Arab friends who are my new family in Manchester, I have spent a lot of joyful and fruitful times with you guys. My brothers, Saied and Mohammad, and my friends in Syria have always been encouraging and inspiring, thanks for reminding me of that light at the end of tunnel!

Finally, this work would have not started nor would have not been completed without the endless sacrifices my wife ‘Asmaa’ and our children Yasin, Yaser, Sumaya, and Huda have made. The prayers of my father and my mother have always been the guiding light. May Allah reward you with all what you wish for.

Dedication

I would like to dedicate this thesis to the hard working people of Syria, including farmers. I feel I have gained from your sacrifices twice; by funding my studies at Manchester University and by rising against the dictatorship and injustice in our country. Your blessed revolution is getting us our dignity back. I will surely live and die at your service.
# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACh</td>
<td>Acetylcholine</td>
</tr>
<tr>
<td>AChE</td>
<td>Acetylcholinesterase</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>AHS</td>
<td>Agricultural Health Study</td>
</tr>
<tr>
<td>BSE</td>
<td>Bovine Spongiform Encephalopathy</td>
</tr>
<tr>
<td>CFS</td>
<td>Chronic Fatigue Syndrome</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CIS</td>
<td>Clinical Interview Schedule</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>COT</td>
<td>Committee on Toxicity of Chemical in Food, Consumer Products and the Environment</td>
</tr>
<tr>
<td>CPHN</td>
<td>County Parish Holding Number</td>
</tr>
<tr>
<td>DAP</td>
<td>Dialkylyphosphates</td>
</tr>
<tr>
<td>DEDTP</td>
<td>Diethylthiophosphate</td>
</tr>
<tr>
<td>Defra</td>
<td>Department of Environment, Food and Rural Affairs</td>
</tr>
<tr>
<td>DEP</td>
<td>Diethylphosphate</td>
</tr>
<tr>
<td>DETP</td>
<td>Diethylthiophosphate</td>
</tr>
<tr>
<td>DMDTP</td>
<td>Dimethylthiophosphate</td>
</tr>
<tr>
<td>DMP</td>
<td>Dimethylphosphate</td>
</tr>
<tr>
<td>DMTP</td>
<td>Dimethylthiophosphate</td>
</tr>
<tr>
<td>DREAM</td>
<td>Dermal Exposure Assessment Method</td>
</tr>
<tr>
<td>EPA</td>
<td>Environmental Protection Agency</td>
</tr>
<tr>
<td>FMD</td>
<td>Foot and Mouth disease</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma Amino-butyric Acid</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>HSDS</td>
<td>The Health and Sheep Dipping Survey</td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>NOAH</td>
<td>National Office of Animal Health</td>
</tr>
<tr>
<td>OC</td>
<td>Organochlorine</td>
</tr>
<tr>
<td>OP</td>
<td>Organophosphate</td>
</tr>
<tr>
<td>OPIDPN</td>
<td>Organophosphate induced delayed polyneuropathy</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>P</td>
<td>P value for significance</td>
</tr>
<tr>
<td>PD</td>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td>PON1</td>
<td>Paraoxonase</td>
</tr>
<tr>
<td>PPE</td>
<td>Personal Protective Equipment</td>
</tr>
<tr>
<td>PSD</td>
<td>Pesticides Safety Directorate</td>
</tr>
<tr>
<td>P&lt;sub&gt;i&lt;/sub&gt;</td>
<td>P-for-trend</td>
</tr>
<tr>
<td>PUS</td>
<td>Pesticide Usage Survey</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>SARSS</td>
<td>Suspected Adverse Reaction Surveillance Scheme</td>
</tr>
<tr>
<td>SHAPE</td>
<td>Survey of Health and Pesticide Exposure</td>
</tr>
<tr>
<td>SHAW</td>
<td>Study of Health in Agricultural Work</td>
</tr>
<tr>
<td>SP</td>
<td>Synthetic Pyrethroid</td>
</tr>
<tr>
<td>sRR</td>
<td>Summary Risk Ratio</td>
</tr>
<tr>
<td>VMD</td>
<td>Veterinary Medicines Directorate</td>
</tr>
</tbody>
</table>
Chapter 1: Introduction

1.1 Rationale of this PhD project

Pesticides have become well known environmental and occupational pollutants during the second half of the last century. While people may be exposed to pesticides environmentally through consumption of food and water contaminated with pesticides or living near places where pesticides are applied, levels of pesticide exposure are potentially higher through using pesticides occupationally or in the home and gardens\(^1\). In addition to exposure in home use and in the control of different human diseases (\textit{e.g.} malaria and river blindness)\(^2\), pesticide exposure can occur in many occupations such as pesticide manufacturing and veterinary medicine, but farming is an occupation in which important exposure to pesticides may occur routinely\(^3\).

Farmers are exposed to pesticides mainly when they apply pesticides to crops and other plants or when they apply pesticides to animals\(^4\). Because of the importance of sheep farming as an industry in the UK, sheep dipping is one of the main pesticide applications in the UK\(^5\). Sheep dipping consists of immersing sheep in a dilute pesticide to prevent or treat sheep scab and other ectoparasites that affect sheep\(^6\). During sheep dipping, farmers can get exposed to pesticides and several British studies have focused on this application since preliminary data indicated that it may be associated with acute and chronic neurological effects amongst these farmers\(^7\)-\(^11\).

Organophosphates (OPs) were one of the main insecticides used in agriculture throughout the world in the last three decades of the last century\(^8\) and they have also been the main ingredients of sheep dips in the UK since 1970s\(^12\). Sheep dipping was compulsory in the UK from 1984 to 1991 and as a result many current sheep farmers have been exposed to OP compounds in the past\(^13\). Therefore, sheep farmers are considered as a good epidemiological population to study the potential health effects from long-term low-level exposure to OPs\(^14\).

The health effects of acute pesticide poisoning of many pesticides, especially OPs, are very well documented\(^15\)-\(^17\) whilst the effects of long-term low-level exposure are still unclear\(^18\)-\(^23\). This gap in our understanding of side effects of long-term low-level exposure to pesticides can be attributed to the many difficulties facing any study on long-term effects. The relatively weak association between pesticide exposure and health effects is one of the difficulties but the difficulties of retrospective long-term
pesticide exposure assessment has been suggested to be one of the most important causes of this uncertainty\textsuperscript{24,25}. Undocumented work conditions and changes in the pesticides used and in the application methods are examples of the reasons for this difficulty\textsuperscript{26}.

Studies of pesticide health effects have depended on different methods to estimate long-term pesticide exposure. Some studies have depended on simple surrogates like ever/never working with pesticides\textsuperscript{11} or residential pesticide exposure\textsuperscript{27} while other studies have used more sophisticated models\textsuperscript{28,29}. Sometimes the difference in exposure assessment methodologies is a result of the difference between study types\textsuperscript{24,30} (i.e. exposure variables that can be recalled by a participant in a retrospective case-control study may be different from exposure variables that can be collected in a prospective cohort study). Problems in the retrospective assessment of pesticide exposure primarily result in non-differential exposure misclassification, which generally reduces the study power and bias the estimates of relative risks towards the null\textsuperscript{31}.

As a result, for an increased understanding of health effects in human population that may be associated with long-term low-level pesticide exposure, there is a great need to develop better techniques to assess past exposure to pesticides and it is important to validate these techniques. Therefore, this PhD study focuses on the assessment of long-term pesticide exposure, mainly assessment of OP exposure among sheep dippers, to be subsequently applied to epidemiological studies on the health effects of this exposure.

Many chronic health illnesses and symptoms such as cancers, dermatologic problems, neurologic deficits and miscarriages have been associated with long-term exposure to pesticides in many studies\textsuperscript{18-23}. However, the assessment of neurologic and neuropsychiatric effects has been used to illustrate the difficulties that face studies of health outcomes in farming communities exposed to pesticides\textsuperscript{24,30}. The Study of Health in Agricultural Work (SHAW) is a previously conducted study described in detail in Chapter 2 that has explored the neurologic and neuropsychiatric effects of long-term pesticide exposure among UK farmers. Therefore, the SHAW study was used in this thesis to investigate the impact of using the newly developed exposure assessment methodologies on the association between exposure and health outcomes.

In the SHAW study four health outcomes were of interest namely, depression, neuropathy, Parkinsonism and dementia. These four illnesses can be classified in different ways, but generally depression and dementia are classified as neuropsychiatric
ill-health while Parkinsonism and neuropathy are classified as neurological ill-health. However, in the text of this thesis and mainly for simplicity these four illnesses were referred to as ‘neuropsychiatric’ ill-health.

1.2 Main aim and specific objectives of this PhD project

The main aim of this thesis was therefore to develop long-term occupational pesticide exposure models for UK farmers, specifically for OP exposure among sheep dippers, and to apply them to the SHAW study in order to examine the associations between long-term pesticide exposure and neuropsychiatric ill-health.

To achieve this aim, the objectives are:

1- To develop a comprehensive conceptual exposure model to assess pesticide exposure during sheep dipping (as described in Chapter 3).

2- To evaluate this new developed exposure model of sheep dipping (as described in Chapter 4).

3- To develop a probabilistic model from the new exposure model of sheep dipping and to examine the effect of unavailable data on exposure determinants on exposure assessment (as described in Chapter 5).

4- To describe the occupational practices of the farmers of the SHAW study related to pesticide exposure and to estimate their occupational pesticide exposure using different methodologies (as described in Chapter 6).

5- To validate self-reported occupational exposures among farmers in the SHAW study (as described in Chapter 7)

6- To apply the new models to examine the association between neuropsychiatric ill-health and long-term pesticide exposure in different farming sectors (as described in Chapter 8).
1.3 Assessment of long-term occupational exposure to pesticides

1.3.1 Pesticides

Pesticides have been defined by the Food and Agriculture Organisation as “any substance or mixture of substances intended for preventing, destroying or controlling any pest, including vectors of human or animal disease, unwanted species of plants or animals causing harm during or otherwise interfering with the production, processing, storage, transport or marketing of food, agricultural commodities, wood and wood products or animal feedstuffs, or substances which may be administered to animals for the control of insects, arachnids or other pests in or on their bodies”32.

Before the development of synthetic organic pesticides in the first half of the twentieth century, farmers used different methods like crop rotation, crop diversity, mechanical pest removal and host removal to control pests33. Inorganic materials such as lead, copper, and arsenic and botanical compounds like nicotine and pyrethrum were also used. However, the old methods and materials were expensive and not always practical, and the introduction of synthetic pesticides made pest control more effective and economic33.

Each year around 3 billion kilograms of pesticide are applied worldwide and nearly 40 billion US dollars are spent to purchase pesticides34. 26 primary benefits and 31 secondary benefits from pesticides have been described35, and the main benefits include the increment of crop and livestock yields, improvement in food safety and human health, and a reduction in energy use and environmental degradation. In contrast, pesticide application can also cause economic losses mainly due to groundwater contamination, public health effects (acute poisoning and chronic effects), crop losses caused by pesticides themselves, and other environmental losses34.

During pesticide application to crops and other plants or to farm animals, farmers are exposed to pesticides4. Pesticide manufacturers usually focus on making the products extremely effective against the targeted pests but this aim sometimes contradicts with human and the environmental safety36. Therefore the use of new pesticides has been regulated by pesticide regulatory agencies such as the Pesticides Safety Directorate (PSD) and the Veterinary Medicines Directorate (VMD) in the UK37 and the Environmental Protection Agency (EPA) in the USA38.
1.3.2 Main categories of pesticides

Pesticides can be categorised in different ways but the main two ways are either according to the chemical classes of the active ingredients (OPs, organochlorines, pyrethroids, etc.) or according to their functions (insecticides, herbicides, fungicides, etc.). In the following sections, the main categories of pesticides will be described with a special attention to insecticides since they are applied, in addition to crops, to farm livestock including sheep and cattle.

1.3.2.1 Insecticides

Many methods and natural materials have been used to get rid of insects which affect human health and wealth (crops and animals) and the first known use is documented to be around 2500 B.C\textsuperscript{39}. However, the world saw the most significant growth in the use of synthetic insecticidal compounds after World War II. The main groups of insecticides are OPs, carbamates, organochlorines, synthetic pyrethroids, and avermectines\textsuperscript{39,40}.

1.3.2.1.1 Organophosphates

All chemicals which contain carbon and phosphorus are described as organophosphorus compounds. However, the term OPs is used to refer to those organophosphorus compounds that inhibit acetylcholinesterase (AChE), the primary target enzyme\textsuperscript{13}. The structure of OPs in general is represented in Figure 1-1:

\[
\begin{align*}
\text{X} & \text{P} \quad \text{L} \\
\text{R}_1 & \\
\text{R}_2 & \\
\end{align*}
\]

\textbf{Figure 1-1: General structure of OP pesticides}  
Adapted from Chambers \textit{et al.}\textsuperscript{41}

“L” indicates the “leaving group”, which is the most reactive substituent and is displaced when the OP phosphorylates AChE. X denotes either oxygen in the phosphates compounds (sometimes referred as oxons) or sulphur in the phosphorothioate compounds (sometimes referred as thions). R\textsubscript{1} and R\textsubscript{2} are alkyl, aryl, alkylthio, or alkylamino, but most commonly alkoxy groups\textsuperscript{41}.

Nerve agent gases (\textit{e.g.} sarin and tabun) are also OPs but have a different chemical structure with a low molecular weight. Their R\textsubscript{1} and R\textsubscript{2} are simple groups and their
leaving groups (fluoro- and cyano-) are readily displaceable and bound directly to the phosphorus without an intermediate oxygen or sulphur atom. This direct chemical bond gives a high degree of stability to the OP-inhibited acetylcholinesterase *in vivo* and this stability is, to a great extent, behind the very high toxicity of these compounds compared to that of the OP pesticides. Throughout this thesis, the term “OPs” refers in particular to those organophosphorus compounds used as pesticides and that inhibit AChE.

The volatility of OPs depends on the structure of X, R₁, and R₂ but generally is low and usually they are solids at room temperature and stable in aqueous solutions¹³. Most OPs have high lipid-solubility⁴² specially those used in sheep dips like diazinon (Figure 1-2) which need to be retained in the sheep fleece¹³.

![Figure 1-2: Structure of diazinon](image)

*Adapted from Rougier et al.⁴³*

A number of OPs were synthesised in the early years of the 20th century but the toxicity of these compounds were only recognised in the 1930s when many highly toxic compounds were produced as chemical warfare agents⁴¹. After World War II the use of OP insecticides increased and as OPs degrade quickly by hydrolysis in the environment this made them attractive alternatives to the organochlorines which persist in the environment for a long time¹³. In 1970 there were more than 200 OP compounds used as insecticides in the worldwide market⁴¹ while 24 OP insecticides were approved in the UK in 1998¹³. Figure 1-3 shows the amounts (in tonnes) of OP pesticides applied to crops in Great Britain between 1965 and 1997. The amount of OPs used increased rapidly until the mid 1970s and then plateaued until the late 1980s when use increased again until 1995 when it fell again¹³. About 230 tonnes of OPs were applied on all crops in Great Britain in the year 2000 and the amount then decreased gradually to reach 130 tonnes in 2010⁴⁴. OP compounds (mainly diazinon and propetamphos) have been the predominant pesticides used in sheep dips in the UK since 1970¹², and in 2011 diazinon was the only permissible active ingredient in sheep dips authorised by the VMD⁴⁵.
OP pesticides inhibit AChE enzyme in synapses and on red cell membranes and inhibit butyrylcholinesterase in plasma. The inhibition of AChE accumulates the neurotransmitter, Acetylcholine (ACh), in the target tissues (i.e. synapses of the autonomic nervous system, Central Nervous System (CNS), and neuromuscular junctions) which results in the paralysis of ACh receptors\(^46\). Figure 1-4 displays the key reaction occurring between OP compounds and AChE. AChE is an efficient enzyme that can rapidly regenerate its active form after inactivating ACh, but the phosphorylated enzyme is hydrolysed back to the active form at a slower rate than the normal enzyme\(^47\). The phosphorylated enzyme may undergo a process known as “aging” when it loses one alkyl group and becomes irreversibly inactivated\(^13\).

**Figure 1-3: The amounts of OPs (in tonnes) applied to crops in Great Britain (1965-1997)**
Adapted from the COT report\(^13\)

**Figure 1-4: Reaction between OPs and acetylcholinesterase**
Adapted from Kamanyire and Karalliedde\(^42\)
OPs are metabolised in mammals through different pathways which involve various enzyme system and these pathways may vary between OP compounds. The most common pathway of OP metabolism is through hydrolysis that leads to the removal of the leaving group and this hydrolysis results in different dialkylphosphates (DAP)\textsuperscript{13}. About 80% of the approved OPs in the UK increase one or more DAP and the most frequent metabolites are diethylphosphate (DEP), diethylthiophosphate (DETP), diethyl-dithiophosphate (DEDTP), dimethylphosphate (DMP), dimethylthiophosphate (DMTP) and dimethyl-dithiophosphate (DMDTP)\textsuperscript{48}. The present of one or more of these metabolites in the urine provides an indication of exposure to specific OPs. Dimethoxy OPs (\textit{e.g.} malathion and dichlorovos) are metabolised to DMP and DMTP, whilst diethoxy OPs like diazinon are metabolised to DEP and DETP\textsuperscript{49}.

The metabolism of a specific OP into a specific metabolite or another varies according to the metabolic pathways. For example, diazinon, that is itself weakly toxic, is activated when it is oxidised into diazoxon which is a toxic metabolite with a high potency to phosphorylate AChE. This activation pathway is carried out by cytochrome P450s mainly in the liver and produces the DEP metabolite. The cytochrome P450s can also hydrolise diazinon into non toxic products and this pathway produces the DETP metabolite\textsuperscript{13,50}. Figure 1-5 shows the metabolic pathway of diazinon. The toxic diazoxon is inactivated by Paraoxonase (PON1) and other serum esterase and the rate of hydrolysis of the toxic metabolites by serum PON1 is found to be an important determinant of OP toxicity in mammals\textsuperscript{51}.

DAP urinary excretion varies according to the route of exposure. About 60% of an oral dose of diazinon and only 1% of a dermal dose has been reported to be excreted as urinary DAP, whilst approximately 90% of the dermal dose was recovered from the skin surface\textsuperscript{52}. OPs deposited in the lungs after inhalational exposure are absorbed rapidly and almost completely and they reach the general circulation with limited metabolism\textsuperscript{13}. A rapid absorption, metabolism and excretion usually follow oral exposure. The urinary DAP levels were shown to peak 2 hours after exposure and 90% of the excreted oral dose was recovered within 14 hours. In contrast, urinary excretion of DAP was shown to peak at 12 hours after the start of exposure to an occluded dermal dose or after 4 hours after it was washed off and 60% of the excreted DAP was recovered between 6 and 26 hours. This suggested that the elimination half- lives of the DAP metabolites of diazinon are 2 and 9 hours following oral and dermal exposures respectively\textsuperscript{52}. These elimination half-lives were relatively close to the urinary
metabolite elimination half-lives of propetamphos (1.7 and 3.8 hours following oral and dermal doses respectively)\textsuperscript{\ref{footnote53}} but much shorter than those of DAP metabolites of chlorpyrifos (15 and 37 hours following oral and dermal doses respectively)\textsuperscript{\ref{footnote54}}.

![Figure 1-5: Metabolic pathways of diazinon](image)

\textit{Adapted from Poet et al.}\textsuperscript{\ref{footnote50}}

The worldwide number of deaths per year due to self-poisoning with OPs has been estimated to be around 200,000 while unintended poisoning is less common\textsuperscript{\ref{footnote55}}. In the UK only about 30 cases of OP intoxication among people aged 16-69 years were admitted to hospitals between 1998 and 2003\textsuperscript{\ref{footnote56}}. The effects of OP intoxication can be classified into three syndromes, namely the acute syndrome, the intermediate syndrome, and delayed polyneuropathy\textsuperscript{\ref{footnote13}}. Acute syndrome, which is a result of accumulated ACh in the target tissue, includes three groups of effects based on a physiological basis; namely central, muscarinic, and nicotinic effects\textsuperscript{\ref{footnote57}}. Central effects include anxiety, giddiness, headache, tremor, confusion, convulsions and respiratory depression. Muscarinic effects result from the accumulation of ACh within the postganglionic synapses of the parasympathetic nervous system. These effects include sweating, salivation, lachrymation, bronchorrhea, miosis, failure of accommodation, diarrhea,
abdominal cramp, and bradycardia. The accumulation of ACh at autonomic ganglia and neuromuscular junctions results in the nicotinic effects. The main nicotinic effects are pallor, weakness, tachycardia, hypertension and fasciculation\textsuperscript{42}. Acute symptoms usually appear immediately or within hours after exposure and rarely appear after more than 24 hours post exposure. The symptoms usually last for hours but after high exposure, severe symptoms may last for days and mild symptoms may last for weeks. The diagnosis of severe poisoning is easy but the diagnosis of very mild toxicity might be difficult\textsuperscript{58}.

The intermediate syndrome starts one to four days after OP poisoning. In this syndrome, a muscle weakness occurs in the limbs and the neck and might reach the respiratory muscles resulting in respiratory failure. These effects, which may be due to muscle necrosis, lasts from 5 to 18 days\textsuperscript{59,60}.

OP-induced delayed polyneuropathy (OPIDPN) is a rare syndrome resulting from intoxication with certain OPs (\textit{e.g.} dichlorvos, fenthion, and trichlorfon). In this phenomenon, a degeneration of some long axons in the central and peripheral nervous system occurs 2-3 weeks after exposure and results in ataxia and paralysis\textsuperscript{42,61}. The mechanism of this syndrome is well-established and is associated with the inhibition of the neuropathy target esterase enzyme (NTE) within neurons. OPIDPN happens in all mammalian species tested since NTE is found in all mammalian species including humans, however the hen is more sensitive than other species to the development of an OPIDPN, and clinical signs developed in hens are similar to those occur in humans. OPs that produce more than 70\% inhibition of NTE give positive results in the hen test, and to be approved or licensed by the UK regulatory agencies (VMD or PSD) OP pesticides should be negative in the hen test. Therefore, OPIDPN is not expected to be seen in the UK in the absence of acute toxicity\textsuperscript{13}.

1.3.2.1.2 Carbamates

Carbamates are derivatives of carbamic acid and categorised into three classes; aryl N-methylcarbamate esters of phenols (\textit{e.g.} carbaryl), N-methyl and N-dimethylcarbamate esters of heterocyclic phenols (\textit{e.g.} carbofuran), and oxime derivatives of aldehydes (\textit{e.g.} aldicarb)\textsuperscript{2}. The structures of the three examples are presented in Figure 1-6. The synthesis of carbamate insecticides started in 1950s and carbaryl, one of the most common and successful carbamates, was introduced in 1956\textsuperscript{4}. Most carbamate insecticides have poor volatility but the volatility of few of them like aldicarb quickly
increases with temperature and most of them also have low water solubility\textsuperscript{62}. Only a slight accumulation of carbamate insecticides are found in the environment and in the food chains\textsuperscript{63}.

![Structure of Carbaryl, Carbofuran, and Aldicarb](image)

**Figure 1-6: Structure of carbaryl, carbofuran and aldicarb**
Adapted from Hassall\textsuperscript{2}

Carbamates were increasingly used in 1960s and 1970s with a large number of its compounds being synthesised, but only less than 20 compounds have been used in the pesticide market worldwide\textsuperscript{62}. The total annual usage of carbamate in England and Wales was about 66 tonnes in the period of 1971-1974, 314 tonnes in the period of 1975-1979, and 444 tonnes in the period of 1980-1983\textsuperscript{64}. Figure 1-7 shows the total annual usage of carbamates (in tonnes) applied to all crops in Great Britain during 1990-2010. In general, the amount of carbamates applied has decreased over the time\textsuperscript{65}.

![Total annual usage of carbamate](image)

**Figure 1-7: The total annual usage of carbamate (in tonnes) applied to all crops in Great Britain (1990-2010)**
Adapted from Pesticide Usage Survey\textsuperscript{65}
The mode of action of carbamate insecticides is the same as OPs in that they inhibit AChE resulting in the accumulation of ACh in nerve synapses\textsuperscript{66}. However, the carbamyl-acetylcholinesterase combination which results from carbamates is hydrolysed faster than phosphoryl-acetylcholinesterase produced by OPs. Therefore, in the absence of continued exposure, regeneration of free AChE in synapses would start in a few minutes and would be complete after several hours\textsuperscript{39}.

Carbamate intoxication is less frequent than OP intoxication and symptoms of carbamate poisoning are generally similar to those of OP poisoning but the duration of poisoning is limited and the toxicity is less compared to OPs\textsuperscript{62}. The recovery from carbamate poisoning is usually complete after only a few hours with no delayed neurotoxic effects\textsuperscript{39}. Symptoms of CNS depression (\textit{e.g.} coma and seizures) and nicotinic effects (\textit{e.g.} hypertension) and cardiorespiratory depression are the main manifestations of a serious intoxication and death may occur from respiratory failure\textsuperscript{66}.

\subsection*{1.3.2.1.3 Organochlorines}

Chlorinated hydrocarbons or organochlorine insecticides (OC) can be divided into three main classes: chlorinated ethane derivatives (\textit{e.g.} dichlorodiphenyltrichloroethane (DDT)), hexachlorocyclohexanes (\textit{e.g.} lindane), and cyclodienes (\textit{e.g.} aldrin) (Figure 1-8)\textsuperscript{2}. The chemical stability of most of OC insecticides and their metabolites is high which makes them relatively chemically inactive in the environment. A second important characteristic of the OCs is that their solubility in water is low and their affinity for lipids is strong. This characteristic means that OCs tend to accumulate in lipids of animals and plants. The volatility of most OCs is low and usually OCs are waxy solids at room temperature, however, the volatility of compounds like lindane and aldrin is enough for them to be used as soil fumigants\textsuperscript{2,4,67}.

![Figure 1-8: Structure of DDT, lindane and aldrin](image)

\textit{Adapted from Hassall}\textsuperscript{2}
OC compounds started to be used as insecticides in the Second World War and were widely used in the 1940s to 1960s. These compounds were used on crops and animals and many sheep dips contained OC compounds, especially lindane, from the early 1940s until the use of OCs was banned in 1985. DDT, the most famous OC compound, was considered at some point as the perfect insecticide being cheap, effective, and safe to man and animals. However, due to their environmental persistence and toxicity, OCs were prohibited in Europe and North America in the early 1980s. However, OC insecticides are still in use in many developing countries especially in Asia since these compounds are inexpensive and effective. In the USA, a few OC compounds are still used for specific situations; like lindane which is prescribed for treating scabies and pediculosis. Lindane also continued to be used in the UK as a seed treatment after the ban of OCs but use has stopped recently.

The total annual usage of OCs in England and Wales was about 131 tonnes in the period of 1971-1974, 166 tonnes in the period of 1975-1979, and 130 tonnes in the period of 1980-1983. Figure 1-9 presents the total annual usage of OCs (in tonnes) applied to all crops in Great Britain during 1990-2010. The applied amount ranged between 110 and 250 in this period except in the years 1996 and 1997 when the applied amount was about 425 tonnes. Less than a tonne of OCs has been applied after the year 2008.

![Figure 1-9: The total annual usage of organochlorines (in tonnes) applied to all crops in Great Britain (1990-2010)](Adapted from Pesticide Usage Survey)

31
OC insecticides act by interfering with nerve impulse transmission across axons, and although there are differences in their physiological actions, generally all OCs destabilise the neural activity causing hyperexcitability in nerves and muscles. DDT, for example, affects mainly the peripheral nervous system by affecting sodium channel function. A decrease in sodium permeability usually follows the action potential; DDT prevents this decrease and thereby facilitates repetitive neuronal discharges. Lindane and aldrin, on the other hand, attack mainly the CNS by interacting with γ-aminobutyric acid (GABA) receptors to modify chloride flow resulting in neuronal stimulation\(^2\)\(^,\)\(^72\). The general results of DDT poisoning in insects include violent tremor, ataxia, loss of movements, paralysis and finally death\(^{39,40}\).

Acute OC poisoning is still reported in developing countries\(^70\). The acute toxic action of OCs in human is similar to those in pests. The main manifestation of intoxication is convulsions usually expressed as violent seizures. Other signs of acute OC poisoning are paraesthesia, tremor, hyperreflexia, ataxia, headache, and mental confusion. Death might happen if the convulsions are followed by respiratory depression and pulmonary gas exchange is seriously affected. DDT and methoxychlor are associated with less severe seizures and fatalities than lindane and cyclodienes where the convulsions may happen again over several days after the intoxication\(^66\). Although OC insecticides are less acutely toxic than OPs and carbamates, OC compounds are well known to have a greater chronic toxicity and the International Agency for Research on Cancer (IARC) have classified many of OCs as “probable human carcinogens”\(^{18,66,73}\).

1.3.2.1.4 Synthetic pyrethroids

*Chrysanthemum cinerariafolium*, which is a plant that is characterised by a lethal effect on flying insects, has been used against flies and mosquitoes for long time in domestic sprayers\(^2\). Pyrethrin (Figure 1-10, A) is a natural derivative of this plant and has been used mainly against indoor flying insects due to its low stability in light and heat\(^66\). Synthetic pyrethroids (SP) have been introduced since 1949 due to their increased stability which render them more effective in the natural environment\(^74\). SPs are classified into either type I pyrethroids when the pyrethroid has a basic cyclopropane carboxylic ester structure (*e.g.* permethrin) and type II pyrethroids that contain alpha-cyano group to enhance their activity (*e.g.* cypermethrin and deltamethrin)\(^2\). Figure 1-10 shows the structures of these examples.
After the introduction of SPs their worldwide usage to control agricultural pests increased rapidly due to their high efficacy against insects and very low toxicity to mammals compared to other insecticides. They are now widely used as insecticides in agriculture and homes\textsuperscript{39,66}. In the UK, less than one tonne of pyrethroids was applied to all crops in England and Wales in 1970, and about 8 tonnes were applied in 1980 and then use increased rapidly to reach 50 tonnes in 1990\textsuperscript{64,76}. The annual usage of SPs applied to all crops in Great Britain during 1990-2010 is presented in Figure 1-11. The applied amount was about 55 tonnes in 1993, 32 tonnes in 1994 and then increased to 70 tonnes in 1996. Except for the increase in 2004 and 2005, the use of SPs has remained relatively stable between 1996 and 2010: 62 tonnes were used in 2010\textsuperscript{65}.

\textbf{Figure 1-11: The total annual usage of synthetic pyrethroids (in tonnes) applied to all crops in Great Britain (1990-2010)}

\textit{Adapted from Pesticide Usage Survey\textsuperscript{65}}
SPs were licensed in the UK for the control of sheep ectoparasites in the mid 1980’s. Cypermethrin has been licensed as sheep dips and pour-ons while deltamethrin has been licensed as a pour-on only. However, in 2006 cypermethrin was suspended as sheep dips following many reports of their toxicity to fish and other aquatics and subsequently the manufacturers withdrew the authorisation voluntarily in 2010.

The mechanism of pyrethroid toxicity is complex. Pyrethroid insecticides alter neurological function by targeting the sodium and chloride channels. Pyrethroids modify the characteristics of sodium channels delaying their closure. This will lower the action potential threshold causing hyperexcitability followed by paralysis. Type II pyrethroids also decrease chloride flow through channels and at high concentrations they can act on GABA-gated chloride channels resulting in seizures.

The toxicity of SPs to human is low especially through inhalation or dermal absorption. However, they can cause peripheral effects at low doses and might affect the CNS at high doses. The main peripheral effects of SPs are sensory and paraesthesia is the most common effect of SP exposure. Numbness of the extremities and mucous membranes and burning sensation on skin have also been reported. Exposures to high doses might result in loss of consciousness, convulsions and seizures that can last up to 2 to 3 weeks. Pyrethroid poisoning is very rare in the UK and long-term health effects are not well described.

1.3.2.1.5 Avermectins

Avermectins are a group of macrocyclic lactones naturally generated from the fermentation of the soil actinomycete *Streptomyces avermitilis* and they are also generated by synthetic modifications. Avermectins were initially introduced in 1979 as antihelmintics but then their insecticidal activities were discovered.

![General structure of avermectins](image)

*Figure 1-12: General structure of avermectins*

Adapted from Tom and Foster.
Ivermectin is a mixture of two related avermectins with a high antiparasitic activity. It has been used for several years in human medicine to control several endo and ectoparasites especially *Onchocerca Vlovulus*, the nematode causing river blindness disease\(^{82}\). Avermectins have been licensed in the UK since the early 1980s as veterinary medicines to control different arthropods and nematodes\(^{80}\). Ivermectin achieved a significant success in controlling warble fly infestation in cattle in the UK at that time\(^{83}\). Avermectins have been licensed as injectable products to control sheep scab and other ectoparasites in sheep, and as oral medicines to treat and control roundworms and arthropods (but not scab mites)\(^{45}\). They were also licensed as injectable and pour-on products to control roundworms and arthropods in cattle\(^{84}\).

The mode of action of avermectins mainly comes from stimulating the release of GABA. This will lead to increased chloride ion transmission leading to hyperpolarisation and subsequent paralysis of the neuromuscular systems\(^{2,77}\).

Little information is available on the toxicity of avermectins in humans\(^{80}\). In humans, GABA receptors are found only in the CNS and avermectins have poor penetration of the blood-brain barrier which explains the low toxicity of these insecticides in human\(^{77}\). Although ivermectin has been used to treat millions of people from river blindness with little harm with any reported symptoms from this treatment being mild and have been attributed to immunological reactions to the dead parasites rather than the ivermectin itself. Headache, fever and other mild symptoms were reported by healthy volunteers given 0.1 mg/kg. Dermatitis has been reported after dermal exposure while, vomiting, mydriasis, somnolence and tachycardia has been reported after accidental oral exposure to ivermectin\(^{77,82}\).

### 1.3.2.2 Herbicides

Herbicides or weedkillers are chemical products used to kill unwanted plants. They are not only used in farms but also used to remove undesired plants from many areas like gardens, roadsides and irrigation canals\(^4\). Herbicides can be classified in different ways. They are classified as ‘selective’ when they kill only the undesired weeds and leave the crops unharmed and as ‘unselective’ when they kill all types of plants. Herbicides are also classified as ‘contact’ when they kill only the part of the plants in contact with the chemical and as ‘translocated’ or ‘systemic’ when they are absorbed by the roots or the upper parts of the plants and kill all the plant\(^2,4\). Herbicides can also be grouped by their agricultural function, effect, and chemical classification as presented in Table 1-1.
Table 1-1: Classification of herbicides

<table>
<thead>
<tr>
<th>Agricultural function</th>
<th>Effect</th>
<th>Chemical classification</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Applied to foliage</td>
<td>Kill all foliage unless directionally sprayed</td>
<td>Quaternary ammonium Glyphosate Aminotriazole</td>
<td>Paraquat Glyphosate Aminotriazole</td>
</tr>
<tr>
<td></td>
<td>Kill broad-leaf weeds in cereals and grass</td>
<td>Phenoxyacetic acids Chlorinated benzoic acids Phenolic nitriles Bentazon</td>
<td>2,4-D Dicamba Ioxynil Bentazon</td>
</tr>
<tr>
<td></td>
<td>Kill grasses</td>
<td>Dalapon Fluazifop and sethoxydim</td>
<td>Dalapon Fluazifop</td>
</tr>
<tr>
<td></td>
<td>Kill grasses in cereals</td>
<td>Carbamates Others</td>
<td>Barban Difenzoquate</td>
</tr>
<tr>
<td></td>
<td>Kill broad-leaf weeds in various dicotyledonous</td>
<td>Phenoxybutyric acids Dinitrophenols Others</td>
<td>MCPB Dinoseb Pentanochlor</td>
</tr>
<tr>
<td>Group 2: Foliar and soil action on young weeds</td>
<td>Inhibit photosynthesis</td>
<td>Ureides Triazines Uracils and pyridazinones</td>
<td>Diuron Atrazine Bromacil</td>
</tr>
<tr>
<td></td>
<td>Affect cell division</td>
<td>Phenylcarbamates Sulphonylureas</td>
<td>Chlorpropham Chlorsulfuron</td>
</tr>
<tr>
<td></td>
<td>Disrupt membrane structure or function</td>
<td>Diphenyl ethers</td>
<td>Nitrofen</td>
</tr>
<tr>
<td>Group 3: Soil-acting</td>
<td>Disrupt fatty acid metabolism</td>
<td>Thiocarbamates</td>
<td>EPTC</td>
</tr>
<tr>
<td></td>
<td>Affect meristematic growth</td>
<td>Dichlobenil and chlorthiamid Chloroacetamides Dinitroanilines</td>
<td>Dichlobenil Alachlor Trifluralin</td>
</tr>
</tbody>
</table>

Farmers have used inorganic compounds to control weeds for many centuries. The importance of herbicides has increased since the end of World War II because agriculture has become highly mechanised and without herbicides, the mechanised production of many crops such as cotton and sugar beets is impossible. Therefore, about 40% of the worldwide pesticide sales are spent on herbicides. 2,4-dichlorophenoxyacetic acid (2,4-D) (Figure 1-13, A) is the most used herbicide in the world. It has a systemic action and is a selective herbicide that is used to control broadleaf weeds in cereal crops. It was introduced in 1944 and was the first widely used herbicide. MCBA (Figure 1-13, B), another phenoxy herbicide, is more preferred in Europe than 2,4-D probably due to the low cost of raw materials in this region. Paraquat (Figure 1-13, C), which is a dipyridil compound, was synthesised in 1882 but it was not used as an herbicide until 1962. It is a very effective herbicide that kills a wide spectrum of broad-leaved weeds and annual grasses and hence it became one of the most widely used herbicides in the world. Glyphosate (Figure 1-13, D) which is an organophosphorus herbicide introduced in 1971 is very popular to the extent that its sales comprise 60% of global unselective herbicide sale.
The total annual usage of herbicides in England and Wales was about 15,250 tonnes in the period of 1971-1974, 19,925 tonnes in the period of 1975-1979, and 26,360 tonnes in the period of 1980-1983. The use then decreased to reach 15,579 tonnes in 1986.

Figure 1-14 displays the amount of herbicides in tonnes applied to all crops in Great Britain during 1990-2010. There was a trend to reduce use with the applied amount decreasing gradually from about 12,000 tonnes in 1990 to about 8,000 tonnes in 2010.

Herbicides vary widely in their acute toxicity with health effects ranging from irritation to skin and mucous membranes to death. For example, 2,4-D has been classed by WHO as a moderately hazardous pesticide since high-level exposure may irritate the skin and mucous membranes and can cause vomiting, headaches and confusion. A
sensory-motor peripheral neuropathy has also been reported after high dose exposure. The IARC has classified 2,4-D as possible carcinogenic to humans (class 2B). Glyphosate has been considered by EPA as a non carcinogenic chemical with relatively low acute toxicity causing only irritation of skin and mucous membranes. Paraquat is acutely toxic to humans and more so than any other widespread used herbicide. Pulmonary effects are the most lethal and untreatable effects of paraquat toxicity. Paraquat generates free radicals that damage lung tissue and cause acute pulmonary oedema within a few hours, whereas the pulmonary fibrosis, which is the usual cause of death, takes 7-14 days to occur. Chronic exposure to paraquat has been associated with Parkinson’s disease.

1.3.2.3 Fungicides

A fungicide is any chemical used to kill or to stop the development of fungi. Fungal diseases are more difficult to control than the diseases caused by insects and usually fungicides have to be applied repeatedly and during different stages of plant life. Fungicides are heavily used in agriculture and industry for many purposes like seed treatment, crop protection, and the suppression of mildews on painted surfaces. In crop protection, fungicides are grouped into two main categories; namely ‘non-systemic’ compounds which remain near the application point and ‘systemic’ compounds which enter the plant through the leaves or the root and are transported within the plant. The main chemical groups of each category are presented in Table 1-2.

The global market of fungicides comes second after the market of herbicides and the UK market is about 10% of the EU market. 2,400 tonnes of fungicides were applied every year in England and Wales in the period of 1971-1974 and use approximately doubled that (4,341 tonnes) in the period of 1980-1983 and tripled (7,124 tonnes) in the year 1986. The annual use of fungicides applied to all crops in Great Britain during 1990-2010 is shown in Figure 1-15. There was a gradual decrease in the amount of fungicides applied every year from about 7,000 tonnes in 1990 to about 5,500 tonnes in 2010.

The acute health effects of fungicides vary from one fungicide to another but are generally considered to be low. Many severe and fatal poisonings reported in the past especially in developing countries were due to the use of mercurial fungicides. However, most recent fungicides rarely cause severe systemic poisoning due to their...
low toxicity in mammals and due to their formulation as powders or granules. The main and most common effect of short-term high exposure to fungicides is the irritation of skin, eyes, mucous membranes and respiratory tract and they can also cause dermal sensitisation.

Table 1-2: Chemical classification of non-systemic and systemic fungicides

<table>
<thead>
<tr>
<th>Category</th>
<th>Chemical group</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-systemic</td>
<td>Organosulphur compounds:</td>
<td>Thiram, zineb</td>
</tr>
<tr>
<td></td>
<td>(a) Dithiocarbamates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(b) Phthalimides</td>
<td>Captan, folpet</td>
</tr>
<tr>
<td></td>
<td>Dinitrophen derivatives</td>
<td>Dinocap, binapacryl</td>
</tr>
<tr>
<td></td>
<td>Chlorinated aromatics:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(a) Chlorinated nitro compounds</td>
<td>Quintozene</td>
</tr>
<tr>
<td></td>
<td>(b) Chlorinated amino compounds</td>
<td>Dicloran</td>
</tr>
<tr>
<td></td>
<td>(c) Chlorinated nitriles</td>
<td>Chlorothalonil</td>
</tr>
<tr>
<td></td>
<td>(d) Chlorinated quinones</td>
<td>Dichlorone</td>
</tr>
<tr>
<td></td>
<td>Other:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(a) Guanidine derivatives</td>
<td>Dodine acetate</td>
</tr>
<tr>
<td></td>
<td>(b) Imidazoles</td>
<td>Imazalil, prochloraz</td>
</tr>
<tr>
<td></td>
<td>(c) Dicarboximides</td>
<td>Iprodione, vinclozolin</td>
</tr>
<tr>
<td>Systemic</td>
<td>Benzimidazoles</td>
<td>Benomyl, carboxanidate</td>
</tr>
<tr>
<td></td>
<td>Oxathiins or carboxamides</td>
<td>Carboxin, oxycarboxin</td>
</tr>
<tr>
<td></td>
<td>Morpholines</td>
<td>Tridemorph</td>
</tr>
<tr>
<td></td>
<td>Inhibitors of steroid C-14 demethylation:</td>
<td>Triadimefon</td>
</tr>
<tr>
<td></td>
<td>(a) Triazoles</td>
<td>Fenarimol</td>
</tr>
<tr>
<td></td>
<td>(b) Pyrimidines</td>
<td>Buthiobate</td>
</tr>
<tr>
<td></td>
<td>(c) Pyridines</td>
<td>Triforine</td>
</tr>
<tr>
<td></td>
<td>(d) Piperazines</td>
<td>Imazalil</td>
</tr>
<tr>
<td></td>
<td>(e) Imidazoles</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydroxyaminopyrimidines</td>
<td>Ethirimol</td>
</tr>
<tr>
<td></td>
<td>Antibiotics</td>
<td>Streptomycin</td>
</tr>
<tr>
<td></td>
<td>Phenylamides</td>
<td>Metalaxyl</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>Chloroneb, prothiocarb</td>
</tr>
</tbody>
</table>

Figure 1-15: The total annual usage of fungicides (in tonnes) applied to all crops in Great Britain (1990-2010)

Adapted from Pesticide Usage Survey.
1.3.3 Pesticide exposure in sheep farming and other farming sectors

The World Health Organisation has defined agriculture as “all forms of activity connected with growing, harvesting, and primary processing of all types of crops; with breeding, raising, and caring for animals; and with tending gardens and nurseries”\textsuperscript{93}. From this definition, two general categories of farm work related to pesticide exposure can be recognized; applying pesticides to crops and other plants and applying pesticides to animals. Both categories contain the same broad activities during which a farmer may be exposed to pesticides. The main activities are the mixing of pesticides, applying them, the disposal of excess, the maintenance of application equipment and dealing with animals or plants that have been treated with pesticides\textsuperscript{94}.

1.3.3.1 Sheep farming

Sheep farming is an important industry in the UK, and the UK is the European Union member state with the largest number of sheep\textsuperscript{5,95}. The total number of sheep and lambs in the UK increased gradually from about 26 million in 1970 to about 44.5 million in 1992, after which the number decreased to reach 31 million in 2010\textsuperscript{96}.

Sheep farmers treat sheep with pesticides against many ectoparasites such as scab mites (\textit{Psoroptes ovis}), lice (\textit{Bovicola ovis}), keds (\textit{Melophagus ovinus}) and ticks (\textit{Ixodes ricinus}) (Figure 1-16)\textsuperscript{97}. Sheep farmers use different methods to control ectoparasite infestations. These methods include sheep dipping, showering, injection, and pour-ons methods (Figure 1-17)\textsuperscript{12}. The National Office of Animal Health (NOAH) reported that the relative sale of pour-ons and injectable sheep treatments sold in the UK increased from less than 1\% in the early 1990s to reach about 40\% at the end of that decade\textsuperscript{98}.

Sheep dipping (Figure 1-17, A) has been used for around 200 years and it has been considered the most effective method to control many ectoparasites including sheep scab\textsuperscript{12,77}. Sheep dipping is a dirty and exhausting procedure in which the farmers dilute the utilised pesticides in the water of the dipping bath and submerge all sheep completely in that bath. Sheep dipping may finish in one day or may take several days. Three well defined dipping tasks have been described in this procedure; the helper who collects the sheep and makes them ready for the chucker who guides the sheep into the dip bath, and the paddler (or plunger) who stands alongside the bath and immerses each sheep under the surface of the water with an implement or with his feet and hands\textsuperscript{99}.
The ingredients of sheep dips have changed over time. Before the introduction of OCs, sheep dippers used mainly arsenic and sulphur compounds. Sheep dips contained mainly OC compounds, especially lindane, since it was approved in 1948 until a number of OP compounds were introduced in the early 1960s. Since that time the number of OP sheep dips increased and OPs became predominant among pesticides after 1970, whilst the number of OC dips decreased until they were banned in 1985. The main OPs used in sheep dips were diazinon, propetamphos, and chlorfenvinphos. In the mid-1980s SP dips (e.g. cypermethrin) were introduced. However, in February 2006 cypermethrin was suspended as a sheep dip following many reports of serious pollution incidents and therefore since 2006 diazinon has been the only permissible sheep dip.

Sheep dipping was compulsory in the UK twice a year from 1984 to 1988 and the compulsory dipping continued once a year until 1991 when it was terminated. As a result most elderly current sheep farmers have carried out sheep dipping in the past with OP compounds being the predominant pesticides. As a result, many studies have used sheep dippers as subjects to study the long-term effects of OP pesticides.
In pour-ons, a specific applicator is used to apply the pesticide to specific parts of the animal body\textsuperscript{77} (Figure 1-17, B). These parts of body vary according to the infestation controlled. For example, when apply cypermethrin for lice control, it should be applied from the shoulders to the rump, whilst for tick control it should be applied from the crown of the head to the rump\textsuperscript{109}. Sheep pour-ons have to date been mainly SPs although other active ingredients included triazines and dicyclanil\textsuperscript{45,109}. Showering methods (Figure 1-17, C) have been rarely used in the UK because it is effective for controlling blowfly but not for sheep scab\textsuperscript{12,77}. There is no guidance for this treatment and currently there are no products approved for this method in the UK\textsuperscript{45}. Sheep injections (Figure 1-17, D) can be given intramuscularly or subcutaneously. The main advantages of this method are that it is not exhausting like sheep dipping and does not
require special facilities (i.e. dip bath or shower unit). Sheep injections have to date been mainly avermectins and in 2011 sheep injectables for sheep scab and other ectoparasites in sheep included ivermectin, moxidectin, and doramectine.

1.3.3.2 Cattle and other livestock farming

Cattle and other livestock farming are also important industries in the UK and the UK is the third amongst the European countries in terms of number of cattle after France and Germany. Figure 1-18 presents the total number of cattle, pigs and poultry in the UK during the period 1970-2010. The total number of cattle and calves in the UK was about 12.5 million in 1970 and increased to around 15 million in 1974, after which it decreased gradually to about 10 million in 2010. The number of pigs in the UK fluctuated between 7.5 million and 9 million during the period 1970-1998 and it has decreased after that to 4.5 million in the year 2011. The total number of breeding and laying fowl and table chicken ranged between 121 and 149 million in the period 1970-1996 whilst it increased after that to range between 153 and 182 million. The total number of all other livestock (horses, goats, and farmed deer) in 2011 was 459 thousand.

Pesticides are used to treat cattle for a variety of internal and external parasites, and this treatment is very important from an economic point of view. All other livestock (pigs, horses, etc.) can be infested as well with insects and parasites and can be treated by pesticides.

![Figure 1-18: The total number of cattle, pigs and poultry in the UK (1970-2010)](image)

Adapted from Defra
Pests can affect both beef and dairy cattle. Infestations of beef cattle which are raised for weight gain can affect meat productivity while the infestation of dairy cattle can affect milk productivity. Different types of pesticides (OCs, OPs, pyrethroid insecticides, etc.) have been used to treat pests in cattle such as horn flies, face flies, lice. However, parasite control in dairy cattle is problematic since there are regulations that prevent the use of many pesticides in cattle producing milk for human consumption (e.g. ivermectin).

One of the main usages of OP pesticide in cattle sector in the past was for treating warble fly infestation. *Hypoderma bovis* (known as warble fly) which belongs to oestridae bee-like insects (Figure 1-19) causing irritation to cattle which may lead to financial consequences due to a reduction in the yield of both milk and meat. The infestation can also damage the hide which can affect its use in the leather industries and may, in extreme cases, lead to the death of the cow. In 1978 The Ministry of Agriculture, Fisheries and Food started the warble fly eradication scheme as about 40% of cattle in Britain were infested in that year. As a result of that scheme the infestation went down to the prevalence of 0.01% in 1986.

![Warble fly](image)

**Figure 1-19: Warble fly**

*Dermestes hortensis*

Derris powder was used as an organic treatment for warble flies in 1950s. In the early 1960s when OP pesticides were used to control warble flies in cattle, and under the eradication policy, farmers were required to treat all infested cattle with one of four OPs (phosmet, fenthion, famphur, and crufomate). The use of OPs has decreased dramatically by the approval of the injectable avermectins in 1981 which achieved a significant success in controlling warble fly infestation in cattle in the UK at that time. The peak usage of OPs was between 1979 and 1982.
1.3.3.3 Crops and grains

The utilised agricultural area in the UK was about 16 million hectares in the mid 1980s and decreased slightly in the mid 1990s (15.5 million hectares) while it reached about 17 million hectares in 2010. About a third of this area is cropable and most of the rest is grassland\textsuperscript{26,95}.

In 1990 around 34.5 thousand tonnes of pesticides were used for all crops in Great Britain. This number increased to about 35.7 thousand tonnes in the mid 1990s then decreased gradually to reach around 16.8 thousand tonnes in 2010\textsuperscript{65}. Of the 14,000 tonnes applied to arable crops in the UK in 2010, 44% were herbicides, 32% were fungicides, 19% were growth regulators, 2% were insecticides and nematicides, and 3% were molluscicides and for seed treatments. These ratios have been relatively the same for all years between 2000 and 2010\textsuperscript{116}.

Methods of applying pesticides to crops and grains in the UK include boom sprayers, airblasters, backpack sprayers and hand sprayers (Figure 1-20) and boom spraying is the most widely used method to apply pesticides on arable crops in the UK\textsuperscript{1}. Although it is used widely in the USA and other areas in the world, aerial spraying is rarely used in the UK\textsuperscript{117}. Moreover, the total area treated by aerial application has sharply decreased from around 162,000 hectares in 1988 to around 11,000 hectares in 2010. Prior to 2000, aerial application was used to apply pesticides to arable crops especially potatoes, while in the last decade it was almost restricted to bracken control\textsuperscript{116}.

The number of times pesticides are applied to crops varies significantly between farms due to the variation in crops. Some crops like corn need only one or two applications, while others, such as bulbs, need more than ten applications\textsuperscript{118}. Besides applying pesticides, farmers can be exposed to pesticides during harvesting, weeding or many other activities in crop farming\textsuperscript{119}.
1.3.4 Techniques used to assess long-term exposure

While recent pesticide exposure can be measured using ambient monitoring techniques (e.g. personal sampling pump) and biological measurements (e.g. pesticide urinary metabolites), retrospective quantification of past exposure has depended on the use of alternative means such as work history and governmental databases because measurement data were often not available.

Assessment methods for long-term pesticide exposure have developed from simple surrogates, like ever working on a farm, to integrated exposure metrics which
incorporate all available determinants of past exposure into one estimated score\textsuperscript{18}; an example of this development is shown in Figure 1-21. In this example, pesticide exposure from sheep dipping can be estimated using a very simple surrogate like ever/never living in a rural area or the duration of living in such an area. The estimation can be developed by asking specifically about being involved in sheep farming or sheep dipping and in applying pesticides in that treatment while using integrated exposure metrics may be the best method to estimate pesticide exposure in sheep dipping.

![Figure 1-21: Evolution of exposure measures to assess occupational pesticide exposure through sheep dipping](image)

Modified from Alavanja \textit{et al.} \textsuperscript{18}

### 1.3.4.1 Self-reported exposure

Self-reported occupational history is often the only available resource to assess life-time occupational exposure in retrospective epidemiologic studies\textsuperscript{125,126}. Exposures can be estimated simply based on the data provided by the participants (\textit{e.g.} whether they worked in specific occupations or they can be asked to estimate their exposure themselves). However, workers can also provide more details about their occupational practices and exposures that can subsequently be used by other developed methods (\textit{e.g.} job exposure matrices or exposure algorithms) to estimate long-term exposure\textsuperscript{127}. 47
The validity and reliability of self-reported occupational exposure have been investigated in many studies in non-farming occupations\textsuperscript{128-130} and they varied between studies and between agents within studies\textsuperscript{131}. Fewer studies have investigated the accuracy of self-reported pesticide exposure. The percentage agreement between data of pesticide suppliers and data reported by farmers regarding their pesticide use was 52.4\% for herbicides and 68\% for insecticides\textsuperscript{118}. Blair \textit{et al.}\textsuperscript{132} compared the baseline and repeat interviews (after 1 year) from 4,088 Iowa pesticide applicators who took part in the Agricultural Health Study (AHS) study. For the use of specific pesticides and application practices (ever/never), percentage agreement was high (70\%-90\%) and the results were not affected by age, farm size, or educational level. For frequency, duration, and decade of first use of those pesticides the agreement was lower (50-60\%).

Engle \textit{et al.}\textsuperscript{126} asked 185 orchardists to fill in a detailed questionnaire in 1997 about their lifetime use of pesticides and compared the answers with their answers they gave previously when they had been interviewed for a cohort study between 1972 and 1976. Farmer’s recall was good to excellent for the broad categories (insecticides, herbicides, \textit{etc.}) and for heavily used chemical classes like OPs and OCs (sensitivity: 0.6–0.9), while for specific pesticides the sensitivity was lower and more variable (0.1–0.6). Therefore, the researchers concluded that self-reported exposure can be used in epidemiologic studies for broad categories of pesticides, but not for exposure to specific pesticides.

Researchers have tried to find methods to improve the subject’s recall. One of these methods is the use of checklists and a list of exposures which can prompt recall and result in more accurate results than open-ended questions\textsuperscript{131}. Another method to improve the recall is event history calendars. Event history calendars are tools used to obtain more accurate information from the respondents about his personal exposure by using easily remembered milestones in the respondent’s life (\textit{e.g.} births, graduations, weddings) to help them in ordering life activities in time\textsuperscript{133}. The event history calendar has been used with farmers and in a pilot study 17 out of 18 farmers found it a useful tool to enhance their recall of lifetime farming activities\textsuperscript{26}. The same method has also been applied in agricultural studies but with recording the life events by icons on the calendar and was similarly found more effective than the traditional questionnaires in obtaining complex occupational history (\textit{i.e.} farmers recalled more information about their work history especially for the earliest time period)\textsuperscript{125}. 48
1.3.4.2 Exposure measurement

Various methods of ambient pesticide exposure monitoring can be carried out during the application of pesticides or any other farming activities. Those methods vary according to the routes of the exposure. There are three approaches to dermal exposure monitoring: the absorbent patches method, removing residuals of the pesticides by wiping or washing, and the fluorescent tracer technique. To determine pesticide exposure by inhalation many techniques are available starting from using respirators with gauze pads and ending by the use of personal sampling pumps with attached filter cassettes. Exposure through the oral route is difficult to be monitored and no feasible technique has been applied to estimate pesticide exposure through oral ingestion. Exposure measurement methods are only applicable for recent and not for long-term exposure. However, sometimes these measurements can be obtained if available from governmental or companies databases but such databases are very rare in farming occupation.

1.3.4.3 Biological markers

Biological monitoring is one of the most accurate indicators of the actual recent absorbed dose of pesticides. This monitoring could be performed by measuring pesticide metabolites in body fluids, urine or in other excreta or by measuring biochemical markers; the latter may be called “biological effect monitoring”.

Biological monitoring and biological effect monitoring have been used to assess, for example, OP exposure of farmers. A reduction of blood cholinesterase activity (biological effect monitoring) has been used to monitor OP exposure but it was found that this reduction is an insensitive indicator of actual exposure. Therefore, an alternative approach which depends on measuring the OP metabolites in urine is more common in exposure assessment. Urinary levels of one or more alkyl phosphate metabolites (DEP, DETP, DEDTP, DMP, DMTP, DMDTP) increase by the use of about 80% the OPs approved in the UK.

To assess short-term pesticide exposures, biological markers are usually measured in workers the day before applying pesticides and then 1 or more days after (depending on the half life of the pesticide applied); and the differences will give an approximate estimation for the exposure. Although biological monitoring can be used efficiently to assess long-term exposures to chemicals that persist long in human body such as certain metals, the use of this monitoring to assess long-term exposure to pesticides is
not applicable due to the short biological half-life of the majority of pesticide biomarkers\textsuperscript{127}. However, biological monitoring was used to validate other pesticide assessment techniques of long-term exposure\textsuperscript{138,139}. This validation method will result in some errors mainly because of the short half-life of the biomarkers and due to the considerable amount of undetectable levels of biomarkers\textsuperscript{123}.

1.3.4.4 Expert assessment

Using experts (like occupational hygienists, chemists, engineers, etc.) to assess occupational exposure from job histories or to estimate the exposure on the basis of the information reported by the worker has increased\textsuperscript{131}. The first application of this technique was to study the relation between occupational exposure and the risk of cancers and afterwards it has been applied in other occupational epidemiology studies\textsuperscript{140}.

Experts are usually more knowledgeable about occupational exposures (mechanism, routes, modifying factors, etc.) than workers. They also know exposures which are relevant and the range of jobs in which exposures have to be estimated\textsuperscript{141}. On the other hand, not all jobs and occupations in the occupational history of the subjects are always familiar to the experts, and if they do not have detailed information about those jobs from the subjects or from the industries, most likely their estimations will be not that good\textsuperscript{131,142}. Specificity of expert assessment was generally reported as high (0.91-0.98) while the sensitivity was found to be moderate to high (0.48-0.79)\textsuperscript{128,143}.

Expert assessment was used to assess pesticide exposure in farming\textsuperscript{144,145}. In the study of Garcia \textit{et al.}\textsuperscript{144} and by using a 4-point scale, two experts (a public health medical doctor and an agricultural engineer) assessed the probability and the level of exposure to each pesticide. The interrater agreement expressed by kappa-weighted values was 0.36 for probability and 0.39 for level of exposure. Much lower interrater agreements were found when other exposure categories (non-applicators and herbicides) were analysed. Similar low agreements were observed in the study of de Cock \textit{et al.}\textsuperscript{145}. Three groups of 15 occupational hygienists were asked to estimate pesticide exposure in fruit growing. Although the interclass correlation for each group of experts was high when fruit growing tasks were ranked by increasing exposure level, the interrater agreement on factors influencing the internal dose generally decreased when more exposure information was provided. Clear differences were found between experts when they ranked 15 specific sprayings with a fungicide which were due to the differences in their expertise.
1.3.4.5 Job exposure matrix

The use of Job exposure matrices (JEMs) in occupational epidemiology started in the 1980s\textsuperscript{131}. JEMs can be used as a method of assessing occupational exposures when industrial or biological measurements are unavailable or inaccurate\textsuperscript{25}. JEMs generally consist of two axes; one for a list of job history variables, and another for a range of exposures, and sometimes a third axis of calendar period may be included in the matrix. The presence, frequency and intensity of exposure to a specific agent in a specific occupation, may be recorded in the cells of the matrix\textsuperscript{141}. In the past, exposure in each cell was generally presented as dichotomous or ordinal variable (exposed/unexposed or high/medium/low) but more recent research suggest that using the value of the exposure probability in the matrix may increase the accuracy of risk assessment\textsuperscript{146}. JEMs can be developed using many sources; expert judgment usually helped by published literature, observations of potential exposures, communication with the workers and the industry personnel, and databases of exposure measurements when they are available\textsuperscript{131,141}.

Most generic JEMs have not performed well in evaluation. Their sensitivity was low and the agreement between two generic JEMs or between JEMs and more credible methods (\textit{e.g.} exposure measurements and expert assessment based on self-report history) was only slight or fair\textsuperscript{131}.

Several studies have used JEMs to assess pesticide exposure in the evaluation of dose-response relationships in case-control studies of, for example, pancreatic cancer\textsuperscript{147}, reproductive disorder\textsuperscript{148}, and neurotoxicity\textsuperscript{25}. As an example, London and Myers\textsuperscript{25} used the JEM shown in Figure 1-22 to assess OP exposure among farm workers. In this JEM the frequency and duration of exposure to possible pesticides were explored for every job in the life of the farmer with a special attention to OPs. This JEM combined in a weighting factor both job activity and type of crop on which the farmer worked using data derived from expert opinion and industrial hygiene assessments.

JEMs generally ignored exposure variability between farmers working in the same workplace which may result in misclassification\textsuperscript{149}. Nonetheless, specifically for the assessment of pesticide exposure London and Myers\textsuperscript{25} found that when compared with erythrocyte cholinesterase concentrations, the JEM provided a reasonable ranking of pesticide exposure that can be used to compare groups especially when farmers are unlikely to recall specific names and dates of pesticide use or when no data available on chemical application and biological monitoring. Young \textit{et al.}\textsuperscript{150} reached the same
conclusion for the use of their developed JEM. Their JEM exposure estimates were robust and high correlations were found between three types of estimates based on original, conservative and maximum weights for the JEM variables.

Figure 1-22: Assessing exposure to OPs among farm workers with a JEM. Adapted from London and Myers.25
1.3.4.6 Exposure intensity algorithm

Exposure intensity algorithms can be seen as a natural development of JEMs. Although the same sources used to weight variables within the cells of JEMs are used in exposure algorithms, the algorithms can include more variables than can be included in a JEM\textsuperscript{18}. Algorithms which estimate cumulative exposures usually assumed a linear dose-response relation since cumulative exposure depends on duration and intensity of exposure\textsuperscript{151}.

Instead of depending on general practices which usually occur in JEMs, exposure intensity algorithms have the advantage of using the individual information of each farmer regarding his pesticide usage\textsuperscript{18}. The algorithms can be designed to assess a specific-pesticide exposure, or to assess pesticide exposure in groups (insecticides, herbicides, \textit{etc.}) or in general (\textit{i.e.} any pesticides). On the other hand, farmworkers may not know the nature of the pesticides they are applying or the type of pesticides applied on the farm in which they are working\textsuperscript{152}. In such situations, JEM and expert assessment methods may have an advantage.

Developers of exposure algorithms try to include in their models as many exposure determinants as they can, recognising that these will vary between the different farming sectors. However, the information about these determinants is not always available which makes most of the developed algorithms limited to a few exposure determinants.

Algorithms have been used in pesticide exposure assessment in the agricultural field\textsuperscript{7,99,124,151,153,154}. Table 1-3 summarises seven examples of exposure algorithms chosen to represent exposure algorithms in different farming sectors while two of them are described in detail. The first algorithm was chosen because it was developed empirically to estimates pesticide exposure in sheep dipping treatment specifically, whilst the second algorithm was chosen because it was designed for pesticide applicators in different farming sectors and it combines exposures in different sectors into one final exposure estimate.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Farming sector</th>
<th>Algorithm</th>
<th>Definitions</th>
<th>Validated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchanan et al. 2001</td>
<td>Sheep dipping</td>
<td>( \text{EXP} = 3.6 \times \text{CONC} + 0.2 \times \text{SPLASH} )</td>
<td>( \text{EXP} = \text{cumulative exposure to OP sheep dips} )</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>( \text{SPLASH} = \sum_{j=1}^{J} \text{ND}_j \left( % \text{PLNG}_j \times 66 \right) + % \text{CHCK}_j \times 44 + % \text{HELP}_j \times 10 )</td>
<td>( \text{CONC} = \sum_{j=1}^{J} \text{ND}_j \left( % \text{HAND}_j \times 8 \right) )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{CONC} = \text{exposure through handling concentration} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{SPLASH} = \text{exposure through splashing} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( % \text{PLNG}_j, % \text{CHCK}_j \text{ and } % \text{HELP}_j = \text{estimated percentage of dipping in job j spent working as a plunger, chucker, and helper respectively} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{ND}_j = \text{number of dipping days spent in job j} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( % \text{HAND}_j = \text{estimated number of occasions spent as principal concentrate handler in job j} )</td>
<td></td>
</tr>
<tr>
<td>Tahmaz et al. 2003</td>
<td>Sheep dipping</td>
<td>( E_{ak} = C_{ak} \times t_{ak} \times S_{ak} )</td>
<td>( E_{ak} = \text{dermal exposure} )</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( C_{ak} = \text{concentration of the chemical in the skin contamination layer} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( t_{ak} = \text{the duration of exposure} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( S_{ak} = \text{the area of skin contaminated} )</td>
<td></td>
</tr>
<tr>
<td>Brouwer et al. 1994</td>
<td>Bulb farmers</td>
<td>( \text{EI}<em>{ij} = \sum \sum \sum</em>{mnq} \left( E_{mnq} \times N_{mnq} \times A_{mn} \right) \times (1 - PF_{mnq}) )</td>
<td>( \text{EI}_{ij} = \text{exposure index (mg) for individual i in year j} )</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( m = \text{method of crop protection} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( n = \text{method of mixing and loading} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( q = \text{method of bulb disinfection} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( E = \text{specific level of potential exposure (mg/ha)} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( A = \text{bulb acreage (ha)} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( N = \text{number of crop protection applications (mn), respectively, the number of containers handled for bulb disinfection per year (q)} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( PF = \text{protection factor} )</td>
<td></td>
</tr>
<tr>
<td>Stewart et al. 2001</td>
<td>Crops sector</td>
<td>( \text{EXP} = \text{RAR} \times \text{H-L} \times \text{Task} \times \left( \frac{\text{Dur}}{PF} \right) \times \text{ND} )</td>
<td>( \text{EXP} = \text{lifetime estimate of the pesticide exposure} )</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{RAR} = \text{recommended application rate} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{H-L} = \text{half-life} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( \text{Dur} = \text{duration of the task} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( PF = \text{protection factor} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>( ND = \text{number of days spent at each job} )</td>
<td></td>
</tr>
</tbody>
</table>

* See Table 1-4 for more information on the studies that used these algorithms
Table 1-3: Summaries of examples of pesticide exposure algorithms in different farming sectors (continued)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Farming sector</th>
<th>Algorithm</th>
<th>Definitions</th>
<th>Validation</th>
</tr>
</thead>
</table>
| Tielman et al.  | Greenhouses    | MLA = 0.47 \times MLA_{\text{hand}} + 8.54 \times MLA_{\text{body}}       | MLA = monthly exposure through mixing, loading or application activities through the hand and the rest of the body.  
| 2007\(^{54}\)   |                | MLA_{\text{hand}} = \sum_{c=1}^{m} \sum_{a=1}^{n} I_{H_{ca}} \times PH_{ca} \times D_{ca} | \text{IH}_{ca} = the hand exposure intensity through activity a and chemical c in a particular month, and IB_{ca} for the body.  
|                 |                | MLA_{\text{body}} = \sum_{c=1}^{m} \sum_{a=1}^{n} IB_{ca} \times PB_{ca} \times D_{ca} | D_{ca} = the duration.  
|                 |                |                                                                          | \text{PH}_{ca} = the clothing protection factor for the hand, and PB_{ca} for the body.        | No         |
| Monge et al.    | All farming    | EI_{pti} = U_{ptcr} \times C_{ti} | EI_{pti} = estimate of the subject's intensity of exposure. U_{ptcr} = quantity by liters/hectares of active ingredient where p=pesticides, t=calendar year, c=crop, and r=geographical region. C_{ti} = scores of determinants d during time window t for subject i. W_{d} = relative weight for determinant d. H_{d} = hazard value of category of determinants. | No         |
| 2005\(^{24}\)   | sectors        | C_{ti} = \sum_{d=1}^{5} W_{d} \times H_{d} | C_{ti} = scores of determinants d during time window t for subject i. W_{d} = relative weight for determinant d. H_{d} = hazard value of category of determinants. | No         |
1.3.4.6.1 Sheep dipping model

As a first step of a study of UK sheep dippers, a hygiene study of sheep dippers was carried out to derive an empirical model of OP exposure to be used in the main phase of the epidemiological study. On the dipping day, each of 20 farms using diazinon was visited by two professional occupational hygienists. The hygienists recorded general information on dipping practices for each farm and noted the tasks carried out by each worker during the dipping day focusing on handling the concentrate, splashing with dilute dip and indirect ingestion (through smoking or eating).

Three urine samples were collected from each dipper; one before the beginning of the dipping session, one immediately after dipping, and the last early the following morning. The increase in the urinary concentration of diazinon metabolites, namely DEP and DETP, from the sample before the start to the sample of the following morning was used to estimate diazinon exposure during the observed dipping session.

The mean±SD increment of the urinary metabolites in plungers was 40.8±9.8 nmol/mmol creatinine, compared to 7.3±3 nmol/mmol creatinine in chuckers and 5.3±3.7 nmol/mmol creatinine in helpers. In general plungers in this study were responsible for handling concentrate throughout the dipping session and they also had the highest observed exposure to diluted dip splashes. The estimated linear regression coefficients for variables representing concentrate handling and diluted dip splashing were highly significant (P<0.001) and the results after correcting exposure for Personal Protective Equipment (PPE) were similar because the farmer did not wear the recommended protective gloves in 93% of the 132 observed concentrate handling events. The number of smoking and ingestion events was not correlated with the increment in the urinary metabolites (P=0.92). From these observations, a simple linear model for exposure (EXP) during a single dipping session was developed:

\[ \text{Eq. 1.1: EXP} = \alpha + \beta C + \gamma S \]

Where:

C = number of events in which concentrate was handled; S = time weighted splash score for dilute dip; and \( \alpha, \beta \) and \( \gamma \) = parameters. The fitted regression models for the increments in urinary concentrations resulted in \( \beta =3.6 \), \( \gamma =0.2 \) and \( \alpha \) close to zero so it was neglected.

To use this exposure model to estimate past exposure by a questionnaire, it was necessary to find other variables which can be related to the model variables and could
be accurately recalled. Mean time weighted splash scores were predicted from a two factor ANOVA model that included the principal task and bath type (linear, circular and mobile). Simple surrogate inputs were determined; a mean of 8 handling events per session for the principal concentrate handlers and the task specific means for linear bath for splash exposure (66 for plunger, 44 for chucker, and 10 for helper). Researchers validated the exposure model with similar data of 51 dippers who took part in two previous hygiene studies. Observed and predicted exposure using the simple surrogate variables (i.e. eight handling events and task specific means for linear bath) was significantly correlated ($r = 0.39; P = 0.005$).

The equation of cumulative exposure to OP sheep dips was derived from the single session exposure model:

\[
\text{Eq. 1.2: EXP} = 3.6 \times \text{CONC} + 0.2 \times \text{SPLASH}
\]

Eq.1.2.1: \[\text{CONC} = \sum_{j=1}^{J} \text{ND}_j \times (% \text{HAND}_j \times 8)\]

Eq.1.2.2: \[\text{SPLASH} = \sum_{j=1}^{J} \text{ND}_j \times (% \text{PLNG}_j \times 66 + % \text{CHCK}_j \times 44 + % \text{HELP}_j \times 10)\]

Where: \%HAND$_j$ = the estimated number of occasions spent as principal concentrate handler in job j, \%PLNG$_j$, \%CHCK$_j$ and \%HELP$_j$ = the estimated percentage of dipping in job j spent working as a plunger, chucker, and helper respectively, and ND$_j$ = the number of dipping days spent in job j.

This specific model for long-term OP exposure during sheep dipping has included three main variables (i.e. handling concentrate, task, and number of dipping days) which are easy to recall. Another advantage of this model is that it was extracted from an empirical study not from a hypothetical judgment.

However, this model has ignored many important variables of exposure in sheep dipping. For example, the use of PPE had limited effect in this study and thus it was omitted from the model. Such omission may lead to estimation errors in other circumstances when the farmers wear the PPE properly and their exposure to pesticides may nearly be eliminated. Another important variable neglected in this model was the number of dipped sheep. This number may range from 1 to 2000 sheep which affects hugely number of handling the concentrate events and the amount of dip splashes from the bath.
1.3.4.6.2 Pesticide applicator model

A semi-quantitative model was built by Dosemeci et al.\textsuperscript{153} to estimate long-term exposure to pesticides for the AHS which had enrolled more than 58,000 pesticide applicators in North Carolina and Iowa\textsuperscript{28}. Most studies which were subsequently based on the AHS data have used this model\textsuperscript{156-159}.

The researchers designed two questionnaires; an enrolment questionnaire and a take-home questionnaire which was more detailed. On enrolment into the study, pesticide applicators completed a questionnaire and provided information on the duration of work (\textit{i.e.} number of working years and average number of days per year) for 22 pesticides (selected because of their importance in that region), the frequency of pesticide handling, the frequency of mixing pesticides, the method of application, the repairing of application equipment and the use of PPE. All applicators were also requested to fill in a self-administered take-home questionnaire which looked for more information on pesticide handling, the mixing system, the type of tractor, replacing old gloves, personal hygiene, cleaning procedures, and lifestyle variables. The second questionnaire added a further 28 chemicals to the original 22. Using questionnaire responses the researchers applied two algorithms; the general algorithm used the variables of the enrolment questionnaire and the detailed one used those of the take-home questionnaire.

The general algorithm was:

\textbf{Eq. 1.3: Intensity Level} = \((\text{Mix} + \text{Appl} + \text{Repair}) \times \text{PPE}\)

Where the variables and their assigned scores were:
\begin{itemize}
  \item Mix = mixing status (0, 3, 9);
  \item Appl = application method (1, 2, 3, 4, 5, 6, 7, 8, 9);
  \item Repair = repairing application equipment (0, 2);
  \item PPE = personal protective equipment use (1.0, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.1).
\end{itemize}

The detailed algorithm was:

\textbf{Eq. 1.4: Intensity Level} = \([\text{(Mix} \times \text{Enclosed}) + (\text{Appl} \times \text{Cab}) + \text{Repair} + \text{Wash}] \times \text{PPE} \times \text{Repl} \times \text{Hyg} \times \text{Spill}\)

Where the variables and their assigned scores were:
\begin{itemize}
  \item Enclosed = using enclosed mixing system (0.5, 1.0);
  \item Cab = tractor with enclosed cab and/or charcoal filter (0.1, 0.5, 1.0);
\end{itemize}
Wash = status of washing pesticides equipment after application (0.0, 0.5, 1.0, 3.0);
Repl = replacing old gloves (1.0, 1.1, 1.2);
Hyg = personal hygiene use (0.2, 0.4, 0.6, 0.8, 1.0);
Spill = changing clothes after a spill (1.0, 1.1, 1.2, 1.4, 1.8)

Since the mixing, applying, repairing and washing variables independently contribute to exposure of the whole body, an additive model was used for these variables. On the other hand, a multiplicative model was used for the protective variable (PPE, Enclosed, etc.) since they are dependent on the main exposure determinants.

Three sources of information were utilised by the researchers to assign exposure weights (i.e. scores) for each variable in the algorithm. The published scientific literature was the main source where more than 100 articles containing exposure measurements in agricultural settings were reviewed. The second source was the Pesticide Handlers Exposure Database. This database was non-chemical-specific developed by the EPA, American Crop Protection Association and Health and Welfare Canada to investigate dermal and inhalation exposure during mixing, loading and application activities. The final source was a pilot exposure monitoring survey undertaken by the EPA. The weights of the algorithm variables were generated by making comparisons between the results of different monitoring data within each variable (e.g. for ‘Appl’ variable: backpack versus hand spray) and also between different variables (e.g. applying versus mixing). Available measurement data on human exposure during pesticide application to livestock was very limited.

After estimating exposure intensity level, a lifetime cumulative exposure score was calculated for each pesticide using frequency of exposure (i.e. number of days/year) and the duration (i.e. number of years):

Eq. 1.5: Cumulative exposure = Intensity level × Frequency × Duration

The second questionnaire was returned from 40% of the enrolled applicators. When the results of the two algorithms were compared, a high concordance was found especially for cumulative exposure estimates (50-57% exact percent agreement). Therefore, the study suggested that although the general algorithm included less exposure information, it could be used instead of the detailed one in evaluating disease risks.

The general algorithm has been evaluated twice at least. Coble et al. used the data of 126 farmers who applied one of two herbicides, namely MCPA and 2,4-D in the
Pesticide Exposure Assessment Study. In the evaluation analysis, exposure scores estimated by the general algorithm were compared with pesticide concentrations in post-application 24-h urine samples. For the MCPA applicators, the geometric mean of pesticide urinary concentration in the highest exposure group was 20 μg/l compared to 5 μg/l in the lowest exposure group (P =0.03) while for the 2,4-D applicators the 2,4-D concentration was 29 μg/l in the highest group compared to 2 μg/l in the lowest group (P =0.007). These results suggest a good validity for the general algorithm among those applicators. The study also showed a significant correlation in the 2,4-D applicators between the algorithm scores and the urine concentrations (r_s =0.45, P =0.003), while the correlation in the MCPA applicators was not significant (r_s =0.17, P =0.11). The difference between the two pesticides suggests that the algorithm worked better with 2,4-D compared to MCPA. The study justified that partially by the differences in the physical-chemical properties of the two pesticides.

Acquavella JF et al. evaluated the general algorithm using 24-h composite post-application urinary pesticides concentrations for 116 farmers who applied glyphosate, 2,4-D or chlorpyrifos and who participated in the Farm Family Exposure Study. The formulation of all applied glyphosate and 2,4-D pesticides was liquid whilst the formulation of applied chlorpyrifos was either liquid or granular. The intensity scores were calculated twice; once based on information collected by trained observers and once based on information given by the farmers. Moderate correlations were found between exposure scores relying on the observers’ assessment and urine concentrations for glyphosate (r_s, 95%CI= 0.47, 0.21-0.66) and 2,4-D (r_s, 95%CI= 0.45, 0.13-0.68), while the correlations were lower when the scores depended on farmers’ self-reports (glyphosate: r_s, 95%CI= 0.23, -0.07-0.48, 2,4-D: r_s, 95%CI= 0.25, -0.10-0.54). Contrasting correlations were found for liquid chlorpyrifos (r_s, 95%CI= 0.42, 0.01-0.70) and granular formulations (r_s, 95%CI= -0.44, -0.83-0.29) based on both assessments (the results were identical). The study concluded that type of pesticide formulation should be collected and that using a generic model that does not consider the physical and chemical properties of pesticides will likely result in exposure misclassification.

The main strength of this model is that it can be used for different farming sectors. However, it was designed to assess exposure among pesticide applicators and therefore it cannot be used to estimate exposure among other farmworkers like harvesters. Furthermore, although it contained a separate scoring for the animal insecticides (ear
tags, inject animal, dip animal, etc.), exposure determinants in animal treatment were very limited in this model.

This detailed model combined 10 exposure determinants in one intensity score and the determinants were weighted by using several methods and databases. However, determinants such as farm area or application rate were not included although it was used in other models\textsuperscript{124,151}. Evaluation studies found that the performance of the model was poor in some situations\textsuperscript{138,139}. Although these studies suggest that the performance of such a generic model is not good with all types and formulations of pesticides, this poor assessment could be also a result of incorrect weighting of the model variables.

1.3.5 **Routes of occupational exposure to pesticides**

Pesticides can enter the body through the skin, or via inhalation, and ingestion.

1.3.5.1 **Dermal**

Dermal exposure is the predominant route of occupational pesticide exposure\textsuperscript{162,163}. The rate of dermal absorption varies from one part of the body to another. The forearm absorption rate is usually considered as a baseline (1.0), and compared to this baseline dermal absorption rate of certain areas like genital area and forehead is very high (11.8 and 4.2 respectively)\textsuperscript{164,165}.

Dermal absorption might happen as a result of splashes or spills during handling the concentrate or during applying the pesticide. It might happen also from contacting contaminated application equipment, protective clothing or treated animals or plants\textsuperscript{164,165}. Handling OP pesticide concentrate was found to be a major source of exposure in sheep dipping studies\textsuperscript{12,99}. Contaminated parts of the body differ according to the type of activity. During mixing and loading of pesticide powders 45-75\% of the total estimated dermal exposure was through the hands\textsuperscript{151}. During downward pesticide application by vehicles 65-75\% of the total estimated dermal exposure was through the hands and the forearms and 10-15\% was through the upper torso, while during upward application only 10\% was through the hands and the forearms and 65\% was through the upper torso\textsuperscript{94}.

In the dermal route, it is important to distinguish between the potential dermal exposure and the actual exposure. Potential exposure is the amount of pesticide that ends on the farmer’s skin, on his clothes or on his protective clothes, while the actual dermal
exposure is the total amount of pesticide that comes into contact with bare skin and is available for percutaneous absorption\(^3\). Considering the importance of dermal route compared to other routes has made many researchers focus on dermal exposure only, especially through hands. Therefore occupational pesticide assessment has been based on variables related to dermal exposure rather than those related to exposure through inhalation\(^7,12,29,99\).

### 1.3.5.2 Inhalation

Respiratory exposure to pesticides constitutes not more than 1% of the total occupational exposure in agricultural work\(^162,163\). The inhalation route can be ignored in the mixing and loading of liquid pesticides if closed mixing systems are used. However this route will become significant when volatile pesticides, fumigants, or dusts are used especially in confined spaces\(^3\). In an occupational hygiene assessment of sheep dipping practices and processes, airborne diazinon concentrations were measured for 6 dippers and all were less the detection limit (0.01 mg/m\(^3\)) which is tenth of the UK occupational exposure standard (0.1 mg/m\(^3\)) indicating that inhalation route was not that significant in sheep dipping\(^12\). Although inhalation exposure is generally less important than dermal exposure in occupational exposure to pesticides, it is important to mention that proportion of the inhaled dose retained systemically is very high (may reach 75\%\(^166\)) compared to the proportion absorbed through dermal route (1% or less of the actual dermal exposure\(^3\)).

### 1.3.5.3 Ingestion

The major route of pesticide exposure in the general population is oral\(^167\), but most studies have ignored this route when assigning occupational exposure to farm workers, primarily because inadvertent oral occupational exposure was considered unlikely\(^7,99,154\). Also, little information is available about the oral route of occupational exposure since it is difficult to measure\(^168\). Inadvertent ingestion exposure to pesticides as a result of the contact between contaminated hands or objects and the mouth is probable in workplace; however no research has explicitly investigated this route in adult workers\(^169\). To demonstrate the relationship between dermal and ingestion exposure, Gorman et al.\(^168\) has developed a conceptual model for inadvertent ingestion exposure that follows hands-to-mouth or object-to-mouth events by integrating two previously published models; a conceptual model for inadvertent ingestion exposure\(^169\) and a conceptual model for dermal exposure\(^170\). This integrated conceptual model has been developed as
a framework for building a predictive model for estimating occupational inadvertent ingestion exposure. Airborne particles may also enter the mouth or be trapped in the nose and subsequently ingested. This oral exposure may be included in the inhalation exposure measurements since it measures airborne particles whether they were inhaled or ingested3.

1.3.6 Main determinants of occupational pesticide exposure used in epidemiological farming studies

Pesticide exposure can be affected by many determinants, some of them can easily be defined in epidemiological studies such as application methods, whereas others are more difficult to define such as physical workload and meteorological conditions124. The determinants which can be easily assessed retrospectively, either by a questionnaire or by reviewing accessible data, are of most interest in the epidemiological studies. Table 1-4 presents the determinants included in exposure algorithms mentioned earlier in Table 1-3, while the main determinants of pesticide exposure that can be used in epidemiological studies will be described briefly.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place</th>
<th>participants and sample size</th>
<th>Determinants *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buchanan et al.</td>
<td>UK</td>
<td>Sheep dipping sessions at 20 farms using diazinon</td>
<td>x x x</td>
</tr>
<tr>
<td>Tahmaz et al. 2003</td>
<td>UK</td>
<td>63 sheep dippers</td>
<td>x x x x</td>
</tr>
<tr>
<td>Brouwer et al. 1994</td>
<td>Netherlands</td>
<td>137 farm workers</td>
<td>x x x x x</td>
</tr>
<tr>
<td>Stewart et al. 2001</td>
<td>-</td>
<td>Theoretical study on farmworkers</td>
<td>x x x</td>
</tr>
<tr>
<td>Tielemans et al.</td>
<td>Netherlands</td>
<td>64 greenhouse workers</td>
<td>x x x x x</td>
</tr>
<tr>
<td>Dosemecci et al.</td>
<td>USA</td>
<td>58,000 pesticide applicators</td>
<td>x x x</td>
</tr>
<tr>
<td>Monge et al. 2005</td>
<td>Costa Rica</td>
<td>227 employees in agriculture or livestock breeding</td>
<td>x x x x x</td>
</tr>
</tbody>
</table>

* Determinants: 1=PPE, 2=task, 3=duration of task, 4=application rate, 5=re-entry or handling treated sheep, 6=application technique, 7=personal hygiene, 8=application frequency, 9=area treated, 10=repairing and washing application equipment, 11=pesticide half-life.
### 1.3.6.1 Pesticide class

Pesticide class is important as chemicals can differ in their ability to penetrate the skin. Acquavella JF *et al.*\(^{138}\) (described in section 1.3.4.6.2), found contrasting results for liquid chlorpyrifos and granular formulations when they validated the exposure algorithm used in the AHS study and Coble *et al.*\(^{139}\) (described in section 1.3.4.6.2) found exposure differences between two similar herbicides; MCPA acid and 2,4-D. This indicates that the ignorance of the physical-chemical properties of the pesticides during the exposure assessment may result in significant misclassification. However, it is not easy for farmers always to recall the type of pesticides used especially over a long period of time\(^{118,126,132}\).

### 1.3.6.2 Type of activity

Application, mixing, loading and harvesting can expose farmer to pesticides differently. For example, during sheep dipping farmers who deal with OP concentrates were more likely to be exposed to pesticide than farmers who just deal with diluted pesticides\(^99\). Dermal exposure from weeding\(^{171}\) was found to be 9-10 times higher than the exposure from harvesting\(^{172}\) while the exposure through thinning was found to be 2 times higher than exposure from harvesting and pruning\(^{171}\). Job title is obtained as a surrogate of the type of activity undertaken as it is easier to remember and defined. In exposure assessment, not every farmer can define the percentages of every activity carried out and most farmers have carried out all the activities\(^{25,150}\).

### 1.3.6.3 Method of application

These methods vary between crops and animal farms, and between countries\(^{117}\). Exposure of the farmer can vary according to these methods; for example, airblast and hand spray applications were reported to generate about three times higher exposure levels to the applicator than boom sprayer application\(^{173}\), and the last has been reported to generate three times that generated by aerial spraying\(^{174}\). The exposure received from pesticide application on animals varies according to the application method\(^{175}\). The bath type used in dipping sheep can also play a role in the exposure; exposure with a linear bath was 1.3 times higher than with a circular one\(^{99}\). Method of application is easy to remember but it may have changed over the time and some farmers may use more than one method\(^{26}\).
1.3.6.4 Farm area and flock size

Farm area or flock size can be a surrogate for the amount of pesticide applied. A good correlation was found between the whole body dermal exposure and number of boxes filled during the harvesting in a day \((r_s =0.41-0.76)\)\(^{176}\). The estimated total number of sheep dipped was used as a surrogate for exposure in the study of Stephens et al.\(^8\). Brouwer et al. found that more mechanized equipment was used in larger farms and that this led to lower levels of pesticide exposure per unit of area suggesting that the use of acreage as the only surrogate for exposure may result in misclassification\(^{151}\).

1.3.6.5 Application rate

In the crops and grains sector, application rate means the weight of active ingredient per acre. Zweig et al. found that when the amount of pesticide applied increased four times, the exposure on skin increased 7.2 times\(^{177}\). The application rate can be used as a surrogate of exposure intensity since it may be available and can be obtained from the farmers or from the records of some institutes and agencies\(^{124}\); the specific crop and pesticide has to be known to get this rate. However, manual equipment is usually used when applying small amount of pesticide \((i.e. \text{ in small farms})\) while more mechanized equipment is used when applying larger amounts \((i.e. \text{ in bigger farms})\)\(^{151}\). This means that pesticide exposure when applying a large amount of pesticides might be less than when applying a smaller amount and that the application rate and application method should be considered together in assessing pesticide exposure.

1.3.6.6 Frequency of application

In order to know the cumulative exposure, the number of days the farmer has been in contact with pesticides should be known. However, the meaning of a day of pesticide use can vary greatly and has to be defined\(^{178}\).

1.3.6.7 Re-entry to sprayed area or dealing with treated animals

Farmers have to re-enter the sprayed area (or deal with treated animals) for many reasons \((e.g. \text{ harvesting, shearing animals and dairy milking})\). However this re-entry should happen days after applying pesticides with the specific time depending on the type of pesticide and its half-life otherwise the farmer will be exposed to an additional exposure\(^{152}\). Re-entry time was found to be an important determinant of dermal exposure to captan and tolyfluanid (variance of regression models was 0.30-0.87)\(^{179}\). Data indicate that not all farmers comply with this time so the time of re-entry to the
treated area or handling the treated animals should be considered as one of the
determinants of pesticide exposure.  

1.3.6.8 Use of protective equipment

Protective equipment either general or personal, can affect exposure significantly. For
example, exposure to parathion and dimethoate during application to citrus trees
differed according to the airblast spray equipment. Exposure was reduced by 50% by
closed cabs on tractors and by 90% by closed cabs with air filters compared to non-cab
tractors. PPE include mainly gloves, respirators, face-shields, boots, aprons and
overalls. PPE can nearly eliminate dermal exposure if they are used properly but this
does not often happen. In an occupational hygiene assessment of OP exposure in
sheep dipping, the dermal protection factor of PPE ranged from 4 to >1000 and the
penetration of the pesticides through the PPE was generally very low. However, if the
PPE are not used correctly or they have become old they may increase the exposure to
pesticides. Therefore this determinant has to be approached carefully.

1.3.6.9 Personal work habits and hygiene

Changing clothes, taking a bath after work and washing hands before eating or smoking
are examples of habits which can affect exposure through skin or ingestion. In sheep
dipping, chucker who threw the sheep into the bath or allow too many sheep into the
bath in the same time and plungers who used their hands or feet to immerse the sheep
instead of using a special instrument were exposed to greater amounts of splashing.
Among farmers who applied insecticides to livestock, those who had poor work
practices like using leaking equipment or contacting the wet fences had significantly
higher exposure levels than others; geometric mean of active ingredients on their skin
was 1188.15 and 3.34 µg respectively.

1.4 The neurotoxicity of long-term pesticide exposure

Many chronic health outcomes like cancers, neurologic and dermatologic problems, and
miscarriages have been linked with long-term pesticides exposure in previous studies.
However, researchers have used the assessment of neurotoxic effects to demonstrate
the difficulties in studying the health outcomes in farming communities exposed to
pesticides. Likewise, this thesis has used the SHAW study, which had focused on
neuropsychiatric ill-health, to examine the impact of using the newly developed
exposure models on the association between pesticide exposure and health effects.
A wide range of nonspecific neurologic and neuropsychiatric symptoms including fatigue, headache, dizziness, nausea, weakness, insomnia, concentrating difficulties and confusion have been associated with long-term pesticide exposure even without a history of poisoning whilst only few specific neuropsychiatric illnesses have been mentioned to be related to long-term pesticide exposure\textsuperscript{16,18,182}. Long-term exposure to OP specifically has been linked with many neurotoxic effects and in 1999 the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) published a report about the long-term adverse health effects of OP pesticides\textsuperscript{13}. In that report the Working Group of the Committee summarized 27 studies published up to June 1999 relevant to potential toxicity of low-level exposure to OPs. The COT report divided the putative neurotoxic effects of long-term low-level OP exposure into five categories; neuropsychological abnormalities, peripheral neuropathy and neuromuscular dysfunction, electroencephalographic abnormalities, psychiatric illness, and the effects on the autonomic nervous system\textsuperscript{13}. The COT committee received testimonies from individual who believed that they had suffered from long-term ill-health as a result of their exposure to OPs. Those individuals have listed a range of symptoms and signs that mainly included anxiety, confusion, depression, suicidal thoughts, sleep disorders, headache, fatigue, impaired concentration, memory loss, Irritability, numbness of the extremities, and muscular pains and spasms. However, the COT committee concluded in their report that no firm conclusion could be drawn.

Pesticides regulatory agencies have their own schemes for reporting adverse reactions to pesticides and other veterinary medicines. The main two schemes are the Pesticides Incidents Reports which provides information on incidents and complaints involving pesticides investigated by the Field Operations Directorate of the Health and Safety Executive\textsuperscript{183} and the Suspected Adverse Reaction Surveillance Scheme (SARSS) which is a national surveillance run by the VMD\textsuperscript{184}. In the SARSS, for example, 651 reports of suspected adverse reactions due to OP sheep dips were received between 1985 and 1998. The reports received each year were 5 to 19 reports every year before 1991 then the number dramatically increased in 1991, 1992 and 1993 to be 127, 129 and 180 reports respectively and then considerably fell to 17 reports in 1998\textsuperscript{13}. Figure 1-23 shows the number of cases by reported year of onset of the adverse reaction that might differ from the year of reporting and shows annual sales of OP sheep dips over the same time period. The total sales of OP sheep dips in the UK increased until 1986 and then steadily declined until 1998. It should be mentioned that between 1988 and 1991 it was compulsory to dip sheep twice a year and once a year after that until 1991 when
compulsory dipping was discontinued\textsuperscript{185}. Therefore, this figure would suggest that there was no association between the sales of sheep dips and the reported effects.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Total sales of OP sheep dip products in the UK and annual numbers of human Suspected Adverse Reactions to sheep dips by year of onset of the adverse reaction.}
\end{figure}

Adapted from the COT report\textsuperscript{13}.

The Department of Health recognised in 2002 Chronic Fatigue Syndrome (CFS)/Myalgic Encephalopathy as a chronic ill-health and recommended that health workers should deal with it as such. The most common symptom of CFS is a profound, persistent and debilitating fatigue and it typically becomes worse after physical or mental exertion. The aetiology and risk factors of this syndrome remain unclear; however there were concerns based on limited evidence that long-term low-level exposure to OPs may result in CFS\textsuperscript{7,8}.

The SHAW study used in this PhD project has focused on four neuropsychiatric illnesses, namely depression, neuropathy, Parkinsonism, and dementia. Therefore, the relationship between these four illnesses and long-term pesticide exposure will be described in the following sections with a special focus on the research on sheep farming. The comparison between published reports mentioned below is difficult for many reasons. A term such as “depression” can be used to report a psychiatric symptom among many other psychiatric symptoms\textsuperscript{186} and can be used to report a clinically diagnosed disease\textsuperscript{187}. Researchers might also depend on different screens to diagnose
neuropsychiatric illnesses while others might depend on clinical diagnosis. Moreover, neuropsychiatric health effects might be investigated by the performance of the farmers in neurobehavioral tests or by the impairment in the electrodiagnostic tests. Such tests should be considered indications of possible ill-health and not necessarily a manifestation of one specific disease. Thus neurobehavioural test performance might be impaired in both dementia and Parkinson's disease.

### 1.4.1 Depression

Depression is a major disabling disease among elderly people affecting more than 120 million people worldwide while 50% of people are affected by a kind of psychiatric disorder, mainly a major depressive disorder, during the age period 18-44 years. The lifetime prevalence rate of depression is estimated at 17% making it one of the most common disorders in the primary care services, while the prevalence rate among UK people aged over 55 has been reported to be 0.9-4.3% for major depression and 8.3-13.5 for minor depression. About 6% of men and 9.5% of women are estimated to experience a depressive episode every year.

A major depressive disorder can be diagnosed by one or more major depressive episodes. The episode is characterized by criteria developed by a number of organisations; one of the most common utilised is the DSM-IV criteria (Table 1-5).

<table>
<thead>
<tr>
<th>Group</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Five or more of the following symptoms present during the same 2-week period nearly every day and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. (1) Depressed mood most of the day, nearly every day. (2) Markedly diminished interest or pleasure in almost all activities. (3) Significant weight loss or weight gain, or decrease or increase in appetite. (4) Insomnia or hypersomnia. (5) Psychomotor agitation or retardation. (6) Fatigue or loss of energy. (7) Feelings of worthlessness or excessive or inappropriate guilt. (8) Diminished ability to think or concentrate, or indecisiveness. (9) Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.</td>
</tr>
<tr>
<td>B</td>
<td>The symptoms do not meet criteria for a Mixed Episode.</td>
</tr>
<tr>
<td>C</td>
<td>The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.</td>
</tr>
<tr>
<td>D</td>
<td>The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).</td>
</tr>
<tr>
<td>E</td>
<td>The symptoms are not better accounted for by bereavement. The symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.</td>
</tr>
</tbody>
</table>

Table 1-5: DSM-IV Criteria for major depressive episode

---

69
A high prevalence of psychiatric disorders has been found in rural communities\(^{195}\) and changes in mood and affect have been linked particularly with long-term pesticide exposure\(^{18,196}\). Short-term high and moderate levels of pesticide exposure may lead to permanent psychological consequences including depression but the effects of long-term exposure to low levels remains unclear\(^{182,197}\).

In 1999 the COT published a report in which they summarized 27 epidemiological studies published up to June 1999 relevant to the potential toxicity of low-level exposure to OPs\(^{13}\). Whether or not there was an association between psychiatric disorders and long-term pesticide exposure was mentioned in four studies in the COT report\(^{8,22,198,199}\).

Two cross-sectional studies suggested that OP pesticides have psychiatric effects and one of them was carried out on sheep dippers\(^{8,198}\). The study of Stephens et al.\(^{8}\) compared neuropsychological performance between 146 sheep farmers who dipped sheep using OPs and a control group of 143 quarry workers. OP exposure was estimated by a surrogate measure namely the average number of sheep in flock\(\times\)number of dips per year\(\times\)number of years using OPs. Vulnerability to psychiatric disorder (\(i.e.\) reporting five psychiatric symptoms at least) was greater among farmers who worked with OPs than their controls (Odds Ratio (OR), 95% Confidence Interval (CI): 1.50, 1.31-1.69). In this study, the use of a simple surrogate to estimate long-term OP exposure (\(i.e.\) the cumulative number of dipped sheep) might result in exposure misclassification. Moreover, the selection of the controls is also questionable since many of them have worked in sheep farms during free time.

In contrast, the COT reported another two studies that did not find significant psychiatric effects\(^{22,199}\). One of them was cross-sectional\(^{22}\) and the second was an ecological study\(^{199}\) but both of them were not on sheep farmers. The COT report concluded that it was difficult to draw useful conclusions regarding the relationship between low-level OP exposure and psychiatric illnesses\(^{13}\).

After the publication of the COT report few studies investigated the association between psychiatric disorders and long-term pesticide exposure; two of them have been carried out in the UK sheep dippers\(^{11,186}\). Graham Dunn\(^{186}\) analysed 646 reports of suspected adverse reactions to OP sheep dips in the SARSS database of the VMD in 2001. Using a developed exposure metric, levels of both short-term exposure (\(i.e.\) peak exposure likely to have occurred shortly before the onset of symptoms) and long-term cumulative
exposure were estimated and a wide variation in levels was found. Psychiatric disorders were the fourth most common reported symptoms (203 reports of at least one symptom) after the nervous disorders, the general disorders, and the gastrointestinal disorders. The most common psychiatric disorder symptoms were depression and amnesia. Associations between several symptoms and both short and long-term exposures were significant but the most marked were for psychiatric disorders (depression in particular) (OR, 95%CI: 1.86, 1.42-2.45 and 1.73, 1.43-2.09 for short and long-term exposure, respectively) and musculoskeletal disorders (especially myalgia). However, the associations became weaker, but remained significant, after adjustment for age of onset of ill health and year of the report (OR, 95%CI: 1.46, 1.08-1.97 and 1.35, 1.08-1.68 for short and long-term respectively). These data were voluntarily reported only, and as such this study should be considered as descriptive and exploratory and can only be used as a hypothesis-generating study.

Solomon et al. 11 carried out a postal survey to investigate neuropsychiatric symptoms in past users of sheep dip and other pesticides in three rural areas of England and Wales. 9844 men were recruited, of whom 1913 had worked with sheep dips, while 832 had worked with other insecticides and 990 with other pesticides but never with sheep dip or insecticides. There was no association between past use of pesticides (whether sheep dips, insecticides or other pesticides) and depression (Prevalence Ratio (PR), 95%CI was 1.2, 1.0-1.4, 0.9, 0.7-1.1, and 0.9, 0.8-1.1 respectively). No association was also found with current anxiety (PR, 95%CI was 1.1, 1.0-1.2, 1.0, 0.8-1.2, and 1.1, 0.9-1.2 respectively). A low response rate which can lead to a participation bias and exposure misclassification due to the use of simple surrogates (ever/never) are two of the limitations of this study.

Away from sheep farming, clinical neuropsychiatric and laboratory examinations were performed in a follow-up study200 on 37 tobacco farmers who had been exposed to low levels of OP pesticides for three months. The same examinations were repeated on 25 of them after three months without exposure to OP pesticides. Psychiatric diagnoses were found in 18 subjects (48%) in the first interview including 13 cases of generalised anxiety and 8 cases with major depression. In the second interview and after three months without using OPs, the number of subjects who had any psychiatric diagnosis decreased from 11 to 7 indicating that exposure to low-levels of OPs might induce psychiatric disorders. However, the exposure assessment (i.e. being exposed for 3 months and not exposed for another 3 months) was very simplistic.
Two nested case-control studies, nested in the AHS, aimed to study the association between chronic pesticide exposure and depression; one has focused on the private pesticide applicators and the second has focused on their female spouses. Lifetime pesticide exposure among private pesticide applicators was compared between 534 cases of self-reported a physician-diagnosed depression and 17,051 controls. An increased risk of depression was associated with pesticide poisoning (OR, 95%CI: 2.57, 1.74-3.79) but not with high cumulative exposure (OR, 95%CI: 1.11, 0.87-1.42). However, when those subjects with a history of pesticide poisoning were excluded, the association with high cumulative exposure became significant (OR, 95%CI: 1.54, 1.16-2.04). In the second study, depression was also associated with pesticide poisoning among female spouses of the pesticide applicators (OR, 95%CI: 3.26, 1.72-6.19) but not with high cumulative exposure (OR, 95%CI, 1.09, 0.91-1.31). These two studies suggest that the effect of previous high-exposure events should be considered in any study of long-term exposure effects.

Major depression is known to be one of the main risk factors of attempting suicide. Suicide is a noticeable problem among farmers and committing suicide has been linked with farming life and pesticide exposure in different studies. The COT reported that a Canadian case-control study found no association between committing suicide and pesticide exposure in different studies. The COT reported that a Canadian case-control study found no association between committing suicide and pesticide exposure, whilst another ecological study found significant increased rate of suicide in the British county of Devon where OP exposure among sheep farmers had been common. Exposure assessment depended simply on the regional pesticide usage in the first study and type of farming carried out in the second study.

In 2005, London et al. performed a literature review of studies which investigated the relationship between suicide and both short-term and long-term OP exposure. This report reviewed also human and animal toxicological studies of the effect of OPs on the CNS. A high rate of suicide among farming communities was reported and epidemiological studies and case series suggest a causal association between suicide and short-term and long-term OP exposure. The review reported that, based on animal studies, OP exposure may cause disturbance of serotonin in the CNS which may in turn correlates in human with suicide and depression. Another literature review was performed by Fraser et al. in the same year on 52 papers that came from Europe, Australia, Canada, and the USA between 1985 and 2005 which investigated mental health in farming populations. The review concluded that suicide incidents among farmers are higher than general population.
A recent Spanish ecological study conducted in different health districts found that the prevalence rates for suicide attempts was significantly higher in the districts with higher environmental pesticide exposure compared to those of low exposure (99.6 and 53.4 respectively, \( P = <0.001 \))\(^{27} \). Pesticide exposure was determined according to the number of agricultural hectares and pesticide sales per capita. The prevalence of affective psychosis did not differ significantly between both high and low exposure areas (147.1 and 144.9 respectively, \( P = 0.70 \)).

On the other hand, a prospective cohort study on the pesticide applicators and their spouses based on the AHS study found no association between suicide and past pesticide exposure\(^{208} \). Exposure assessment depended on the cumulative lifetime days of use of individual pesticides and overall pesticides. The results of no association were consistent across all types of pesticides in this study.

In conclusion, there is evidence of high risk of psychiatric disorders and suicide among farmers who have been exposed to pesticides; however it is difficult to reach a firm conclusion regarding the relationship between low-level OP exposure and psychiatric illnesses. Whether this high risk among farmers is related to pesticide exposure in particular or related to other risk factors in the farming life is also a concern.

**1.4.2 Neuropathy**

Peripheral neuropathy, which refers to a group of diseases, describes damage to the nerves outside the CNS and this damage might be inherited or acquired\(^{209,210} \). The prevalence of peripheral neuropathy is about 2.4% and increases to 8% in people over 55 years old\(^{211} \). Diabetes mellitus is the main cause of this condition with about 15% of diabetes patients developing neuropathy within 20 years after diagnosis\(^{209} \). Other causes of neuropathy can include other systemic diseases (e.g. kidney disorders and cancers), physical injury, and toxins (e.g. heavy metals and carbon disulfide)\(^{209,210} \).

Peripheral neuropathy causes a variety of symptoms related to the affected nerve. Numbness, tingling, burning pain, lack of coordination and muscle weakness are examples of the common symptoms\(^{211,212} \). Diagnosis is usually difficult due to the variability of symptoms and electrodiagnostic tests (e.g. motor and sensory nerve conduction) are an important component in evaluating patients with suspected peripheral nerve disorders in epidemiological studies\(^{212,213} \).
The nervous tissue in both central and peripheral nervous system is directly targeted by high-level exposure to several pesticides, especially OPs and carbamates which might be followed by persistent nervous damage, but nervous tissue damage due to a chronic low-level pesticide exposure is still controversial\textsuperscript{13,72}. In the OPID, which is a rare phenomenon caused by intoxication with certain OPs, a degeneration of some long axons in the central and peripheral nervous system occurs 2-3 weeks after exposure\textsuperscript{42,61} (See Section 1.3.2.1.1 for details).

Four studies mentioned in the COT report, all of them cross-sectional, found that long-term exposure to OP pesticides had some effects on peripheral nerve functions\textsuperscript{214-217, 218-221}, however OPs rarely caused severe disability. On the other hand, another four examined cross-sectional studies did not support an association between OPs and peripheral neuropathy or impairment in neuromuscular functions\textsuperscript{218-221}. None of those eight studies was carried out on sheep farmers.

After the publication of COT report, additional studies have been published on the relationship between occupational pesticide exposure and neuropsychological illnesses. Four of them were of particular interest because they focused on sheep farmers\textsuperscript{9,11,29,186}. Pilkington et al.\textsuperscript{9} carried out a cross-sectional study to investigate the neuropsychological effects of chronic low-level OP exposure among sheep dippers. An empirical dermal exposure model (described in section 1.3.4.6.1) derived from work of the first phase of the study was used to estimate long-term OP exposure. The prevalence of neurological symptoms (muscle weakness, sweating, fainting, etc.) was significantly higher among sheep dippers who applied OPs than ceramics workers (OR, 95%CI: 3.85, 1.51-9.82). However, the significance depended on the inclusion of farmers who had very high exposure. A higher prevalence of symptoms especially of the sensory type was found only among sheep dippers who handled the OP concentrate (OR, 95%CI: 3.43, 1.63-7.23). Sensory and vibration thresholds were also higher among sheep dippers who handled the OP concentrate than those who had never handled the concentrate but only the difference in cold thresholds was significant (OR, 95%CI: 1.20, 1.00-1.45). Although significant OP effects were still found after adjustment for age and other confounders, the magnitude of the OP effect was relatively low compared with the effect of age, sex and county. Errors in exposure estimates might result from generalizing the empirical model to all sheep dipping processes.

The study by Graham Dunn\textsuperscript{186} described in Section 01.4.1 showed that, among the 646 reports of suspected adverse reactions to OP sheep dips, nervous disorders were the
most common reported symptoms (447 reports of at least one symptom). The most common symptoms (at least 50 reports) of the nervous disorders were headache, dizziness, and paraesthesia.

The postal survey of Solomon et al.\textsuperscript{11} also described in Section 01.4.1 reported that the prevalence of neurological symptoms was higher among past users of sheep dip and those men who had worked only with pesticides other than sheep dip or insecticides than in men who had never worked with pesticides. Compared to the farmers who never used pesticides, reporting of three or more neurological symptoms was more common among the farmers who used sheep dips (OR, 95%CI: 1.3, 1.0-1.6), the farmers who used other insecticides (OR, 95%CI: 1.4, 1.0-1.8) and the farmers who used other pesticides (OR, 95%CI: 1.3, 1.0-1.7).

In the Survey of Health and Pesticide Exposure: The Telephone Survey (SHAPE), Fletcher et al.\textsuperscript{29} described the health and exposure of the members of four UK organisations that have been supporting sheep farmers and others who had ill-health attributed by themselves to OP exposure. Information about the health and exposure of 367 participating members was collected by telephone interviews. Expert judgment was used to estimate OP concentrations in various tasks then to make developed exposure models for those tasks. Cumulative OP exposure was estimated using these models and according to the farmers’ frequency and duration of exposure. The health of the participants in this telephone survey was generally poor with 75% of them describing their overall health as fair or poor. The range of symptoms was wide with 62% of participants reporting numbness, burning and tingling in their hands, 47% in their feet and 34% elsewhere. The overall neuropathy scores were higher among the participants who had a high-level OP exposure episode; nevertheless those who had no high-level exposure also had many signs and symptoms of neuropathy. Since the members of the support groups are self-selected depending on their feeling that they had been affected by OPs, it is not possible to generalise the result of this study. Furthermore many of the findings of this survey might be related to the short-term high exposure more than to the long-term exposure since 80% of participants had a short-term high exposure in the past.

Kamel and Hoppin\textsuperscript{196} performed a summary review on 39 studies on neurotoxicity of chronic pesticide exposure which included comparison groups and were carried out between 1974 and 2003. The researchers found that most evidence indicates that vibration sensitivity, one of the most used tests to evaluate peripheral somatosensory
function, is not affected by low-level pesticide exposure. Motor function was rarely studied and mostly not affected by pesticide exposure and most studies which evaluated nerve conduction found negative results. The report concluded that pesticide exposure may affect CNS more than peripheral nervous system. A summary review report of Alavanja et al.\textsuperscript{18} that depended mainly on the same studies used by Kamel and Hoppin\textsuperscript{196} reached the same conclusion that there is little evidence of peripheral neurological effects of long-term pesticide exposure.

1.4.3 Parkinson's disease

Parkinson’s disease (PD), which is a common idiopathic disease affecting the CNS, has been described clinically by Parkinsonism that includes bradykinesia, rigidity, chronic progressive tremor, and postural instability\textsuperscript{222}. However, the definition of PD has changed over the time and the definitions aimed to distinguish between the parkinsonian syndrome which may occur due to many illnesses and PD which usually needs a movement disorder specialist to be accurately diagnosed\textsuperscript{223}. The UK Parkinson’s Disease Society Brain Bank set a few decades ago clinical diagnostic criteria for PD\textsuperscript{224} (Table 1-6) but many of these criteria were neglected and new definitions of PD have been described that include pathological changes and genetic mutations\textsuperscript{223}. Clinical symptoms of PD are frequently accompanied by cognitive dysfunctions and the pattern of cognitive dysfunctions described in the early stages of PD is similar to those seen when the frontal lobe is damaged\textsuperscript{225}. About one in five PD patients develop a frank dementia at some point of the illness\textsuperscript{226}.

<table>
<thead>
<tr>
<th>Type</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Bradykinesia and one of the following: rigidity, rest tremor, and postural instability not caused by other dysfunctions</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>History of repeated strokes, history of repeated head injury, history of definite encephalitis, oculogyric crises, neuroleptic treatment at onset of symptoms, more than one affected relative, sustained remission, strictly unilateral features after 3 years, supranuclear gaze palsy, cerebellar signs, early severe autonomic involvement, early severe dementia with disturbances of memory, language, and praxis, Babinski sign, presence of cerebral tumour or communicating hydrocephalus on CT scan, negative response to large doses of levodopa, and MPTP exposure.</td>
</tr>
<tr>
<td>Supportive prospective positive criteria</td>
<td>Three or more required for diagnosis of definite PD: unilateral onset, rest tremor present, progressive disorder, persistent asymmetry affecting side of onset most, excellent response (70-100%) to levodopa, severe levodopa-induced chorea, levodopa response for 5 years or more, and clinical course of 10 years or more.</td>
</tr>
</tbody>
</table>
In 2005, the number of people over 50 years old who have PD in the UK was estimated to be around 90,000. The prevalence of PD cases in 2005 was estimated to be 76/100,000 for ages 50-54, 664/100,000 for ages 70-74, and 1,044/100,000 for those over 80 years old\(^2\)\(^2\)\(^7\).

The aetiology of PD is not well established and PD has been related to many genetic and environmental factors including pesticide exposure\(^2\)\(^2\)\(^8\). The relationship between pesticide exposure and cognitive dysfunctions will be discussed in Section 1.4.4. Le Couteur et al.\(^2\)\(^2\)\(^9\) reviewed many studies published before 1999 and noted that 12 out of 20 case-control studies had found a positive association between PD and pesticide exposure, with odds ratios in the range of 1.6-7.0. However, many of those studies had defined the exposure as ever/never which can imply significant exposure misclassification. Furthermore, only a few studies identified specific pesticides which were OCs, OPs and carbamates in one study\(^2\)\(^3\)\(^0\) and paraquat in another two\(^2\)\(^3\)\(^1\),\(^2\)\(^3\)\(^2\). Two ecological studies also reported a positive association between the usage of pesticides in different regions and the prevalence of PD and the same association was suggested by five case reports. On the other hand, two cohort studies which investigated the health effects of long-term exposure to DDT\(^2\)\(^3\)\(^3\) and to paraquat\(^2\)\(^3\)\(^4\) did not report PD among those effects which may be due to the weak study power since a sample of many thousands is needed to detect a relative risk equalling 2. Le Couteur et al. suggested that although the modulation of xenobiotic metabolism is a possible hypothesis for the mechanism of association between pesticides and PD, the simplest mechanism is that pesticides are working as neurotoxins and directly impair the mitochondria\(^2\)\(^2\)\(^9\).

A more comprehensive review about the relation between pesticide exposure and PD was done by Brown et al.\(^2\)\(^2\)\(^2\). Epidemiological and toxicological studies between 1983 and 2003 were reviewed. The review concluded that the epidemiological data indicate a consistent association between PD and pesticide exposure. This relationship appeared to be stronger for exposure to insecticides and herbicides (paraquat in particular), especially after a long duration of exposure. Toxicological data indicated that paraquat and rotenone may have played a role in developing PD through neurotoxic actions, but there was limited data for other pesticides. Methodological weaknesses were found in both types of studies. In epidemiological studies PD was diagnosed by criteria which varied from one study to another. Pesticide exposure was estimated mainly by self-reported exposure history with a number of studies simply defined the exposure as ever/never. Many confounders that are associated with the development of PD (e.g.
rural living and farming as an occupation) were not adjusted for almost in all studies due to the difficulty of such adjustment. The main problem in the toxicological studies was that they used high doses of pesticides which are not comparable with those used by farmers or other pesticide users. The review concluded that the weight of evidence was sufficient to determine that there was an association between PD and pesticide exposure, although not sufficient to determine that there was a causal relationship.

In 2010, a systematic literature review and meta-analysis were performed by van der Mark et al. to investigate the association between pesticide exposure and PD and to investigate the role of methodological differences in the heterogeneity of study results. The review which included studies until November 2010 identified 4 cohort studies, 39 case-control studies, and 3 cross sectional studies and a Summary Risk Ratio (sRR) for pesticide exposure was calculated. An increased risk of PD was associated with general pesticide exposure (ever/never) and with insecticides and herbicides in particular (sRR, 95%CI: 1.62, 1.40-1.88, 1.50, 1.07-2.11, and 1.40, 1.08-1.81 respectively) but not with exposure to fungicides (0.99, 0.71-1.40). Heterogeneity in study results was not related to methodological differences (such as study design, adjustment for confounders, and geographical area) but suggestive effects were found for sample size and for the methodology of exposure assessment. Smaller studies tended to have higher sRRs compared to larger studies whilst studies which estimated pesticide exposure according to job titles tended to report higher sRRs than those studies which estimated the exposure based on self-report (sRR, 95%CI: 2.50, 1.54-4.05, and 1.50, 1.26-1.78 respectively). The report concluded that future studies should focus on developing more accurate exposure assessment methods and not to rely simply on self-reported exposure.

Seven recent studies (three case-control studies and four ecological studies) in different countries suggested a relationship between PD and pesticide exposure. An Indian case-control study included 175 PD patients and 350 non-PD controls matched for age and sex. The multivariate analysis indicated that pesticide exposure and rural living were among factors that were associated with an increased risk of PD (OR, 95%CI: 17.12, 4.97-58.84 and 4.05, 2.53-6.49 respectively). In a Norwegian case-control study, 212 PD patients and 175 non-PD age-sex matched controls were included. This study revealed that among many occupations, only agricultural work was related to PD (OR, 95%: 1.75, 1.03-3.0). A nested case-control study from the AHS studied 110 PD cases diagnosed by specialists in movement disorders and 358 controls. PD was associated with the use of a group of pesticides which impair mitochondrial function (OR, 95%:
1.7, 1.0-2.8 and for rotenone specifically: 2.5, 1.3-4.7) and with use of a group of pesticides which cause oxidative stress (OR, 95%: 2.0, 1.2-3.6) and for paraquat specifically (OR, 95%: 2.5, 1.4-4.7)91.

A Thai ecological study using the Thailand Registry of PD found a higher prevalence of PD among residents of the central plain valley where a large amount of pesticide is used compared to other regions237. Similar findings were found in a French ecological study where a higher prevalence of PD was found among those who live in farms specializing in fruits and permanent crops238. These farms usually use more insecticides per hectare compared to other type of farms in France. A Spanish ecological study described in Section 01.4.1 found that the PD prevalence rate per 100,000 population was significantly higher in the Andalusian health districts with higher environmental pesticide exposure compared to those of low exposure (prevalence rate was 259.5 and 199.3 respectively, P = <0.001)27. Ambient exposures to three pesticides (ziram, maneb, and paraquat) of 362 incident PD cases and 341 controls living in the Central Valley of California were estimated using a geographic information system model239. Exposure to the three pesticides and exposure to ziram and paraquat together were associated with an increased risk of PD (OR,95%: 3.09, 1.69-5.64 and 1.82, 1.03- 3.21). The risk estimates were greater for workplace exposure than for residential exposure and were higher when exposed in both locations.

On the other hand, one cohort study and one case control study did not support the association between pesticide exposure and PD. A Danish cohort study of 3124 male gardeners reported that the standardised hospitalisation rate ratios for PD among gardeners was similar to that among general population, however the number of PD cases was only 28240.

A Canadian case-control study found that although farming work was associated with PD (OR, 95%CI: 2.47, 1.18-5.15), pesticide exposure itself was not (OR, 95%CI: 0.83, 0.43-1.61)241. This study showed the effect of exposure assessment method on the association results since the association between PD and pesticide exposure was significant when exposure was estimated based on self-reports (OR, 95%CI: 1.76, 1.15-2.70). A recall bias was suggested (cases thought that PD was caused by chemicals more than controls).

In conclusion, the systematic review reports and following association studies give evidences of a positive relationship between pesticide exposure and PD. However, this
relationship needs further research especially regarding the type of pesticides and duration and level of exposure.

1.4.4 Dementia

Dementia is a general term which includes different impairments in memory and cognition processes and can be caused by different diseases\(^ {242,243} \). Alzheimer’s Disease (AD) is the main cause of dementia (the reason for two thirds of dementia cases) followed by vascular dementia\(^ {244} \). 24 million people were estimated to have dementia all over the world in 2001, while the prevalence of dementia in Western Europe in 2001 was estimated to be 4.9\% between people over 60 year-old\(^ {245} \). In England, dementia affects about 600,000 people and costs the National Health Service and social care services more than eight billion sterling pounds\(^ {246} \).

The diagnosis of AD has been heavily depended on memory impairment as the central deficit since the anterograde episodic memory is the most earliest and prominent neuropsychological impairment in AD patients and the typical clinical pattern progresses after that to other cognitive impairments\(^ {247} \). However, it has been found that AD does not start with memory problems in about a third of patients but with other behavioural and executive dysfunctions, and therefore generally those patients are likely to have been incorrectly diagnosed\(^ {248} \).

The impairment in the cognitive functions may be considered as an early predictor of dementia and may accompany other illnesses like PD\(^ {188} \). Cognitive dysfunctions have been linked with pesticide exposure in different studies\(^ {8,249,250} \). Researchers have used different batteries of neurophysiological and neurobehavioural tests to investigate the neurotoxicity of pesticide exposure; a sample of these batteries used by Stephens \textit{et al.}\(^ {8} \) is presented in Table 1-7. In this study that described in Section 01.4.1, the performance of the sheep farmers who used OP pesticides to dip sheep was statistically worse than the controls in three cognitive tests; Simple Reaction Time, Symbol-Digit Substitution and Syntactic Reasoning Test, while no differences in short-term memory and learning tests were found. When subjects were divided into five groups according to the estimated OP dose and considering the lowest dose-group as a reference, a significant effect of dose was found in the Syntactic Reasoning Test but no significant effects were observed in other tests.
Table 1-7: Neuropsychological test batteries used in the study of Stephens et al.

<table>
<thead>
<tr>
<th>Test Battery</th>
<th>Test Name</th>
<th>Cognitive domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurobehavioural Evaluation System</td>
<td>Simple Reaction Time</td>
<td>Visuo-motor speed, psycho-motor function, vigilance</td>
</tr>
<tr>
<td></td>
<td>Visual Digit Span</td>
<td>Auditory short term memory</td>
</tr>
<tr>
<td>Automated Cognitive Testing System</td>
<td>Syntactic Reasoning</td>
<td>Allocation of processing resources, linguistic ability</td>
</tr>
<tr>
<td></td>
<td>Category search</td>
<td>Part 1: Retrieval from semantic store (long-term memory) Part2: Storage and retrieval of information into and out of the semantic store (long-term memory), functioning of episodic/contextual memory</td>
</tr>
<tr>
<td></td>
<td>Spatial recognition</td>
<td>Visual short term memory</td>
</tr>
<tr>
<td></td>
<td>Serial Word Learning</td>
<td>Rate of learning (long-term memory)</td>
</tr>
</tbody>
</table>

In a French cohort study, 614 vineyard workers were followed-up for four years between 1997-1998 and 2001-2003. The workers were categorised based on their lifelong pesticide exposure into three groups, namely directly exposed, indirectly exposed and unexposed group. The risk of having a lower score (two points at least) on the Mini-Mental State Examination after 4-year follow up was higher in the exposed workers compared to the unexposed workers (OR, 95%CI: 2.15, 1.18-3.94)\(^{251}\).

Farahat et al.\(^{252}\) compared 52 male farm workers exposed to OP pesticides to unexposed controls and found that exposed subjects performed significantly lower than the controls in six neurobehavioural tests (Digit Symbol, Similarities, Letter Cancellation, Trailmaking part A and B, Benton Visual Retention, and Digit Span). There was an association between the duration of work with pesticides and lower performance on most of these tests after multiple comparisons were adjusted for. No significant correlation was found between serum AChE and neurobehavioural performance.

In the cross-sectional study of Fiedler et al.\(^{22}\), neuropsychological performance was compared between 57 male tree fruit farmers in New Jersey and their 42 matched controls. OP pesticide exposure was estimated based on a lifetime exposure matrix that depended on the area of each crop in each year treated with OP pesticides and was adjusted for type of activities and for the protective equipment. This study reported that tree fruit farmers who applied OP in their farms had only slower reaction time than their controls while no differences were found in other cognitive tests. The inconsistency in the affected cognitive tests in different studies was affirmed in the summary review of Alavanja et al.\(^{18}\).
With relation to dementia in general and AD in particular, several studies have linked these illnesses with pesticide exposure. A French prospective cohort study followed 1507 subjects aged 65 years or more for six years253. A positive association was found in male subjects between an increased risk of AD and occupational pesticide exposure estimated by a JEM (OR, 95%CI: 2.39, 1.02-5.63). This significant association was not found in women or with environmental pesticide exposure. Another cohort study was performed on 3084 dementia-free residents of Cache County in the USA who were 65 years or older254. Cognitive functions were assessed at the beginning of the study, and after 3, 7, and 10 years. During these 10 years, 500 subjects developed dementia including 344 who developed AD. Occupational pesticide exposure based on self-reported history was associated with dementia from all causes and AD specifically after adjustment for all different possible confounders (HR, 95%CI: 1.38, 1.09-1.76 and 1.42, 1.06–1.91 respectively). When pesticides were categorised according to their types, the association between AD and OP pesticides was slightly higher than the association with OCs (HR, 95%CI: 1.53, 1.05-2.23 and 1.49, 0.99–2.24 respectively).

Different case-control studies aiming to investigate risk factors of dementia have emerged from The Canadian Study of Health and Aging which was performed in ten Canadian provinces over 10,000 elderly people during the last decade of last century255. A population-based case-control study on 258 AD clinically diagnosed cases and 535 controls found that an increased risk of AD was associated with the occupational use of pesticides and fertilisers256. In 1997, another population-based case-control study which included 129 subjects clinically diagnosed as vascular dementia (VD) cases and 535 controls found a positive association between VD and occupational exposure to pesticides and herbicides (OR, 95%CI: 2.60, 1.30-5.23)257. 8623 subjects presumed free of dementia were followed over 5 years, and a nested prospective case-control study was used to study the risk factors of VD. The occupational use of pesticides and fertilisers was also found as a risk factor of VD in this study (OR, 95%CI: 2.05, 1.03-3.85)244.

A Spanish ecological study described in Section 01.4.1 compared the prevalence rates of AD in selected health districts27. AD prevalence rates were significantly higher in the districts with higher environmental pesticide exposure compared to those of low exposure (prevalence rate was 273.1 and 130.1 per 100,000 population respectively, P= <0.001).
On the other hand, a cohort study and two case-control studies have found no relationship between AD and pesticide exposure. A cohort study has followed 694 cognitively intact Canadian subjects for five years. 36 subjects had developed AD while the cognitive functions of the rest remained intact\textsuperscript{258}. An increased risk of AD was not associated with occupational exposure to pesticides and fertilisers (Relative Risk (RR), 95\%CI: 1.45, 0.57-3.68) while it was associated with the exposure to fumigants and defoliants (RR, 95\%CI: 4.35, 1.05-17.90) but only 3 cases was found among the exposed group.

A case control-study of 170 cases of AD and their 170 matched controls found no relationship between AD and any of the reported chemical and physical occupational exposures including exposure to OPs (RR, 95\%CI: 2.54, 0.41-27.06)\textsuperscript{259}. Another case-control study found also no relationship between AD and long-term environmental pesticide exposure based on residential and agricultural census histories (OR, 95\%CI: 0.97, 0.38-2.41)\textsuperscript{260}.

The quality of epidemiological studies of occupational risk factors of AD published up to June 2003 was reviewed by Santibanez \textit{et al.}\textsuperscript{261}. This review concluded that the association between AD and occupational exposure to pesticides is more consistent than the association with other occupational exposures. However, bias opportunities are not limited. This bias may come out from the use of surrogate informants (\textit{i.e.} obtaining personal histories from the family or from a close friend), from disease misdiagnosis due to many differential diagnosis for AD, from exposure misclassification, and from ignoring possible confounders.

Finally it is worth taking into consideration that metrifonate (an OP cholinesterase inhibitor) has been tried as a treatment for the cognitive symptoms of AD since the loss of cholinergic neurons is the basic neurochemical defect in this disease\textsuperscript{262}. This point is important because it means that the OP exposure may play a protective role in dementia illness.

\subsection*{1.4.5 Limitations of previous studies}

Although many positive associations between long-term pesticide exposure and neuropsychiatric effects have been discovered in previous studies, these associations are still indefinite. Different reasons have been suggested to be behind these unconfirmed results, mainly misclassification of both long-term exposure and health outcomes and
the diversity of study designs used in this field, which explains why the assessment of neuropsychiatric effects was used to illustrate the difficulties of the health outcomes studies in farming communities exposed to pesticides. The relatively weak association between pesticide exposure and health effects (if they exist) can be also one of the difficulties since it needs studies of high statistical power to detect any association. Furthermore, in general, studies which searched for pesticide effects categorized the pesticides in classes or groups (insecticides, herbicides, etc. or OPs, carbamates, etc.) and did not deal with every pesticide individually. The combination of different classes of pesticides in one exposure estimation although they might vary in their effects can be one of the reasons of inconsistencies of the epidemiological studies.

Another possible reason of inconsistencies in the previous studies, particularly for depression, is the insufficient adjustment for potential confounders. Farmers who are occupationally exposed to pesticides are usually exposed to other farming-related, relevant factors such as social conditions and ingestion of well water as well as the additional chemicals that are included in many commercial pesticides and fertilisers (e.g. solvents). Such factors have, of themselves, been reported to be associated with neuropsychiatric illnesses but they are not always easy to quantify and adjust for in the relevant models.

However, the difficulty of retrospective assessment of long-term exposure has been suggested to be potentially the main reason behind the uncertainty of disease risks associated with pesticide exposure. Undocumented working conditions and the poor self-recall of pesticide exposure over extended periods especially with the changes in the pesticides and application methods are examples of the reasons for the difficulty of long-term exposure assessment.

Different methodologies have been used to estimate long-term pesticide exposure in the studies of pesticide health effects. Some of these studies have used simple surrogates like residential pesticide exposure or ever/never working with pesticides whereas other studies have developed their own more sophisticated models. The difference in exposure assessment methods is sometimes due to the differences in study types. If the assessment method leads to non-differential misclassification of pesticide exposure, the study power will be reduced and the estimates of relative risks will be biased towards the null.
Accordingly, to increase our understanding of any linkage between occupational long-term low-level pesticide exposure and any possible health effects in human population, the development of better techniques to assess past pesticide exposure is needed. These techniques should also be validated since even developed techniques may result in substantial exposure misclassification for many pesticides\textsuperscript{138}. 
Chapter 2: Description of studied populations

This PhD study has used mainly two previous studies to achieve its specific objectives (Section 1.2). These two studies are the Study of Health in Agricultural Work (SHAW)\textsuperscript{264,265} and the Health and Sheep Dipping Survey (HSDS)\textsuperscript{58}. The occupational practices of the farmers of the SHAW study related to pesticide exposure and their occupational pesticide exposure estimates will be described in Chapter 6 (objective 4). The SHAW study was also used to validate self-reported occupational exposures among farmers (objective 5 in Chapter 7) and to apply the new models to examine the association between neuropsychiatric ill-health and long-term pesticide exposure in different farming sectors (objective 6 in Chapter 8). The HSDS study was only used to evaluate the new developed exposure model of sheep dipping (objective 2 in Chapter 2). All the work described in this chapter for both studies had been already performed before the beginning of this PhD study, and this PhD study has used their data as will be described in the relevant chapters.

2.1 The Study of Health in Agricultural Work (SHAW)

The SHAW Study was a project started in 2002 to study whether chronic low dose exposure to OP pesticides was associated with ill-health in farmers. The SHAW study was undertaken by the Centre for Occupational and Environmental Health, University of Manchester and funded by the Department of Health and the Department of Environment, Food and Rural Affairs (Defra). This project was a historically prospective cohort study of farmers who were in farm work in the UK in 1970s and was carried out in two main phases.

The aims of the SHAW study were 1) to determine the cumulative incidence of depression, neuropathy, Parkinsonism and dementia in farmers; 2) to examine whether there was an excess of these illnesses among farmers who had been exposed to OPs particularly those who handled the concentrate of sheep dips; 3) to estimate the size of the excess when farmers with a history of pesticide poisoning were excluded; and 4) to examine whether there was an association between the investigated illnesses and OP exposure.
2.1.1 Description of Phase 1

In phase 1, a cohort of approximately 19,000 people who were farmers in the 1970s was identified through contemporaneous records held by the National Farmers Union, Sheep and Cattle Associations and through Shepherd’s Guides. Each person in the database was sent a letter describing the study, an information sheet, a consent form, and a health and work history questionnaire. Non-responders were sent a reminder letter and a proportion of those who still did not respond were contacted by telephone to ask if they wished to participate. If they declined, they were asked to answer a short telephone questionnaire. 7691 Responses were obtained but only 1380 completed the screening questionnaire (17.9%), whereas 368 responded to the telephone questionnaire (4.8%), 4635 had died (60.3%), 1102 refused (14.3%) and 206 were ineligible (2.7%). No response was obtained from 11,267 people of which 5870 (51.4%) were known to have moved away from the registered address.

2.1.1.1 Definitions of the health effects

The phase 1 health and work history questionnaire (Appendix 1) was developed in part from questionnaires used in previously published studies. The health section included questions on general health status, neuropathy, Parkinsonism, depression and dementia in addition to questions on seeking medical advice (e.g. for pesticide poisoning) and current treatments. The life style section included questions on smoking and drinking habits.

The answers of the screening questions were used to identify potential cases of depression, neuropathy, Parkinsonism, and dementia according to published or a priori algorithms described in (Table 2-1). Farmers who met the criteria of any of the four illnesses were considered as screen-positive farmers of the relevant illness, and the rest (i.e. the screen-negatives) were considered as controls.

2.1.1.2 Exposure assessment

The working history section included questions on the current employment status, history of working in different farming sectors in addition to brief questions on exposures. Farmers were asked about having sheep or cattle in every year from 1946 to 2003. The same question was also asked for four groups of agricultural crops, namely combinable crops, glasshouse production, outdoor vegetables or potatoes, and top and soft fruits. There were also questions about whether they had ever been involved in
applying pesticides to livestock or crops (e.g. dipping sheep), involved in handling the concentrate for such applications, or involved in activities that might have exposed them to pesticides (e.g. shearing sheep or slaughtering livestock). Finally farmers were asked to what extent their farms were affected by Bovine Spongiform Encephalopathy (BSE) or Foot and Mouth Disease (FMD) in 2001.

### Table 2-1: SHAW Phase 1 ill-health definitions

<table>
<thead>
<tr>
<th>Ill-health</th>
<th>Definition</th>
<th>Based on</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Farmers were considered as screen-positive if: Their answer to A3.1 or 3.2 and four or more of 3.1-3.10 of the Health and Work Questionnaire (with the exception of 3.8 and 3.9 which a response to either was acceptable) were at least “More than half the days”. Question 3.10 was counted if any positive reply was present. Their cumulative score to A3.1-A3.10 was ≥ 10 when the answers were scored as follows: half the days or less = 1, more than half the days = 2, every day or nearly every day = 3 Their answer to A6.3 was positive.</td>
<td>Spitzer et al.270</td>
</tr>
<tr>
<td>Dementia</td>
<td>Farmers were considered as screen-positive if their answer to A4.1, 4.9 or 4.10 was positive and their cumulative score of answers to A4.1-4.11 was ≥ 4 if each positive answer was scored as 1. Values of 2 “don’t know” and 9 “missing” were recoded as 0.</td>
<td>Mundt et al.266</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Farmers were considered as screen-positive if their answer to one or more of A2.2, 2.4, 2.11, 2.13, 2.14, 2.16 and 2.18 was “bothered a lot”.</td>
<td>Clinical judgement by one of the SHAW team</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Farmers were considered as screen-positive if their answer to one or more of A2.7, 2.8 and 2.9 was “bothered a lot”.</td>
<td>Chan et al.269</td>
</tr>
</tbody>
</table>

#### 2.1.1.3 Demographics and farming variables

1380 completed the screening questionnaire of phase 1 of the SHAW study but only those who were 13 or over in 1970 (n=1338) were included in the analysis. Table 2-2 shows the demographics of the respondent population. The mean age of farmers was 69.6 years and the majority of them were men (95%). About a half of the farmers were from the North and North West England (47.2%) and 17.6% were from Scotland. About half of the farmers drank alcohol more than once a week and only 15.7% were current smokers but 37.1% had ever smoked. 70.9% of the farmers had left school before the age of 16. About 64% of the farmers were still working whereas 32% had retired and 3.6% left work due to ill-health. Approximately 70% of the farmers worked on family farms. Less than one third of the farmers had been affected by BSE whereas around half of them had been affected by FMD in 2001.
Table 2-2: Demographics and farming variables of SHAW phase 1 population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>N</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (± SD)</td>
<td>1338</td>
<td>69.6±9.7</td>
</tr>
<tr>
<td>Sex</td>
<td>Male/female (% male)</td>
<td>1338</td>
<td>1271/67 (95.0)</td>
</tr>
<tr>
<td>Region</td>
<td>Scotland (%)</td>
<td>1338</td>
<td>235 (17.6)</td>
</tr>
<tr>
<td></td>
<td>North/North West (%)</td>
<td></td>
<td>529 (47.2)</td>
</tr>
<tr>
<td></td>
<td>Midlands/East Anglia (%)</td>
<td></td>
<td>165 (12.3)</td>
</tr>
<tr>
<td></td>
<td>Wales (%)</td>
<td></td>
<td>103 (7.7)</td>
</tr>
<tr>
<td></td>
<td>South West (%)</td>
<td></td>
<td>186 (13.9)</td>
</tr>
<tr>
<td></td>
<td>South East (%)</td>
<td></td>
<td>120 (9.0)</td>
</tr>
<tr>
<td>Drinker</td>
<td>Number of days per week, &gt;1/&lt;1 (% &gt;1)</td>
<td>1324</td>
<td>698/626 (52.2)</td>
</tr>
<tr>
<td>Smoker</td>
<td>Ever /Never (% ever)</td>
<td>1298</td>
<td>497/801 (37.1)</td>
</tr>
<tr>
<td></td>
<td>Current /Non-smoker (% current)</td>
<td>496</td>
<td>78/418 (15.7)</td>
</tr>
<tr>
<td>Schooling</td>
<td>Leaving age &lt;16/&gt;16 (% &lt;16)</td>
<td>1319</td>
<td>948/371 (70.9)</td>
</tr>
<tr>
<td>Working</td>
<td>Currently/Retired/ Not working due to ill-health (% ill-health)</td>
<td>1140</td>
<td>727/365/48 (3.6)</td>
</tr>
<tr>
<td></td>
<td>On family farm/other (% family farm)</td>
<td>1127</td>
<td>925/202 (69.1)</td>
</tr>
<tr>
<td>BSE\textsuperscript{a}</td>
<td>Affected farm: yes/no (%yes)</td>
<td>1269</td>
<td>382/887 (28.6)</td>
</tr>
<tr>
<td></td>
<td>Affected livelihood slightly/moderately/severely (% severely)</td>
<td>365</td>
<td>203/79/83 (22.7)</td>
</tr>
<tr>
<td>FMD\textsuperscript{b}</td>
<td>Affected farm: yes/no (%yes)</td>
<td>1300</td>
<td>632/668 (47.2)</td>
</tr>
<tr>
<td></td>
<td>Affected livelihood slightly/moderately/severely (% severely)</td>
<td>617</td>
<td>118/192/307 (49.8)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} BSE = bovine spongiform encephalopathy, \textsuperscript{b} FMD = foot and mouth in 2001

### 2.1.2 Description of Phase 2

Phase 2 was a nested case-control study aiming to determine whether screen-positive farmers of depression, neuropathy, Parkinsonism, and dementia have different exposure to pesticides (in general and OP specifically) comparing to the screen-negative farmers\textsuperscript{264}. All cohort members, aged between 54 and 74, screen-positive and screen-negative farmers in phase 1 were sent a letter describing the study, an information sheet and a consent form. 852 farmers from phase 1 were eligible for the second phase of the study. A response was obtained from 746 (87.6\%) farmers (or relatives) of which 412 (48.4\% of total) agreed to participate, 316 (37.1\% of total) refused to participate and 18 had already died. Due to lack of resources it was not possible to interview all the farmers who agreed to participate. Hence, only 234 farmers who lived in the area contained approximately between the England/Scotland border in the North and the M4 corridor in the South were interviewed to complete more comprehensive questionnaires about their occupational histories and their health status.

#### 2.1.2.1 Definitions of the health effects

A general health and lifestyle questionnaire was used to obtain detailed information on the health of the farmers. Farmers who were identified as screen-positive in phase 1 and a random selection of “screen-negative” farmers were interviewed also with specific questionnaires appropriate for the putative ill-health under investigation, and also
physical examinations for investigations on neuropathy and Parkinsonism were carried out. Phase 2 ill-health definitions were based upon previously published scoring schemes, approaches or clinical judgment.

Screen-positive cases of depression and screen-negatives were administered the Clinical Interview Schedule (CIS) and cases were identified if the CIS score was more than 10. Screen-positive cases of neuropathy and screen-negatives were administered a neuropathy questionnaire based on that previously used in another sheep dippers study. The cases were identified either by clinical review of the neuropathy examination or by a previously published scoring scheme. Screen-positive cases of Parkinsonism and screen-negatives were administered the activities of daily living scale. The cases were identified using a previously published scheme which used the results of the physical examination.

Screen-positive cases of dementia and screen-negatives were administered the Cambridge Cognitive Examination (CAMCOG) and the cases were identified by using a previously used cut off (CAMCOG < 79) or by the difference between an adjusted and unadjusted CAMCOG. This difference was calculated using a previously published approach in which a regression equation was developed from phase 2 screen-negative farmers to predict CAMCOG scores from collected demographic information including age and general knowledge. The final model included age and general knowledge but not sex, matrimonial status, social class, age left school, live alone, being a farm owner or depression score from phase 1. Then, the difference between predicted (adjusted) CAMCOG scores and unadjusted scores was determined.

A separate section to assess memory function was included in CAMCOG, and those farmers who had not been requested to complete the full CAMCOG, were administered the memory section of this instrument to allow for an assessment of their memory function. In this section every correct answer was given one mark and the total marks (maximum 27) presented the memory score. The questions examined farmer’s retrieval of remote information (e.g. the name of the leader of the Germans in the Second World War, 6 marks), retrieval of recent information (e.g. the name of the present Queen, 4 marks), ability to incidental learning (recall and recognition of pictures, 12 marks) and ability to intentional learning (recall address, 5 marks).
2.1.2.2 Exposure assessment

A separate questionnaire was designed for occupational pesticide exposure (Appendix 2). All potential sources of pesticide exposure in different farming sectors were addressed in that questionnaire with a focus on sheep dipping practice. The questionnaire was divided into seven parts to obtain information on life events, sheep, cattle, other livestock, crops and grains, other pesticide use, and general farm work.

The questions about treating animals (Part 2-4) focused on flock/herd size, type of treatment, number of treated animals, number of treating days, type of pesticide used for treating livestock and the use of PPE. However, in the section of sheep (Part 2) there was a special focus on sheep dipping treatment and data on that treatment was collected in detail (e.g. description of the dipping bath, the dipper’s task, and the involvement in post dipping activities).

In the crops and grains section (Part 5) the main questions focused on the type of crops, the area of crops, the type of pesticides, the type of applications and the length of application time, whereas questions of Part 6 were about applying pesticides in or around buildings on the farm or for any other farming job. The final section (Part 7) asked about using different farming equipment (e.g. chainsaws and tractors).

To enhance the memory of the farmer, a key life events calendar and different cards of pesticide and activity lists were used. In the calendar, key life events in the history of the farmer were identified and occupational histories were attached to these events. The cards of pesticides and farming activities contained the main pesticides products used in different farming sectors and farming activities related to pesticide exposure extracted from a detailed literature review.

2.1.2.3 Demographics and farming variables

234 farmers were interviewed in phase 2 of the SHAW study. Table 2-3 shows the demographics of the interviewed population. The mean age of farmers was 66.4 years and the majority of them were men (95.7%). Most farmers were from the North and North West England (65.8%) while only one and three farmers were from Scotland and South West England respectively. 38.6% of the farmers drunk alcohol more than once a week and 14.1% were current smokers but 36.3% had ever smoked. About 70% of the farmers had left school before the age of 16. About 64% of the farmers were still working whereas 29.7% had retired and 5.2% left work due to ill-health. Approximately
80% of the farmers worked on family farms. About a third of the farmers had been affected by BSE whereas more than half of them had been affected by FMD in 2001.

Table 2-3: Demographics and farming variables of SHAW phase 2 population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>N</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (± SD)</td>
<td>234</td>
<td>66.4±5.5</td>
</tr>
<tr>
<td>Sex</td>
<td>Male/female (% male)</td>
<td>234</td>
<td>224/10 (95.7)</td>
</tr>
<tr>
<td>Region</td>
<td>Scotland (%)</td>
<td>234</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td></td>
<td>North/North West (%)</td>
<td></td>
<td>154 (65.8)</td>
</tr>
<tr>
<td></td>
<td>Midlands/East Anglia (%)</td>
<td></td>
<td>43 (18.4)</td>
</tr>
<tr>
<td></td>
<td>Wales (%)</td>
<td></td>
<td>17 (7.3)</td>
</tr>
<tr>
<td></td>
<td>South West (%)</td>
<td></td>
<td>3 (1.3)</td>
</tr>
<tr>
<td></td>
<td>South East (%)</td>
<td></td>
<td>16 (6.8)</td>
</tr>
<tr>
<td>Drinker</td>
<td>Number of days per week, &gt;1/&lt;1 (%&gt;1)</td>
<td>232</td>
<td>91/143 (38.6)</td>
</tr>
<tr>
<td>Smoker</td>
<td>Ever /Never (% ever)</td>
<td>234</td>
<td>85/149 (36.3)</td>
</tr>
<tr>
<td></td>
<td>Current /Non-smoker (% current)</td>
<td>85</td>
<td>12/73 (14.1)</td>
</tr>
<tr>
<td>Schooling</td>
<td>Leaving age &lt;16/&gt;16 (% &lt;16)</td>
<td>230</td>
<td>162/70 (69.8)</td>
</tr>
<tr>
<td>Working</td>
<td>Currently/Retired/ Not working due to ill-health (% ill-health)</td>
<td>231</td>
<td>150/69/12 (5.2)</td>
</tr>
<tr>
<td></td>
<td>On family farm/other (% family farm)</td>
<td>194</td>
<td>155/39 (79.9)</td>
</tr>
<tr>
<td>BSEa</td>
<td>Affected farm: yes/no (%yes)</td>
<td>223</td>
<td>70/153 (31.4)</td>
</tr>
<tr>
<td></td>
<td>Affected livelihood slightly/moderately/severely (% severely)</td>
<td>67</td>
<td>41/14/12 (17.9)</td>
</tr>
<tr>
<td>FMDb</td>
<td>Affected farm: yes/no (%yes)</td>
<td>232</td>
<td>130/102 (56.0)</td>
</tr>
<tr>
<td></td>
<td>Affected livelihood slightly/moderately/severely (% severely)</td>
<td>128</td>
<td>20/34/74 (57.8)</td>
</tr>
</tbody>
</table>

*a BSE = bovine spongiform encephalopathy, b FMD = foot and mouth in 2001

2.2 The Health and Sheep Dipping Survey (HSDS)

The HSDS was a prospective cohort study to examine whether sheep treatment result in acute health effects or not. One of the main effects investigated was the so called “dipper’s flu” which is a flu-like illness that reportedly occurs after the treatment of sheep by dipping them in OP dips.

781 sheep farmers who intended to treat their sheep in 2005 and 2006 were recruited through the National Farmers’ Union, Shepherd’s Guide and British Wool Marketing Board (response rate was 9.3%). Sheep farmers were visited and interviewed by a study nurse three times; before treatment, as soon as possible after the start of treatment, and then about two or three weeks after the second visit. All recruited farmers were interviewed in 2005 and 2006.

In the first visit, the nurse collected data on the occurrence of 83 symptoms using a structured health questionnaire. Information about occupational history and health status and baseline blood and urine samples were also collected. 20% (156/781) of the interviewed farmers had a second visit as soon as possible after treatment and 19%
(149/781) had a third visit 2-3 weeks after treatment. Blood and urine samples were obtained at each subsequent visit to measure biological markers of different exposures, particularly to pesticides (OP and SP urinary metabolites) and infectious agents, as well as routine clinical biochemistry parameters.

Farmers were requested to complete a symptom diary for 7 days following the start of treatment and to record their temperature. They were asked also to give detailed information about sheep treatment such as treatment methods, type of pesticides used, handling the concentrate, the number of sheep treated in each day and the farmer’s task during each day. Farmers who dipped their sheep were requested to collect a sample from the dip bath twice, one at the start and one at the end of the dipping session.

Farmers used different methods to treat their sheep. Pour-on treatment was the most common method (50%) followed by dipping (35%). They used also different products with SP being the most common product (31%), followed by OPs (diazinon) (28%) and triazines (19%). More than 80% of the urine samples collected in the second visit contained SP and/or OP metabolites, while only 5% of farmers had a significant fall in AChE activity (>20.8%) between the two blood samples at visit one and two. By analysing blood samples of visit two, little evidence of exposure to infectious pathogens was found. Levels of endotoxin in the dip bath increased in most samples after the end of dipping session.

During the first week after sheep treatment, the number of symptoms was higher in the first two days. 7.3% of farmers felt ill on the day of treatment while only 3% of farmers felt ill in the following three days. However, there was no evidence that symptoms reporting increased after treatment. Only few farmers reported a temperature over 37.7 while general aches, joint stiffness, tiredness, and waking up tired were the most common complaints at all visits. Less than 2% of farmers were identified as dipper’s flu cases. Older age and holding a certificate of competence for handling pesticides were significantly associated with a decreased risk of reporting any symptom.
Chapter 3: A new conceptual model for estimating pesticide exposure through sheep dipping

3.1 Introduction

To study the association between pesticide exposure and health effects among sheep dippers, different methods have been used to assess exposure. For example, the number of dipped sheep has been used as a surrogate for exposure in sheep dipping.\(^8,278\)

Depending on surrogates, however, to estimate the exposure from different sources and ignoring many important modifying factors will lead to exposure misclassification.\(^127,141\)

As a result of recognising the importance of pesticide concentrate handling in pesticide exposure, Buchanan et al.\(^99\) in 1999 developed an empirical model in which exposure to the concentrate and to the diluted pesticide were combined by using the frequency of handling the concentrate as a surrogate for the concentrate exposure and the task of the dipper during the dipping session to represent the exposure to the diluted pesticide.

Cherrie and Robertson\(^134\) developed an exposure metric to assess any chemical exposure through dermal routes by incorporating three factors together, namely the concentration of the chemical in the skin contamination layer (\(C_{sk}\)), the duration of exposure (\(t\)) and the area of skin contaminated (\(S_{sk}\)). Dermal exposure (\(E_{sk}\)) was calculated by this metric:

\[ E_{sk} = C_{sk} \times t \times S_{sk} \]  

Tahmaz et al.\(^7\) used this metric to develop an exposure model specifically for sheep dipping. The use of this dermal metric was justified by the fact that pesticide exposure is essentially dermal; though the developed model also included a part to estimate inhalation exposure which was a constant expressed in the same units as the dermal exposure (\(m^2 \cdot \text{days}\)). The same metric was used by the SHAPE study to establish models for pesticide exposure in different farming sectors with the most developed one being that for the sheep sector.\(^29\) In this model the inhalation route was completely ignored.

Although the dermal route is considered to be the most important route of pesticide exposure during sheep dipping,\(^162,163\) ignoring exposure through ingestion and inhalation as done in the previous models,\(^7,12,29,99\) might lead to exposure misclassification. Development of an aggregate exposure model which incorporates all
exposure sources, exposure routes and modifying factors to estimate the intensity of pesticide exposure has been always a challenge.279

A conceptual model is a framework designed to represent the real human exposure scenarios and processes and is usually illustrated by a comprehensive diagram280. A conceptual model defines the physical, chemical and personal behaviour information which are necessary to describe realistic exposure scenarios. Building this model needs data on the utilised product, strength of the exposure sources, concentrations of the product in different environments, modifying factors and quantitative associations between measured or estimated exposure and different modifying factors280.

Although a conceptual model which takes into account all sources of exposure and deals with all modifying factors would be impractical particularly in retrospective studies, the development of such model would allow identification of the main determinants of exposure intensity and make the development of any further reduced model with only the main factors that drive exposure more systematic. Also, even though in practice usually not all factors can be incorporated, or equally well estimated, the resulting model will also provide systematic insight in likely sources of bias and misclassification.

This chapter aims to develop a conceptual model which describes pesticide exposure during sheep dipping. This conceptual model will be used to derive an exposure algorithm that is able to assess semi-quantitatively pesticide exposure in sheep dipping and so be used in epidemiological studies.

3.2 An explorative farm visit to monitor sheep dipping process

To be fully aware of sheep dipping practices and processes, in addition to a comprehensive literature review, an explorative farm visit to monitor a sheep dipping session was undertaken. In June 2010, seven farmers from those who took part in phase 2 of the SHAW study and whose farms were relatively close to Manchester were contacted again. A letter was sent to them asking for their permission to allow two of the study team to observe sheep dipping sessions at their farm (Appendix 3). Three farmers agreed and would tell us when they plan to dip their sheep. The other four did not respond. However, two of respondents apologised later saying that they had decided to postpone the dipping for many months because there was no need to perform dipping at that time. The remaining farmer informed us on 2nd September that he was planning
to perform the dipping on the following day and two of the study team went to his farm on the following day and attended the dipping session.

The farm was family run located in South Yorkshire. Two persons performed the dipping, the owner of the farm and his son. The father took the job of the plunger whilst his son worked as a chucker and a helper.

The concentrate was only handled by the father (plunger) who used water soluble sachets that contained concentrate. The farmer opened the outside cover of the sachets carefully and the inner package remained intact until dropped into water (Figure 3-1, A). The farmer dropped the sachets into the bath and mixed them with the water in the bath using a long wooded stick (Figure 3-1, B). The concentrate sachets (Coopers Ectoforce Sheep Dip) contained 60% w/w Diazinon. The father handled the concentrate three times; one at the beginning of the session (10 sachets) and two times as a replenishment after about every 50 sheep (2 sachets each time).

The plunger, the father, wore Wellington boots, waterproof leggings, waterproof coat, waterproof apron, and long PVC gloves. During handling the concentrate he also wore a face shield; however he said that he usually did not wear it (Figure 3-1, A). The son (chucker and helper) wore only Wellington boots and waterproof leggings (Figure 3-1,B).

Figure 3-1: Handling the concentrate
The plunger (A) opened the outside cover of the sachets carefully and dropped the inner package into water and then (B) he mixed the pesticide concentrate with the water using a long wood stick.
The bath was circular without an island and there was a curtain around the bath entrance (Figure 3-2, A). The bath had a short slope at the entrance but the chucker pushed the majority of the sheep into the bath and occasionally he threw the sheep in. Usually there were three sheep in the bath at the same time. The bath had a few steps at the exit behind a remote gate (Figure 3-2, B). The chucker was responsible for opening that gate by a rope while the plunger used a metal tool to submerge the sheep, to manoeuvre them round the bath, and to push them out of the bath (Figure 3-2, A). The draining pen was about 4 meters away from the bath and did not have a screen around it. Once out of the bath, the sheep shook their wool which resulted in a fine spray in and around the draining pen. The supply of the clean water came from a pipe connected to an open big container located near the bath.

**Figure 3-2: Dipping bath**

(A) The bath was circular with a splash guard around the entrance, (B) The bath had a few steps at the exit behind a remote gate
150 sheep were dipped in the session which lasted for two hours from about 9:30-11:00 am. At the end of the session the lower part of the leggings of both dippers was soaked with the diluted dip, whilst the splashes reached also the upper part of the leggings and other parts of the plunger clothes (Figure 3-3). The farmer washed his face by clean water once after a major splash. During the session the weather was still and dry. No post dipping activities were performed since the farmer was planning to continue dipping in the afternoon of the same day.

![Figure 3-3: Clothes of the dippers at the end of the session](image)

(A) The chucker, (B) The plunger

**3.3 Conceptual model development**

To build the conceptual model of pesticide exposure in sheep dipping four constituents were defined and identified; sources, routes, transport processes and modifying factors. An assessment algorithm was then developed and the effects of all its components on the exposure were estimated (Figure 3-4).

In this thesis, any activity that leads the subject to be exposed to the pesticide is considered as a **source. Routes** of exposure are the ways in which the pesticide enters the body. In other words, exposure routes are the different receptors in the body (e.g. skin, digestive system, and respiratory system). Pesticides transfer from the source to the receptor in different **processes**, and the relative contributions of these different processes to total exposure may vary between the sources and the exposure routes. A **modifying factor** has been defined as any factor that changes the amount of pesticide
reaching the receptor. These factors could be activities, environmental or behavioural factors \((i.e.\) personal hygiene). The difference between an activity considered as a source and an activity considered as a modifying factor is that the former produces the pesticide while the latter only changes the amount of the pesticide received by the receptor. Although the difference between these two types of activities is artificial, it was found beneficial to make the assessment of their effects on the total exposure more systematic. This model intended to study the exposure \((i.e.\) the amount of pesticide that is ready to absorb into the body\(^{94}\)) therefore all factors related to uptake \((i.e.\) the amount of pesticide actually absorbed into the body\(^{94}\)) such as dermal wounds and nature of the skin will not be discussed.

![Figure 3-4: Development of the conceptual model and the assessment algorithm](image)

To determine all the components \((i.e.\) sources, routes, \textit{etc.}) of pesticide exposure in sheep dipping, previous studies on this process were reviewed and the performed explorative farm visit was used. The developed conceptual model is presented graphically in Figure 3-5 whilst the following sections describe in detail each component. Throughout the following sections, if no scientific literature was available to describe the components of the conceptual model, a personal judgement depending on the explorative farm visit and the common knowledge was relied on.
Figure 3-5: Conceptual model for pesticide exposure from each source in sheep dipping including routes, transport processes and modifying factors

Transport processes were determined as described in Section 3.6 according to previous conceptual models for each route (Schneider’s model for dermal, Cherrie’s model for ingestion, and Tielemans’ model for inhalation.)
3.4 Sources of pesticide exposure in sheep dipping

Activities reported in the literature which may lead to pesticide exposure during sheep dipping were categorized into four main activities; handling the dip concentrate, dipping sheep in the diluted pesticide, handling sheep after dipping and the disposal of sheep dip. Incidental exposure (i.e. fall in the bath or concentrate spillage) was added as a fifth source since it would expose the dipper to an additional exposure.

3.4.1 Handling the concentrate

Dippers can handle the concentrate on many occasions with the minority of these occasions happening during the preparation of the bath and the majority when the farmer adds the concentrate to the bath after a specific number of sheep. Usually it is only one person who handles the concentrate during the dipping session.

Studies have shown that handling the concentrate is the major source of pesticide exposure in sheep dipping. However, the recent use of concentrate sachets might decrease the importance of this source since, as noticed in the farm visit, the probability of contacting the concentrate was very low if the sachets were used properly. Exposure from handling the concentrate occurs essentially through the dermal route however it may occur through the digestive and respiratory tracts.

3.4.2 Dipping sheep in diluted pesticide

Splashes of sheep dip may occur when sheep enter the bath, are immersed under the surface or when the sheep shake themselves after they get out of the bath. Plungers, who submerge the sheep under the surface of the water, may also be exposed to sheep dip if they use their hands or feet to submerge the sheep. Splashes from the dipping bath and immersing part of the body in the bath are the second major source of pesticide exposure. The aerosols originated from this activity can also lead to exposure through inhalation or digestion.

3.4.3 Handling dipped sheep

Handling contaminated surfaces can happen in all main activities in sheep dipping (i.e. handling the concentrate, dipping sheep in the bath, etc.) and therefore this secondary source of exposure has been included in the modifying factors of exposures from the main activities (e.g. size of container in handling the concentrate, and the use of wooden tool to submerge the sheep). Although handling dipped sheep can be considered as an
example of handling contaminated surfaces, it has been previously considered as a standalone source of exposure\textsuperscript{7,29} and it has been considered likewise in this new conceptual model. This is done based on the fact that this activity is separate from other activities and farmers who dip sheep might not be involved in handling them after treatment. Moreover, handling dipped sheep is more recognisable by farmers than other events of handling contaminated surfaces and it may lead to exposure through ingestion and inhalation not only through dermal route.

Sheep fleece may retain pesticides for many days after dipping and therefore farmers could be exposed to pesticides if they handle sheep after they have been dipped but before the pesticide disappears from fleece\textsuperscript{49}. Although this exposure is most likely dermal through the hands, aerosols originated when sheep shake themselves could, in theory, lead to exposure through inhalation or digestion. Due to the small area of skin exposed (mainly the hands) the exposure from handling dipped sheep has shown to be limited comparing to the exposure during the dipping itself; however it should not be neglected\textsuperscript{13}.

### 3.4.4 Disposal of sheep dip

Farmers usually get rid of sheep dip when they end their dipping sessions. A minority of dippers use a drain to soak away the dip, whereas most of them use manual or mechanical methods to dispose of the dip\textsuperscript{12,281}. This process may lead to an additional exposure to pesticides mainly through the dermal route.

### 3.4.5 Incidental exposure

Incidental exposure could happen if the farmer enters the dipping bath either intentionally (e.g. to rescue a sheep) or unintentionally (\textit{i.e.} fall in the bath) or if the dipper spills the concentrate on any part of his body during handling it. If playing with sheep dip by splashing each other is ignored since it is unlikely, other forms of incidental exposure are highly unlikely.

### 3.5 Routes of occupational exposure to pesticide in sheep dipping

The importance of each route of pesticide exposure in farming activities varies from one pesticide to another and will vary according to the application method. Although in sheep dipping the dermal route is considered the most important one, ingestion and inhalation routes have also been included in this conceptual model.
Studies have shown that dermal exposure is the predominant route of pesticide exposure\textsuperscript{162,163} and almost all sheep dipping studies have considered the dermal route as the most important route and exposure models have been built solely for this route\textsuperscript{7,12,29,99}. Exposure through this route comes from all sources although the most important one is considered handling the concentrate. Hands are usually the most contaminated part of the body when the farmer handles the concentrate while legs and torso are usually contaminated during dipping the sheep in the bath and from other sources\textsuperscript{12,104}.

Although the major route of pesticide exposure in the general population is ingestion\textsuperscript{167}, many studies have ignored this route when assigning occupational exposure to farm workers or sheep dippers\textsuperscript{7,99,154}. Estimating exposure through this route is problematic, and no established methodologies to assess this exposure are available\textsuperscript{3}. During sheep dipping pesticides may enter the mouth directly by splashing or more likely indirectly through contaminated surfaces especially the hands and the gloves. Some behaviour like smoking before washing hands and nail biting might increase exposure through ingestion since they increase the chance of ingesting pesticides on the contaminated hands\textsuperscript{169}. Gorman \textit{et al.} have developed a conceptual model for inadvertent ingestion exposure following contact between contaminated hands or objects and worker’s mouth\textsuperscript{168}. This model has integrated two previously published models; a conceptual model for inadvertent ingestion exposure\textsuperscript{169} and a conceptual model for dermal exposure\textsuperscript{170} to demonstrate the relationship between dermal and ingestion exposure.

Studies have shown that respiratory exposure to pesticides constitutes not more than 1\% of the total exposure in farming activities\textsuperscript{151,163}. Niven \textit{et al.} in their study on sheep dipping found that the airborne diazinon concentrations were below the UK Occupational Exposure Standard of 0.1 mg/m\textsuperscript{3} suggesting that inhalation was not a significant route of exposure during sheep dipping\textsuperscript{12}. Nevertheless, Tahmaz \textit{et al.}\textsuperscript{7} included in their model an estimate of inhalation of sheep dip aerosol but as a constant expressed in the same units of the dermal exposure (m\textsuperscript{2}.days). In this conceptual model, the inhalation route will be taken into account with all sources especially with handling the concentrate as the farmer may by exposed to its vapours. It will, however, be neglected in the incidental exposure because the period of this exposure is relatively short.
3.6 Pesticide transport processes

Pesticides reach the receptors from the sources through different processes. Comprehension of these processes will lead to the identification of the modifying factors and subsequently allow them to be given appropriate scores. The terminology used to describe transport processes in the same route (i.e. dermal, inhalation, or ingestion) has varied between models, as well as between different exposure routes.

Schneider et al. “attempted to produce a consistent terminology for assessment of dermal exposure”\(^{170}\). They described three essential transport processes, namely emission, deposition, and transfer. *Emission* was defined as the transport of the pesticide directly from the source of exposure to the skin, clothes or any other materials covering the skin. *Deposition* was defined as the transport of small airborne particles to the skin, clothes or any other materials covering the skin. *Transfer* was defined as the transport of the pesticide by direct contact with contaminated surfaces. Processes which would lead to the pesticide being lost from the skin (e.g. resuspension or evaporation and removal) were further defined by Schneider et al. Van Wendel de Joode et al.\(^{282}\) used the three key processes to establish a semi-quantitative dermal exposure model called DREAM (DeRmal Exposure Assessment Method).

In the sheep dipping model developed in this thesis, all the key processes, namely emission, deposition, and transfer described in Schneider’s model\(^{170}\) are considered, while transport processes in which the pesticide is removed from the body have been included in the modifying factors (e.g. decontamination as a transport process in which the pesticide is deliberately removed from the system has been considered in personal hygiene as a modifying factor). Immersion whereby a part of the body is immersed into the sheep dip is considered as a type of emission process. Pesticide exposure in sheep dipping can occur through emission from all sources. During handling the concentrate, emission can result from splashing, spilling and direct contact with the concentrate. During sheep dipping, disposal of sheep dip and falling in the bath, emission may arise from splashing or immersion, while in handling dipped sheep emission can come from the sheep when they shake themselves and from direct contact with the dipped sheep. Deposition may occur during dipping sheep in diluted pesticides, during the disposal of sheep dip and during handling dipped sheep, while it is not probable during handling the concentrate or during incidental exposure. Transfer may occur during all activities
through contaminated instruments (e.g. jugs, gloves or submerging tools) and other surfaces (e.g. bath walls).

Cherrie et al. mentioned four transport processes for ingesting hazardous substances in workplaces: (i) transfer of contamination by the contact between mouth and contaminated hands or objects, (ii) splashing or direct deposition of substances around or into the mouth (iii) ingestion of inhaled aerosols and (iv) ingestion of contaminated drinks or food, ingestion. These four processes can be considered in pesticide exposure in sheep dipping. Transfer of the pesticide may occur by touching the mouth with contaminated hands or by eating or smoking with contaminated hands from all sources. Exposure can occur directly from the source to the mouth through splashes in all activities, though it might be not that significant, and through immersion if the dipper falls in the bath, while deposition could be neglected in the ingestion route. Ingestion of inhaled pesticide aerosols is possible as well whilst ingestion of contaminated food or drinks is very unlikely since it is very rare to keep food or drinks near the dipping bath.

For the inhalation route emission of vapours and dispersed particles is the main process of contaminants to transport to the airway system. In sheep dipping emission can occur through vapours from the primary source (dip concentrate and diluted sheep dip) or from a secondary source (e.g. contaminated clothes) in handling the concentrate, dipping sheep or disposal of the sheep dip. Incidents do not lead to inhalation exposure because falling of the plungers in the dipping bath will not increase the amount of contaminated air inhaled by them compared to being at the edge of the bath plunging sheep. Dispersed particles can arise during the dipping of sheep, handling dipped sheep or in the disposal of sheep dip while it is not probable from handling the concentrate.

3.7 Modifying factors of pesticide exposure

Factors which may modify the amount of the pesticide received by the receptor vary from source to source. There are general modifying factors that can be applied for different sources such as PPE, personal hygiene and behaviour, and atmospheric conditions. However, most of the modifying factors are specific for one type of sources, such as dipper’s task which is specific for dipping sheep and type of pesticide container which is specific for handling the concentrate. The lists of modifying factors presented in the following tables were developed by reviewing scientific literature related to sheep dipping and when information on a modifying factor was unavailable in the literature, a
hypothesis was made based on a personal judgement or based on information gained during the explorative farm visit. Very few of these factors have been included in the existing models as will be described in Chapter 6, Sections 6.2.4.3 and 6.2.4.4.

Table 3-1 lists the modifying factors in the source of handling the concentrate and the description of these factors. The main factors were thought to be the use of PPE, the type of the concentrate container and the frequency of handling the concentrate.

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPE usage</td>
<td>PPE in this context includes gloves, boots, hats, respirators, face-shields,</td>
</tr>
<tr>
<td></td>
<td>waterproof trousers, waterproof jackets, aprons and overalls. PPE can</td>
</tr>
<tr>
<td></td>
<td>nearly eliminate dermal exposure in sheep dipping if used properly but</td>
</tr>
<tr>
<td></td>
<td>this does not often happen. If PPE are not used properly (size, material,</td>
</tr>
<tr>
<td></td>
<td>cleaning and replacement) they can intensify exposure instead of providing</td>
</tr>
<tr>
<td></td>
<td>protection. Gloves are the most important PPE used since the hands are</td>
</tr>
<tr>
<td></td>
<td>likely to be the most contaminated body area. Using appropriate respirators</td>
</tr>
<tr>
<td></td>
<td>may reduce exposure through inhalation, while using other types of PPE</td>
</tr>
<tr>
<td></td>
<td>(aprons, boots, etc.) is essential in protecting the skin from any</td>
</tr>
<tr>
<td></td>
<td>potential splashes or spills.</td>
</tr>
<tr>
<td>Type and size of container</td>
<td>Can increase or decrease the probability of contact between the dip and</td>
</tr>
<tr>
<td></td>
<td>hands and the probability of spilling the dip onto the body. The</td>
</tr>
<tr>
<td></td>
<td>existence of a pouring mechanism in the container, for example, would</td>
</tr>
<tr>
<td></td>
<td>decrease dermal exposure.</td>
</tr>
<tr>
<td>Frequency of handling the concentrate</td>
<td>Usually depends on the number of sheep to dip since most of the handling</td>
</tr>
<tr>
<td></td>
<td>events are to refill the bath after dipping a certain number of sheep.</td>
</tr>
<tr>
<td></td>
<td>This number is recommended by the dip manufacturer and varies from one</td>
</tr>
<tr>
<td></td>
<td>trade mark to another depending on the ingredient and its concentration</td>
</tr>
<tr>
<td></td>
<td>in the dip.</td>
</tr>
<tr>
<td>Mixing method</td>
<td>Mixing methods have changed over time. There are generally four ways to mix</td>
</tr>
<tr>
<td></td>
<td>the concentrate with the bath; by pouring the concentrate directly in the</td>
</tr>
<tr>
<td></td>
<td>bath, by using a jug or an automatic unit, or sachets containing the</td>
</tr>
<tr>
<td></td>
<td>concentrate. Using the jug can lead to a higher exposure than direct</td>
</tr>
<tr>
<td></td>
<td>pouring into the bath, while both automatic units and sachets may lower</td>
</tr>
<tr>
<td></td>
<td>the exposure if used correctly.</td>
</tr>
<tr>
<td>Volume of the concentrate used</td>
<td>The more concentrate used, the higher the probability of exposure.</td>
</tr>
<tr>
<td>Concentration of the pesticide</td>
<td>The more concentrated the dip, the higher the concentration of the pesticide</td>
</tr>
<tr>
<td></td>
<td>in the skin contamination layer leading to a higher dermal exposure.</td>
</tr>
<tr>
<td>Volatility of chemical and co-formulants</td>
<td>Plays a paradoxical role in the amount of total exposure. High volatility</td>
</tr>
<tr>
<td></td>
<td>can decrease exposure through the dermal route while it can increase</td>
</tr>
<tr>
<td></td>
<td>exposure through inhalation.</td>
</tr>
<tr>
<td>Duration of dipping session</td>
<td>Determines the duration of the contact between the pesticide and the skin</td>
</tr>
<tr>
<td></td>
<td>especially when farmers do not wash their hands or other contaminated</td>
</tr>
<tr>
<td></td>
<td>parts of their bodies for a long time after handling the concentrate.</td>
</tr>
<tr>
<td>Bath location</td>
<td>If the bath is indoors, exposure can be increased through inhalation as an</td>
</tr>
<tr>
<td></td>
<td>indoor location increases the pesticide concentration in the air and</td>
</tr>
<tr>
<td></td>
<td>limits the dipper’s movement.</td>
</tr>
<tr>
<td>Personal hygiene and behaviour</td>
<td>The main factor in this set of modifiers in handling the concentrate can</td>
</tr>
<tr>
<td></td>
<td>be washing hands before eating or smoking.</td>
</tr>
<tr>
<td>Atmospheric conditions</td>
<td>Temperature, humidity and wind can affect exposure. Hot weather, for</td>
</tr>
<tr>
<td></td>
<td>example, can increase the volatility of the concentrate while wind may</td>
</tr>
<tr>
<td></td>
<td>increase dermal exposure through splashes and spills but decrease</td>
</tr>
<tr>
<td></td>
<td>inhalation.</td>
</tr>
</tbody>
</table>

* When scientific literature that describes the modifying factors was unavailable, a hypothesis was made based on a personal judgement or depending on the explorative farm visit.
Table 3-2 presents the factors that affect the exposure from the source of dipping sheep in the diluted pesticide. The main factors were thought to be the use of PPE, the dipper’s task and the number of dipped sheep.

### Table 3-2: Modifying factors in dipping sheep in the diluted pesticide

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPE usage</td>
<td>All types of PPE could be used especially those that cover the feet and the legs since they are the most exposed body parts during this job. Gloves are also important although they can be useless if the plunger uses his hands to plunge the sheep unless the gloves are very long (i.e. over the elbow). A respirator and face shield can reduce the exposure through inhalation and ingestion route.</td>
</tr>
<tr>
<td>Dipper’s task</td>
<td>Generally there are three well defined dipping tasks; plunging, chucking, and helping. A plunger (sometimes called a paddler) is the person who usually immerses the sheep under the surface of the dip bath. A chucker is the person who ushers the sheep one by one into the dip bath, while the helper is the person who gathers the sheep near the bath and makes them ready for the chucker. Sometimes farmers may do more than one task in the same session but only rarely does one farmer do all the tasks. The helper is normally exposed less in the dipping session and is hardly splashed while the plunger and chucker are more exposed to the diluted dip and sometimes they get soaked since both of them stand very close to the bath. However, plungers were splashed more than chukers in two studies.</td>
</tr>
<tr>
<td>Number of dipped sheep</td>
<td>Splashes emerge when each sheep enters the bath and from the plunging of each one under the surface. Therefore when the number of sheep increases the probability of contact with diluted dip increases. Furthermore, dippers become tired after dipping a large number of sheep and that reduces their attention and may increase their wrong practices.</td>
</tr>
<tr>
<td>Proximity to the dipping bath</td>
<td>The closer to the bath the more exposed the farmer. However, this modifying factor can be ignored as theoretically it has a strong relationship with the task. The plunger is usually very close to the bath, the chucker may be further back, while the helper can be much further away from the bath and maybe hardly splashed.</td>
</tr>
<tr>
<td>Concentration of pesticide in the diluted dip</td>
<td>When the pesticide concentration in the diluted dip increases, a higher dermal exposure would be expected from contacting that dip. This factor is a result of amount of the concentrate added to the bath, the concentration of the concentrate dip, and bath volume.</td>
</tr>
<tr>
<td>Number of dippers</td>
<td>The number of dippers may reflect the work burden on the farmers. When there are more dippers they can rely on each other to take a little rest or to be away from the bath for a while which decreases exposure.</td>
</tr>
<tr>
<td>Duration of the session</td>
<td>The longer the duration the more likely exposure will increase as it increases the time between the exposure and washing the body and by increasing the dippers’ tiredness which reduces their carefulness.</td>
</tr>
<tr>
<td>Dip rate (sheep dipped/hour)</td>
<td>When the dip rate increases the farmers are working faster and they may become less careful and allow too many sheep in the bath in the same time which can increase splashes from the bath.</td>
</tr>
<tr>
<td>Splash guard</td>
<td>Fitted across the entry of the bath and aside the bath; these guards can reduce the exposure to the diluted dip extensively.</td>
</tr>
<tr>
<td>Bath type</td>
<td>Exposure to diluted dip is greater when linear baths are used compared to circular or mobile baths. Exposure from using a circular bath can be higher than when a mobile bath is used.</td>
</tr>
<tr>
<td>Bath location</td>
<td>The use of an indoor bath may increase exposure by increasing the pesticide concentration in the air and limiting the area of dipper’s movement.</td>
</tr>
<tr>
<td>Surface area of the bath</td>
<td>Evaporation correlates positively with the surface area of the bath leading to more exposure through inhalation.</td>
</tr>
</tbody>
</table>

* When scientific literature that describes the modifying factors was unavailable, a hypothesis was made based on a personal judgement or depending on the explorative farm visit.
Table 3-2: Modifying factors in dipping sheep in the diluted pesticide (continued)

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep entry</td>
<td>Exposure is greater when the dipper ushers the sheep manually into the bath compared to other methods like using a slope(^{12}). Furthermore exposure varies among farmers who use manual methods according to the way of doing that; let the sheep enter front first or back first or throw the sheep into the bath(^{12})....</td>
</tr>
<tr>
<td>Submerging tool</td>
<td>Dippers who use their hands or their feet to submerge the sheep are exposed to pesticides more than those who use a tool. The use of a wooden tool may lead to more exposure than a metal tool as the wood can absorb the pesticide and result in increased exposure(^{12}).</td>
</tr>
<tr>
<td>Personal hygiene and behaviour</td>
<td>Changing clothes after any incident of getting soaked, changing clothes and taking a bath after work, smoking during work, and washing hands before eating or smoking are the most important factors in this set.</td>
</tr>
<tr>
<td>Atmospheric conditions</td>
<td>Winds may increase dermal exposure through splashes from the bath. Temperature and humidity can affect exposure through inhalation by increasing or decreasing the evaporation of the diluted dip.</td>
</tr>
</tbody>
</table>

Table 3-3 presents the modifying factors in the source of handling dipped sheep with a description of their effects. The duration between dipping and handling, the use of PPE and nature of the handling were considered to be the most important ones.

Table 3-3: Modifying factors in handling dipped sheep

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration between dipping and handling</td>
<td>The duration between dipping and first contact with dipped sheep is crucial in the exposure from this source. This duration depends on the half-life for loss from the fleece which varies according to the type of pesticides; for example half-lives of different OPs ranged from 12 to 53 days(^{49}). Usually manufacturers state this duration on the instruction sheet and it depends on the nature of the handling, for instance, manufacturers advise not to shear sheep in the 3 months after dipping(^{285,286}).</td>
</tr>
<tr>
<td>PPE usage</td>
<td>Gloves are the most important PPE used during handling dipped sheep. However, sheep can shake themselves resulting in splashes which can reach any part of the body.</td>
</tr>
<tr>
<td>Nature of the handling</td>
<td>The contact with dipped sheep could be very slight (e.g. gathering sheep) or intensive (e.g. shearing or milking) which is not likely if the farmers comply with the recommendations of the dip manufacturers.</td>
</tr>
<tr>
<td>Number of dipped sheep handled</td>
<td>Exposure increases with the number of dipped sheep handled.</td>
</tr>
<tr>
<td>Concentration of pesticide in the diluted dip</td>
<td>When this concentration increases pesticide residues in the sheep fleece will increase and so also the exposure.</td>
</tr>
<tr>
<td>Sheep type (length of fleece)</td>
<td>The nature of the fleece and its length may play a role in the quantity of pesticide residues, which can change exposure after any possible contact with the dipped sheep</td>
</tr>
<tr>
<td>Location of gathering dipped sheep</td>
<td>If the dipped sheep are gathered in a closed place, the pesticide concentration in the air of that place will be higher than in the air of an open place.</td>
</tr>
<tr>
<td>Personal hygiene and behaviour</td>
<td>Washing hands immediately after any contact with dipped sheep and especially before eating or smoking can modify exposure from this source.</td>
</tr>
<tr>
<td>Atmospheric conditions</td>
<td>Hot weather, for example, may increase the evaporation of the residue in the fleece and subsequently increase the exposure through inhalation; however it will reduce dermal exposure.</td>
</tr>
</tbody>
</table>

\(^{a}\) When scientific literature that describes the modifying factors was unavailable, a hypothesis was made based on a personal judgement or depending on the explorative farm visit.
Table 3-4 presents the factors which modify the exposure from the source of the disposal of sheep dip where the use of PPE and the disposal method were considered the most important.

**Table 3-4: Modifying factors in the disposal of sheep dip**

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPE usage</td>
<td>All types of PPE should be used in the disposal with more focus on the gloves.</td>
</tr>
<tr>
<td>Method of the disposal</td>
<td>Farmers use different methods to get rid of sheep dip. Some farmers use manual methods like buckets or manual pumps, whilst others use mechanical pumps, tankers or drains to empty the bath. Theoretically, manual methods may lead to more exposure than other methods.</td>
</tr>
<tr>
<td>Volume of sheep dip</td>
<td>If the farmers use manual methods, the volume of sheep dip can affect the exposure while if mechanical methods are used the effect of the volume of sheep dip will be relatively insignificant.</td>
</tr>
<tr>
<td>Duration of disposal process</td>
<td>A long duration will increase the time between any possible exposure and washing which increases the exposure, and it will increase also exposure through inhalation route.</td>
</tr>
<tr>
<td>The age of sheep dip</td>
<td>Old sheep dip may contain less pesticide due to sedimentation, which lead to less exposure, unless the farmer cleans the bath properly after the disposal. However, old sheep dip may also contain more toxic metabolites.</td>
</tr>
<tr>
<td>Bath location</td>
<td>The use of an indoor bath may increase exposure by increasing the pesticide concentration in the air.</td>
</tr>
<tr>
<td>Personal hygiene and behaviour</td>
<td>Washing hands, changing clothes, and taking a bath after the disposal are some of the factors of this set.</td>
</tr>
<tr>
<td>Atmospheric conditions</td>
<td>Winds can increase the probability of exposure to splashes while hot weather may increase the evaporation from dipping bath during the disposal.</td>
</tr>
</tbody>
</table>

*When scientific literature that describes the modifying factors was unavailable, a hypothesis was made based on a personal judgement or depending on the explorative farm visit.*

Table 3-5 presents the modifying factors of the exposure from incidental exposure. The spillage of the concentrate on any part of the body, number of falls in the bath and level of immersion were thought to be the most important.

**Table 3-5: Modifying factors in incidental exposure (falling in the bath and spilling the concentrate on the body)**

<table>
<thead>
<tr>
<th>Modifying factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The spillage of the concentrate on any part of the body</td>
<td>Spillage can add more exposure to that which occurs through normal handling. The frequency of spilling the concentrate, the amount of the concentrate spilled on the body and the concentration of the pesticide are important factors in determining exposure.</td>
</tr>
<tr>
<td>Number of falls</td>
<td>Although it is very rare to fall in the bath more than once in the same session, dermal exposure would increase with the number of falls.</td>
</tr>
<tr>
<td>Level of immersion</td>
<td>Dermal exposure increases with the height of the level of immersion.</td>
</tr>
<tr>
<td>PPE usage</td>
<td>The use of PPE during handling the concentrate reduces the exposure from any potential spills, whilst during dipping can play a negative role if the farmer does not remove the PPE immediately after falling in the bath and washes the body area immersed.</td>
</tr>
<tr>
<td>Personal hygiene</td>
<td>Changing clothes and taking an immediate bath after the fall is the most important factor in exposure from this source. The duration between the spillage and washing is another factor.</td>
</tr>
</tbody>
</table>

*When scientific literature that describes the modifying factors was unavailable, a hypothesis was made based on a personal judgement or depending on the explorative farm visit.*
3.8 Structure of the aggregate exposure algorithm

The conceptual model described above (Figure 3-5) was used to build an exposure algorithm to assess pesticide exposure in one sheep dipping session. Total pesticide exposure through a sheep dipping session is the sum of the exposure from each source. An additive model will be used for the different sources since these are independent. The exposure from each source itself is the sum of the exposure through different routes (i.e. dermal, ingestion, and inhalation). The exposure from each source through each route is a multiplicative function of the modifying factors. However, for incidental exposure the exposure from concentrate spills was added to the exposure from falling in the bath because they are independent incidents.

The same factor can affect the exposure from a source through one route but may not necessarily affect the exposure through another route. For example, the size of the pesticide container affects the exposure from handling the concentrate through the dermal and the ingestion routes but most likely not through the inhalation route. Such factors were not included in the model of the unaffected routes.

The general form of the algorithm and the equations of each part are shown below.

Eq. 3.2: \( \text{EXPOSURE} = \alpha \times \text{CON} + \beta \times \text{DIP} + \gamma \times \text{AFT} + \delta \times \text{DIS} + \varepsilon \times \text{INC} \)

Where:
\( \text{CON} \) = Exposure from handling the concentrate;
\( \text{DIP} \) = Exposure from dipping sheep in the bath;
\( \text{AFT} \) = Exposure from handling dipped sheep;
\( \text{DIS} \) = Exposure from disposal of sheep dip;
\( \text{INC} \) = Exposure from incidental exposure;
\( \alpha, \beta, \gamma, \delta \) and \( \varepsilon \) = Parameters denote exposure weights from each source of the total exposure (each will be described in Section 3.9.4).

Exposure from handling the concentrate was calculated according to the following equations:

**Eq.3.2.1:** \( \text{CON} = \alpha_{\text{der}} \times \text{CON}_{\text{der}} + \alpha_{\text{ing}} \times \text{CON}_{\text{ing}} + \alpha_{\text{inh}} \times \text{CON}_{\text{inh}} \)

**Eq.3.2.1.1:** \( \text{CON}_{\text{der}} = \text{FREQ} \times \text{COVOL} \times \text{CONC}_{\text{con}} \times \text{TYP}_{\text{der}} \times \text{MIX}_{\text{der}} \times \text{VOLT} \times \text{SIZ} \times \text{DUR}_{\text{der}} \times \text{PHB} \times \text{PPE} \times \text{ATM}_{\text{der}} \)

**Eq.3.2.1.2:** \( \text{CON}_{\text{ing}} = \text{FREQ} \times \text{COVOL} \times \text{CONC}_{\text{con}} \times \text{TYP}_{\text{ing}} \times \text{MIX}_{\text{ing}} \times \text{VOLT} \times \text{SIZ} \times \text{DUR}_{\text{ing}} \times \text{PHB} \times \text{PPE} \times \text{ATM}_{\text{ing}} \)
Eq. 3.2.1.3: $\text{CON}_{\text{inh}} = \text{FREQ} \times \text{COVOL} \times \text{CONC}_{\text{con}} \times \text{TYP}_{\text{inh}} \times \text{MIX}_{\text{inh}} \times \text{VOLT} \times \text{LOC} \times \text{PPE}_{\text{inh}} \times \text{ATM}_{\text{inh}}$

Where:

$\text{CON}_{\text{der}}$ = Exposure from handling the concentrate through the skin;

$\text{CON}_{\text{ing}}$ = Exposure from handling the concentrate through ingestion;

$\text{CON}_{\text{inh}}$ = Exposure from handling the concentrate through inhalation;

$\alpha_{\text{der}}$, $\alpha_{\text{ing}}$ and $\alpha_{\text{inh}}$ = Parameters denote exposure weights through each route of the exposure from handling the concentrate (each will be described in Section 3.9.4);

$\text{FREQ}$ = Frequency of handling the concentrate;

$\text{COVOL}$ = Volume of the concentrate used;

$\text{CONC}_{\text{con}}$ = Concentration of the pesticide in the container;

$\text{TYP}$ = Type of container;

$\text{MIX}$ = How mixed with bath;

$\text{VOLT}$ = Volatility of chemical and co-formulants;

$\text{SIZ}$ = Size of container;

$\text{DUR}$ = Duration of the session;

$\text{PHB}$ = Personal hygiene and behaviour;

$\text{PPE}$ = Personal protective equipment;

$\text{ATM}$ = Atmospheric conditions like temperature and wind;

$\text{LOC}$ = Bath location.

Exposure from dipping sheep in bath was calculated according to the following equations:

**Eq. 3.2.2:** $\text{DIP} = \beta_{\text{der}} \times \text{DIP}_{\text{der}} + \beta_{\text{ing}} \times \text{DIP}_{\text{ing}} + \beta_{\text{inh}} \times \text{DIP}_{\text{inh}}$

**Eq. 3.2.2.1:** $\text{DIP}_{\text{der}} = \text{TASK} \times \text{NUM} \times \text{CONC}_{\text{dip}} \times \text{FLOCK} \times \text{DUR}_{\text{der}} \times \text{RATE}_{\text{der}} \times \text{BATH}_{\text{der}} \times \text{LOC}_{\text{der}} \times \text{TOOL}_{\text{der}} \times \text{GUARD}_{\text{der}} \times \text{ENTRY}_{\text{der}} \times \text{PPE}_{\text{der}} \times \text{PHB} \times \text{ATM}_{\text{der}}$

**Eq. 3.2.2.2:** $\text{DIP}_{\text{ing}} = \text{TASK} \times \text{NUM} \times \text{CONC}_{\text{dip}} \times \text{FLOCK} \times \text{DUR}_{\text{ing}} \times \text{RATE}_{\text{ing}} \times \text{BATH}_{\text{ing}} \times \text{LOC}_{\text{ing}} \times \text{TOOL}_{\text{ing}} \times \text{GUARD}_{\text{ing}} \times \text{ENTRY}_{\text{ing}} \times \text{PPE}_{\text{ing}} \times \text{PHB} \times \text{ATM}_{\text{ing}}$

**Eq. 3.2.2.3:** $\text{DIP}_{\text{inh}} = \text{TASK} \times \text{NUM} \times \text{CONC}_{\text{dip}} \times \text{FLOCK} \times \text{DUR}_{\text{inh}} \times \text{RATE}_{\text{inh}} \times \text{BATH}_{\text{inh}} \times \text{LOC}_{\text{inh}} \times \text{TOOL}_{\text{inh}} \times \text{SUR} \times \text{ENTRY}_{\text{inh}} \times \text{PPE}_{\text{inh}} \times \text{ATM}_{\text{inh}}$

Where:

$\text{DIP}_{\text{der}}$ = Exposure through the skin from dipping sheep;

$\text{DIP}_{\text{ing}}$ = Exposure through ingestion from dipping sheep;
DIP\textsubscript{inh} = Exposure through inhalation from dipping sheep; 
\(\beta\text{\textsubscript{der}}, \beta\text{\textsubscript{ing}}\) and \(\beta\text{\textsubscript{inh}}\) = Parameters denote exposure weights through each route of the exposure from dipping sheep in bath (each will be described in Section 3.9.4); 
TASK = Task; 
NUM = Number of dippers; 
CONC\textsubscript{dip} = Concentration of pesticide in the diluted dip; 
FLOCK = Number of dipped sheep; 
DUR = Duration of the session; 
RATE = Dip rate; 
BATH = Bath type; 
LOC = Bath location; 
TOOL = Submerging tool; 
GUARD = Splash guard; 
ENTRY = Sheep entry; 
PPE = Personal protective equipment; 
PH\textsubscript{B} = Personal hygiene and behaviour; 
ATM = Atmospheric conditions like temperature and wind; 
SUR = Area of bath surface.

Exposure from handling dipped sheep was calculated according to the following equations:

\textbf{Eq.3.2.3:} AFT = \(\gamma\text{\textsubscript{der}} \times AFT\text{\textsubscript{der}} + \gamma\text{\textsubscript{ing}} \times AFT\text{\textsubscript{ing}} + \gamma\text{\textsubscript{inh}} \times AFT\text{\textsubscript{inh}}\)

\textbf{Eq.3.2.3.1:} AFT\textsubscript{der} = NAT \times FLOAFT \times DURAFT \times LENGTH \times CONC\textsubscript{dip} 
\times GATHER \times PPE\textsubscript{der} \times PHB \times ATM

\textbf{Eq.3.2.3.2:} AFT\textsubscript{ing} = NAT \times FLOAFT \times DURAFT \times LENGTH \times CONC\textsubscript{dip} 
\times GATHER \times PPE\textsubscript{ing} \times PHB \times ATM

\textbf{Eq.3.2.3.3:} AFT\textsubscript{inh} = NAT \times FLOAFT \times DURAFT \times LENGTH \times CONC\textsubscript{dip} 
\times GATHER \times PPE\textsubscript{inh} \times ATM

Where:
AFT\textsubscript{der} = Exposure through the skin from handling dipped sheep; 
AFT\textsubscript{ing} = Exposure through ingestion from handling dipped sheep; 
AFT\textsubscript{inh} = Exposure through inhalation from handling dipped sheep;
\( \gamma_{\text{der}}, \gamma_{\text{ing}} \) and \( \gamma_{\text{inh}} \) = Parameters denote exposure weights through each route of the exposure from handling dipped sheep (each will be described in Section 3.9.4);

NAT = Nature of the handling;
FLOAFT = Number of dipped sheep handled;
DURAFT = Duration between dipping and handling;
LENGTH = length of fleece;
CONC\text{dip} = Concentration of pesticide in the diluted dip;
GATHER = Place for gathering sheep after dipping;
PPE = Personal protective equipment;
PHB = Personal hygiene and behaviour;
ATM = Atmospheric conditions like temperature and wind.

Exposure from disposal of sheep dip was calculated according to the following equations:

Eq.3.2.4: \( \text{DIS} = \delta_{\text{der}} \times \text{DIS}_{\text{der}} + \delta_{\text{ing}} \times \text{DIS}_{\text{ing}} + \delta_{\text{inh}} \times \text{DIS}_{\text{inh}} \)

Eq.3.2.4.1: \( \text{DIS}_{\text{der}} = \text{METHOD}_{\text{der}} \times \text{VOL}_{\text{der}} \times \text{LOC}_{\text{der}} \times \text{DURDIS} \times \text{OLD} \times \text{PPE}_{\text{der}} \times \text{PHB} \times \text{ATM} \)

Eq.3.2.4.2: \( \text{DIS}_{\text{ing}} = \text{METHOD}_{\text{ing}} \times \text{VOL}_{\text{ing}} \times \text{LOC}_{\text{ing}} \times \text{DURDIS} \times \text{OLD} \times \text{PPE}_{\text{ing}} \times \text{PHB} \times \text{ATM} \)

Eq.3.2.4.3: \( \text{DIS}_{\text{inh}} = \text{METHOD}_{\text{inh}} \times \text{VOL}_{\text{inh}} \times \text{LOC}_{\text{inh}} \times \text{DURDIS} \times \text{OLD} \times \text{PPE}_{\text{inh}} \times \text{ATM} \)

Where:
\( \text{DIS}_{\text{der}} = \) Exposure through the skin from disposal of sheep dip;
\( \text{DIS}_{\text{ing}} = \) Exposure through ingestion from disposal of sheep dip;
\( \text{DIS}_{\text{inh}} = \) Exposure through inhalation from disposal of sheep dip;
\( \delta_{\text{der}}, \delta_{\text{ing}} \) and \( \delta_{\text{inh}} \) = Parameters denote exposure weights through each route of the exposure from disposal of sheep dip (each will be described in Section 3.9.4);

VOL = Volume of sheep dip;
LOC = Bath location;
DURDIS = Duration of disposal process;
OLD = How old sheep dip;
PPE = Personal protective equipment;
PHB = Personal hygiene and behaviour;
ATM = Atmospheric conditions like temperature and wind.
Exposure from incidental exposure was calculated according to the following equations:

**Eq. 3.2.5:** \( \text{INC} = \varepsilon_{\text{der}} \times \text{INC}_{\text{der}} + \varepsilon_{\text{ing}} \times \text{INC}_{\text{ing}} \)

**Eq. 3.2.5.1:** \( \text{INC}_{\text{der}} = \text{FALL} \times \text{LEVEL} \times \text{PHB} \)
\[+ \text{SPIL} \times \text{AMOUNT} \times \text{CONC}_{\text{con}} \times \text{PPE}_{\text{der}} \times \text{PHB}_{\text{der}} \]

**Eq. 3.2.5.2:** \( \text{INC}_{\text{ing}} = \text{FALL} \times \text{PHB} \)
\[+ \text{SPIL} \times \text{AMOUNT} \times \text{CONC}_{\text{con}} \times \text{PPE}_{\text{ing}} \times \text{PHB}_{\text{ing}} \]

Where:

\( \text{INC}_{\text{der}} = \) Exposure through the skin from dipping sheep;
\( \text{INC}_{\text{ing}} = \) Exposure through ingestion from dipping sheep;
\( \varepsilon_{\text{der}} \) and \( \varepsilon_{\text{ing}} \) = Parameters denote exposure weights through each route of the incidental exposure (each will be described in Section 3.9.4);
\( \text{FALL} = \) Number of falls;
\( \text{LEVEL} = \) Level of immersion;
\( \text{PHB} = \) Personal hygiene and behaviour;
\( \text{SPIL} = \) Frequency of spillage of the concentrate on a part of the body;
\( \text{AMOUNT} = \) Average amount of concentrate spills;
\( \text{CONC}_{\text{con}} = \) Concentration of the pesticide in the container;
\( \text{PPE} = \) Personal protective equipment.

### 3.9 Estimating the effects of algorithm components on exposure

Three types of exposure assessment are possible; qualitative assessment (exposed/not exposed), semi quantitative assessment (exposure bands such as no, medium, high, and very high or unitless exposure scores), and quantitative assessment (the exposure in units). In order to obtain an estimate for pesticide exposure from the algorithm, the effects of all algorithm variables on exposure should be estimated and the variables should be assigned values according to their effects.

Exposure metrics such as STOFFENMANAGER and ART were developed to give quantitative estimates for exposures to different chemical substances mainly through inhalation route. However, in this new algorithm exposure through different routes was aggregated and thus it is impossible to assign a unit to the exposure because exposures through different routes are measured in different units (e.g. mg/cm² for dermal route and mg/m³ for inhalation route). Furthermore, no measurement databases were available for most of the exposure determinants that can be used as a base for a quantitative
exposure assessment. Therefore the developed aggregate exposure algorithm will be semi-quantitative using a unitless scale (i.e. scores) similar, for example, to the algorithm used in the AHS study\textsuperscript{153} or to the DREAM model\textsuperscript{282}.

Except for dippers’ task (TASK) and PPE variables, published information which can help to assign scores for all the algorithm variables (i.e. modifying factors) and weights for exposure sources and routes is lacking. Therefore, expert judgment was used to assign the values of scores and weights in this semi-quantitative algorithm except for TASK and PPE where previous studies were used. The intent of developing this new algorithm was to be used as a generic model, thus three chemical-specific modifying factors that need specific pesticides used by the farmer to be known (i.e. CONC\textsubscript{con}, CONC\textsubscript{dip} and VOLT) were excluded from this model by giving them the score of one in the final algorithm. However, this allows for further extension in future development of pesticide-specific algorithms.

3.9.1 Scores of dipper’s task

Scores of tasks have depended essentially on time-adjusted splashing scores found in two previous studies; Niven et al.\textsuperscript{12} and Sewell et al.\textsuperscript{104}. In the first study, a dipper’s body was divided into nine areas and splashing was visually assessed every half an hour. Splashing scores (dry: 0, splashed: 1, soaked: 2) were given to each body part and at the end of the session all scores were summed to give a cumulative splashing score for the whole body in the whole dipping session. A time-adjusted score was calculated by dividing the cumulative score by the number of dipping hours and then multiply the result by 8 hours (a standard reference period). In the second study a similar method was used to obtain splashing scores, except that the body was divided in 10 areas instead of 9, and the assessment was only performed at 4 regular time points in the whole session. The scores were summed at each point and the cumulative score was the average of the four times. At the end the time-weighted splashing score was calculated by multiplying the cumulative score by number of dipping hours. The means of splashing scores in the first study were 42.64 for plunger, 26.45 for chucker, and 9 for helper, while in the second study these means were 57.8 for plunger, 49.4 for plunger/chucker, 47.5 for chucker, 34.9 for chucker/helper, and 9.8 for helper.

By considering the helper task as the reference and by taking the average of these two studies, task scores were assumed as presented in Table 3-6. These scores were based on dermal exposure but they were applied to ingestion and inhalation as well based on the
assumption that the main reason of the exposure difference between tasks is the proximity of the dipper to the dipping bath. This proximity will affect the amount of splashing entering the mouth let alone that when dermal exposure increases, the chance of ingestion exposure by hand-to-mouth contact increases. The same justification is applied to inhalation exposure since the closer the dipper to the bath the more likely the dipper will be exposed to pesticide vapours and dispersed particles.

Table 3-6: Scores of dipper’s task

<table>
<thead>
<tr>
<th>Task</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helper</td>
<td>1</td>
</tr>
<tr>
<td>Plunger</td>
<td>5.5</td>
</tr>
<tr>
<td>Chucker</td>
<td>4</td>
</tr>
<tr>
<td>Plunger/chucker</td>
<td>5</td>
</tr>
<tr>
<td>Chucker/helper</td>
<td>3.5</td>
</tr>
<tr>
<td>All tasks</td>
<td>5</td>
</tr>
</tbody>
</table>

3.9.2 Scores of PPE variable

Scores of using PPE to reduce exposure were based on two previous studies; the SHAPE study\textsuperscript{29} and a proposal for an exposure metric found in the analytical study of OP sheep dip\textsuperscript{186} and used in a subsequent epidemiological study\textsuperscript{7}. To assign PPE scores for the dermal route, the ratio of body part covered with PPE, the proportion of probable skin area to be contaminated in the activity, and the effectiveness of PPE are needed, while for ingestion and inhalation routes the effectiveness is the only information needed.

Eight types of PPE were considered, namely respirator, visor, hat, gloves, jacket, trousers, overall, and boots. Table 3-7 shows the ratio of body parts covered with a single PPE or combinations of PPE\textsuperscript{289}.

Table 3-7: Ratio of body parts covered with single or combinations of PPE \textsuperscript{289}

<table>
<thead>
<tr>
<th>Body Part</th>
<th>Single PPE \textsuperscript{a}</th>
<th>Combinations of PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>R = 0.1667, H = 0.5, V = 0.5, G = 0, J = 0, O = 0, T = 0, B = 0</td>
<td>R+H (0.667), H+V (1)</td>
</tr>
<tr>
<td>Trunk</td>
<td>0 = 0, H = 0, V = 0, G = 0, J = 0, O = 0, T = 0, B = 0</td>
<td>J+T (1)</td>
</tr>
<tr>
<td>Upper arms</td>
<td>0 = 0, H = 0, V = 0, G = 0, J = 0, O = 0, T = 0, B = 0</td>
<td>J/O (1)</td>
</tr>
<tr>
<td>Forearms</td>
<td>0 = 0, H = 0, V = 0.5, G = 1, J = 1, O = 0, T = 0, B = 0</td>
<td>J/O+G (1)</td>
</tr>
<tr>
<td>Hands</td>
<td>0 = 0, H = 0, V = 1, G = 0, J = 0, O = 0, T = 0, B = 0</td>
<td>None</td>
</tr>
<tr>
<td>Thighs</td>
<td>0 = 0, H = 0, V = 0, G = 1, J = 0, O = 1, T = 0, B = 0</td>
<td>None</td>
</tr>
<tr>
<td>Lower legs</td>
<td>0 = 0, H = 0, V = 0, G = 0, J = 0, O = 1, T = 1, B = 0.5</td>
<td>O/T+B (1)</td>
</tr>
<tr>
<td>Feet</td>
<td>0 = 0, H = 0, V = 0, G = 0, J = 0, O = 0, T = 0, B = 1</td>
<td>None</td>
</tr>
</tbody>
</table>

\textsuperscript{a} R = respirator, H = hat, V = visor, G = gloves, J = jacket, O = overall, T = trousers, B = boots
The same scores of PPE were used in this conceptual model for exposure from dipping sheep in bath and for exposure from the disposal of the sheep dip through all routes. The scores of PPE for exposure from handling dipped sheep are assumed to be the same as for exposure from dipping sheep in the bath regarding inhalation and ingestion routes.

The effectiveness of the PPE at reducing exposure varied according to the activity (Table 3-8). Most of these data were taken from the work of Cherrie\textsuperscript{289} while the rest were based on expert judgment. For example, gloves were assumed to offer 70% protection from handling the concentrate compared to 30% from dipping sheep since the former requires less time than the later.

### Table 3-8: Effectiveness of the PPE in sheep dipping activities\textsuperscript{a}

<table>
<thead>
<tr>
<th>PPE</th>
<th>CON</th>
<th>DIP/DIS</th>
<th>AFT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respirator</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>0.60 (inh)</td>
<td>0.60 (inh)</td>
<td>0.60 (inh)</td>
</tr>
<tr>
<td></td>
<td>0.40 (ing)</td>
<td>0.40 (ing)</td>
<td>0.40 (ing)</td>
</tr>
<tr>
<td>Visor</td>
<td>0.80*</td>
<td>0.85*</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>0.30 (inh)</td>
<td>0.30 (inh)</td>
<td>0.30 (inh)</td>
</tr>
<tr>
<td></td>
<td>0.40 (ing)</td>
<td>0.40 (ing)</td>
<td>0.40 (ing)</td>
</tr>
<tr>
<td>Hat</td>
<td>0.80</td>
<td>0.70*</td>
<td>0.80</td>
</tr>
<tr>
<td>Gloves</td>
<td>0.70*</td>
<td>0.30*</td>
<td>0.70</td>
</tr>
<tr>
<td>Jacket</td>
<td>0.95*</td>
<td>0.60*</td>
<td>0.95</td>
</tr>
<tr>
<td>Overall</td>
<td>0.95*</td>
<td>0.60*</td>
<td>0.95</td>
</tr>
<tr>
<td>Trousers</td>
<td>0.95*</td>
<td>0.60*</td>
<td>0.95</td>
</tr>
<tr>
<td>Boots</td>
<td>0.90</td>
<td>0.50*</td>
<td>0.90</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Figures with asterisk are from Cherrie\textsuperscript{289} whereas the rest are based on expert judgment

To determine the reduction of dermal exposure by the use of PPE, the proportion of skin area that could be contaminated in each activity needed to be defined. Table 3-9 presents these proportions which depended essentially on the SHAPE study\textsuperscript{29}.

PPE scores were then calculated as follows:

Eq. 3.3: PPE\textsubscript{der} = 1 - \sum_{PPE=1}^{8} \beta_{PPE} \times \varepsilon_{PPE} \times \eta_{PPE}

Eq. 3.4: PPE\_ing = 0.60 (if visor or respirator was used) and 1 (if neither)

Eq. 3.5: PPE\_inh = 0.70 (if visor was used), 0.40 (if respirator was used), and 1 (if neither)

Where: PPE = one of the eight types of PPE, \( \beta \) = proportion of probable skin area, \( \varepsilon \) = ratio of body part covered with PPE, and \( \eta \) = effectiveness of PPE.
Table 3-9: Skin area (m\(^2\)) that could be contaminated during each activity and as a proportion of the whole body

<table>
<thead>
<tr>
<th>Body Part</th>
<th>Average of skin area (a)</th>
<th>CON (handle)(b)</th>
<th>DIP/DIS(b)</th>
<th>AFT(b)</th>
<th>INC (spill)(b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\delta^c)</td>
<td>Prob.Area(d)</td>
<td>(\beta^e)</td>
<td>(\delta^c)</td>
<td>Prob.Area(d)</td>
</tr>
<tr>
<td>Head</td>
<td>0.188</td>
<td>0.0001</td>
<td>0.004</td>
<td>0.2</td>
<td>0.0376</td>
</tr>
<tr>
<td>Trunk</td>
<td>0.569</td>
<td>0.0005</td>
<td>0.059</td>
<td>0.6</td>
<td>0.3414</td>
</tr>
<tr>
<td>Upper arms</td>
<td>0.143</td>
<td>0.0005</td>
<td>0.015</td>
<td>0.6</td>
<td>0.0858</td>
</tr>
<tr>
<td>Fore arms</td>
<td>0.114</td>
<td>0.0005</td>
<td>0.012</td>
<td>0.8</td>
<td>0.0912</td>
</tr>
<tr>
<td>Hands</td>
<td>0.084</td>
<td>0.05</td>
<td>0.042</td>
<td>1.0</td>
<td>0.084</td>
</tr>
<tr>
<td>Thighs</td>
<td>0.198</td>
<td>0.0005</td>
<td>0.020</td>
<td>0.8</td>
<td>0.1584</td>
</tr>
<tr>
<td>Lower legs</td>
<td>0.207</td>
<td>0.0005</td>
<td>0.021</td>
<td>0.9</td>
<td>0.1863</td>
</tr>
<tr>
<td>Feet</td>
<td>0.112</td>
<td>0.0001</td>
<td>0.002</td>
<td>1.0</td>
<td>0.112</td>
</tr>
<tr>
<td>Total</td>
<td>1.615</td>
<td>0.0048455</td>
<td>1</td>
<td>1.0967</td>
<td>1</td>
</tr>
</tbody>
</table>

\(a\) Average of skin area in m\(^2\) according to EPA, 1992\(^{289}\). Male averages are used since the majority of the dippers are men.

\(b\) CON (handle): Exposure from handling the concentrate, DIP: exposure from dipping sheep in the bath, DIS: exposure from disposal of sheep dip, AFT: exposure from handling dipped sheep, and INC (spill): exposure from concentrate spills.

\(c\) \(\delta\): fraction of skin area that could be contaminated during the activity\(^{29}\). Except \(\delta\) for INC (spill) which is the fraction of skin area that the spill may reach (expert judgment).

\(d\) Prob.Area: Skin area that could be contaminated during the activity.

\(e\) \(\beta\): Proportion of skin area that could be contaminated in each body part from the whole body area that could be contaminated during the activity.
3.9.3 Scores of other algorithm variables

Apart from the variables of dipper’s task and PPE use, all other variables were assigned scores by expert judgment. The following sections describe the methodology of assigning these scores and the final scores assigned by the experts.

3.9.3.1 Methodology of assigning scores for other algorithm variables

Five occupational hygienists were contacted to participate in assigning scores for variables and weights for exposure sources and routes. All had extensive training in occupational hygiene and exposure assessment in general, and had done work in pesticide exposure in agriculture before while two of them had extensive knowledge of sheep dipping practices and processes. Two documents were sent to the experts; the first was the conceptual exposure assessment model with a description of all activities and variables and the derived algorithm and the second was the file with the expert scoring assignments which had to be completed by the experts. The score sheet was based on the following methodology and example.

For each variable one of the categories was already assigned to be the reference value and given the value of 1 while the remaining categories should be assigned values according to their effect relative to the reference category as estimated by each occupational hygienist. For example, the type of container is one of the modifying factors for the source of handling the concentrate. This variable has three categories, namely a container with a pouring mechanism, a container without a pouring mechanism and sachets. The use of containers with a pouring mechanism was assigned the value of 1 as the reference category. If the use of containers without a pouring mechanism is assessed by the expert as increasing dermal exposure by 50% and ingestion exposure by 70% compared to the use of containers with a pouring mechanism, the expert should assign the value of 1.5 to the dermal route and 1.7 to the ingestion route. If the exposure through inhalation is assumed to be slightly affected when the containers had no pouring mechanism, the value of 1.1, for example, could be assigned to the inhalation route. On the contrary, if the expert thinks that the use of sachets would reduce the exposure by 90% in both the dermal and ingestion routes and by 80% in the inhalation route in comparison to the use of containers with a pouring mechanism, the value of 0.1 should be assigned to sachets in first two routes and 0.2 in the last route.
Only variables whose distributions were reported in the literature were sent to the experts; all other variables were assigned the score of one. After receiving the work of the experts, their scores for each variable were combined into one final score by deleting the maximum and the minimum values and take the geometric mean of the other 3 scores. The assignments of all experts are presented in Appendix 4 whilst the final scores are presented in the following section. The methodology of assigning weights for exposure sources and routes is described in Section 3.9.4.

3.9.3.2 Scores of algorithm variable based on expert judgment

Table 3-10 to Table 3-13 present the final semi-quantitative scores of algorithm variables assigned by the experts with their justification of those scores if mentioned. The main variable for each source was identified on the basis of repetitive activity.

For the source of handling the concentrate (Table 3-10), every time the dipper handled the concentrate they might be exposed so the frequency of handling the concentrate was the main variable and the rest of the variables were modifiers. For the source of dipping sheep in the diluted pesticide (Table 3-11), every time the farmer dips a sheep they might be exposed so the number of dipped sheep was the main variable and the rest of the variables were modifiers.

The source of the disposal of sheep dip (Table 3-12) has no main variable since there is no repetitive action in this activity. The main variable in the incidental exposure (Table 3-13) was the number of falls in the dip bath and the frequency of spilling the concentrate on the body. However, the distribution of these two main variables was not reported in the literature. The main variable in handling the dipped sheep was the number of sheep handled after dipping. However, no variables of handling dipped sheep were reported in the literature and therefore the assessment of exposure from this source has depended solely on the scores of using PPE which were mentioned earlier.
Table 3-10: Exposure scores for variables of handling the concentrate assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category *</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of handling the concentrate</td>
<td>All</td>
<td>FREQ</td>
<td>Discrete variable</td>
<td>Number of events of handling</td>
<td>Every time farmer handles the concentrate, they might be exposed.</td>
</tr>
<tr>
<td>Volume of the concentrate used</td>
<td>All</td>
<td>COVOL</td>
<td>1st tertile</td>
<td>1</td>
<td>Exposure increases with the volume of the pesticide dip handled.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd tertile</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd tertile</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Type of container</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td></td>
<td>TYP&lt;sub&gt;der&lt;/sub&gt;</td>
<td>With a pouring mechanism</td>
<td>1</td>
<td>Containers with pouring mechanism lead to reduced contact between the skin and the concentrate and less exposure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td></td>
<td>TYP&lt;sub&gt;ing&lt;/sub&gt;</td>
<td>With a pouring mechanism</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td>TYP&lt;sub&gt;inh&lt;/sub&gt;</td>
<td>With a pouring mechanism</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Size of container</td>
<td>Dermal &amp;</td>
<td>SIZ</td>
<td>5 litres</td>
<td>1</td>
<td>Larger containers are more likely to result in spills due to handling problems, and use of the same container many times leads to more contamination on its walls.</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td></td>
<td>10 litres</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20 litres</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Duration of the session</td>
<td>Dermal</td>
<td>DUR&lt;sub&gt;con.der&lt;/sub&gt;</td>
<td>1st tertile</td>
<td>1</td>
<td>Duration of the session would increase the absorbance of the pesticide through the skin, and would increase the probability of the pesticide getting into the mouth through contaminated hands.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd tertile</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd tertile</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>DUR&lt;sub&gt;con.ing&lt;/sub&gt;</td>
<td>1st tertile</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd tertile</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd tertile</td>
<td>2.2</td>
<td></td>
</tr>
</tbody>
</table>

* The tertiles when mentioned for some variables have been derived from the available data in the literature as will be described in Chapter 5, Section 5.2.3.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>How mixed with bath</td>
<td>Dermal</td>
<td>MIX&lt;sub&gt;der&lt;/sub&gt;</td>
<td>Pouring directly in bath or using sachets Using a jug Using automatic unit</td>
<td>1</td>
<td>1.9 0.5 Using a jug to pour concentrate leads to handling contaminated objects twice, while using automatic units reduces the exposure through handling.</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>MIX&lt;sub&gt;ing&lt;/sub&gt;</td>
<td>Pouring directly in bath or using sachets Using a jug Using automatic unit</td>
<td>1</td>
<td>2.4 0.6</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>MIX&lt;sub&gt;inh&lt;/sub&gt;</td>
<td>Pouring directly in bath or using sachets Using a jug Using automatic unit</td>
<td>1</td>
<td>1.7 0.6</td>
</tr>
<tr>
<td>Atmospheric conditions (wind)</td>
<td>Dermal &amp; Ingestion</td>
<td>ATM&lt;sub&gt;con.der&lt;/sub&gt;</td>
<td>Inside bath or using sachets Still Breezy Gusting</td>
<td>1</td>
<td>1 1.1 1.2 Winds may increase dermal and ingestion exposure through splashes from pouring concentrate, but decrease the exposure through inhalation route because it reduces the concentration of the pesticide in the air.</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>ATM&lt;sub&gt;con.ing&lt;/sub&gt;</td>
<td>Inside bath or using sachets Still Breezy Gusting</td>
<td>1</td>
<td>1 0.7 0.4</td>
</tr>
<tr>
<td>Bath location</td>
<td>Inhalation</td>
<td>LOC</td>
<td>Outside and exposed Outside and sheltered Trailer Inside</td>
<td>1</td>
<td>1.1 1.4 1.7 When the bath is sheltered the concentration of the pesticides in the air would increase a little, especially if the bath was inside a building.</td>
</tr>
</tbody>
</table>
Table 3-11: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category a</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of dipped sheep</td>
<td>All</td>
<td>FLOCK</td>
<td>Discrete variable</td>
<td>Flock/median (369 sheep)</td>
<td>The probability of getting exposed to the dip increases with each sheep dipped in the bath.</td>
</tr>
<tr>
<td>Number of dippers</td>
<td>All</td>
<td>NUM</td>
<td>1-4 5</td>
<td>1-4: 1 5: 0.9</td>
<td>More farmers involved in dipping may lead to less exposure due to shifting or freedom of movement away from the bath.</td>
</tr>
<tr>
<td>Duration of the session</td>
<td>Dermal&amp; Ingestion</td>
<td>DUR_{dip.der} DUR_{dip.ing}</td>
<td>1st tertile 2nd tertile 3rd tertile</td>
<td>1 2 3.3</td>
<td>Duration of the session would increase the absorbance of the pesticide through skin and inhalation\textsuperscript{134}, and would increase the probability of the pesticide of getting into the mouth through contaminated hands.</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>DUR\textsubscript{dip.inh}</td>
<td>1st tertile 2nd tertile 3rd tertile</td>
<td>1 2 3.6</td>
<td></td>
</tr>
<tr>
<td>Dip rate</td>
<td>Dermal</td>
<td>RATE\textsubscript{der}</td>
<td>1st tertile 2nd tertile 3rd tertile</td>
<td>1 2 3.3</td>
<td>When farmers work faster they normally become less careful and allow too many sheep in the bath at the same time which increases the splashes from the bath\textsuperscript{12}.</td>
</tr>
<tr>
<td></td>
<td>Ingestion&amp; Inhalation</td>
<td>RATE\textsubscript{ing} RATE\textsubscript{inh}</td>
<td>1st tertile 2nd tertile 3rd tertile</td>
<td>1 2 3</td>
<td></td>
</tr>
<tr>
<td>Bath type</td>
<td>Dermal</td>
<td>BATH\textsubscript{dip.der} Linear Circular Mobile</td>
<td>1 0.9 1.1</td>
<td>Exposure to diluted dip was greater when linear bath was used compared to circular bath\textsuperscript{12,104}. Bath type affects exposure through skin and ingestion more than inhalation.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>BATH\textsubscript{dip.ing} Linear Circular Mobile</td>
<td>1 0.9 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>BATH\textsubscript{dip.inh} Linear Circular Mobile</td>
<td>1 1 0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} The tertiles when mentioned for some variables have been derived from the available data in the literature as will be described in Chapter 5, Section 5.2.3.
Table 3-11: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bath location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>LOC&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>If the bath is inside exposure through inhalation would increase since the concentration of the pesticide in the air would increase.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>LOC&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>LOC&lt;sub&gt;dip,inh&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td>1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Splash guard</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>GUARD&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td>No</td>
<td>1</td>
<td>0.7</td>
<td>Splash guard reduces the exposure through splashes&lt;sup&gt;12,104&lt;/sup&gt;.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>GUARD&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>No</td>
<td>1</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sheep entry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>ENTRY&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1</td>
<td>1.1</td>
<td>Exposure to diluted dip was greater when the dipper ushers the sheep in manually. Using a slipway method produces more splashes than using a slope&lt;sup&gt;12,104&lt;/sup&gt;.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1.1</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>ENTRY&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1.1</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>ENTRY&lt;sub&gt;dip,inh&lt;/sub&gt;</td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walk in method (Slope or ramp) Manual</td>
<td>1.1</td>
<td>1.7</td>
<td></td>
</tr>
</tbody>
</table>
Table 3-11: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Submerging tool</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td></td>
<td>TOOL_dip_der</td>
<td>NA (if doesn’t plunge sheep)</td>
<td>1</td>
<td>Dippers who used hands or feet to submerge sheep are more exposed than those who used a tool. Wooden tool may lead to more exposure as the wood can absorb the pesticide and make an additional contact to skin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Metal tool</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td></td>
<td>TOOL_dip_ing</td>
<td>NA: 1 (if doesn’t plunge sheep)</td>
<td>1</td>
<td>If the farmer uses his hands it is more probable that the splashes will enter his mouth. Using a wooden tool increases the probability of the pesticide getting into the mouth through contaminated hands.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Metal tool</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>5.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td>TOOL_dip_inh</td>
<td>NA: 1 (if doesn’t plunge sheep)</td>
<td>1</td>
<td>If the farmer uses his hands it is more probable to inhale the dispersed particles since his head will be closer to the surface of the water.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Metal tool</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Personal hygiene and behaviour</td>
<td></td>
<td>PHB_dip</td>
<td>Occasionally or at end of the day</td>
<td>1</td>
<td>Exposure will be reduced if the farmer washes sheep dip off regularly.</td>
</tr>
<tr>
<td>(washing off sheep dip)</td>
<td></td>
<td></td>
<td>Regularly</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td><strong>Atmospheric conditions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(wind)</td>
<td>Dermal &amp;</td>
<td>ATM_dip_der</td>
<td>Inside bath</td>
<td>1</td>
<td>Winds may increase dermal and ingestion exposure through splashes from the bath while it would decrease the exposure through inhalation because it reduces the concentration of the pesticide in the air.</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>ATM_dip_ing</td>
<td>Still</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>ATM_dip_inh</td>
<td>Inside bath</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Still</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>
Table 3-12: Exposure scores for variables of the disposal of sheep dip assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category a</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of the disposal</td>
<td>Dermal</td>
<td>METHOD&lt;sub&gt;dis.der&lt;/sub&gt;</td>
<td>Drain</td>
<td>1</td>
<td>Manual methods may lead to more exposure than mechanical ones, while using drain leads to the least contact.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Manual</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td></td>
<td>METHOD&lt;sub&gt;dis.ing&lt;/sub&gt;</td>
<td>Drain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Manual</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td>METHOD&lt;sub&gt;dis.inh&lt;/sub&gt;</td>
<td>Drain</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Manual</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Volume of sheep dip</td>
<td>Dermal</td>
<td>VOL&lt;sub&gt;dis.der&lt;/sub&gt;</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; tertile</td>
<td>1</td>
<td>Probability of contact with the dip increases with its volume.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; tertile</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; tertile</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Ingestion&amp; Inhalation</td>
<td>VOL&lt;sub&gt;dis.ing&lt;/sub&gt;</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; tertile</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VOL&lt;sub&gt;dis.inh&lt;/sub&gt;</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; tertile</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VOL&lt;sub&gt;dis.inh&lt;/sub&gt;</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; tertile</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Bath location</td>
<td>Dermal</td>
<td>LOC&lt;sub&gt;dis.der&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td>If the bath is inside or in a trailer exposure through skin and ingestion would be more due to the restriction of movement, and inhalation of the pesticide would increase due to an increase in the concentration in the air.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trailer</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inside</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>LOC&lt;sub&gt;dis.ing&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trailer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inside</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LOC&lt;sub&gt;dis.inh&lt;/sub&gt;</td>
<td>Outside</td>
<td>1</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trailer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inside</td>
<td>1.2</td>
<td></td>
</tr>
</tbody>
</table>

* The tertiles when mentioned for some variables have been derived from the available data in the literature as will be described in Chapter 5, Section 5.2.3.
Table 3-13: Exposure scores for variables of incidental exposure assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Score</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal hygiene and behaviour (washing out concentrate spills)</td>
<td>Dermal</td>
<td>PHBspil.der</td>
<td>At the end of the session</td>
<td>1</td>
<td>Exposure increases with increased time between spillage and washing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before meal break</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Immediately</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>Dermal</td>
<td>PHBspil.ing</td>
<td>At the end of the session</td>
<td>1</td>
<td>Washing immediately after spillage should greatly minimise the ingestion risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before meal break</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Immediately</td>
<td>0.1</td>
<td></td>
</tr>
</tbody>
</table>
3.9.4 Weights of exposure sources and routes

To combine all sources and routes in one model of ‘total exposure’ the weight of exposure through each route from each source and the weight of exposure from each source of the total exposure need to be estimated. Since there are different variables with different ranges of scores in each route of exposure from the same source, some form of equalising exposure estimates across routes is required. This equalisation was done based on the developed probabilistic model described in detail in Chapter 5. The probabilistic model was used first to obtain the nine percentiles (10th, 20th, etc.) of the distribution of each individual route components of the model (i.e. CON<sub>der</sub>, CON<sub>ing</sub>, CON<sub>inh</sub>, DIP<sub>der</sub>, etc.). These nine percentiles were used to obtain the same grading scale for exposure through each route (i.e. exposure results were ranked into ten grades (1, 2, 3… 10) based on the determined nine percentiles where 1 denoted exposures under the 10<sup>th</sup> percentile and 10 denoted exposures over 90<sup>th</sup> percentile).

By using the same grading scale for all routes, the parameters of each route (α<sub>der</sub>, α<sub>ing</sub>, α<sub>inh</sub>, β<sub>der</sub>, etc.) will give more weight to one route than another and these parameters were assigned by the experts. The five experts were asked to estimate the contribution of exposure through each route to the total exposure from each exposure source after assuming the maximum expected exposure intensity through all routes and taking into account the difference in the uptake between the different routes. After obtaining the estimates from the experts, the geometric mean of their middle three estimates was calculated and then parameters of exposure through each route in each source were extracted by assuming the dermal route as a baseline (i.e. parameters of dermal route in all sources were set to 1). The parameters of other routes are presented in Table 3-14.

Table 3-14: Weights of exposure routes for each exposure source in sheep dipping

<table>
<thead>
<tr>
<th>Exposure source</th>
<th>Parameters of routes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dermal</td>
</tr>
<tr>
<td>Handling the concentrate</td>
<td>α&lt;sub&gt;der&lt;/sub&gt; = 1.00</td>
</tr>
<tr>
<td>Dipping sheep in the bath</td>
<td>β&lt;sub&gt;der&lt;/sub&gt; = 1.00</td>
</tr>
<tr>
<td>Handling dipped sheep</td>
<td>γ&lt;sub&gt;der&lt;/sub&gt; = 1.00</td>
</tr>
<tr>
<td>Disposal of sheep dip</td>
<td>δ&lt;sub&gt;der&lt;/sub&gt; = 1.00</td>
</tr>
<tr>
<td>Incidental exposure</td>
<td>ε&lt;sub&gt;der&lt;/sub&gt; = 1.00</td>
</tr>
</tbody>
</table>

Then, the probabilistic model was used again to obtain the distribution of exposure from each source (i.e. CON, DIP, AFT, DIS, and INC) but this time by using the grades of each route resulted from the first use of the probabilistic model and using the assigned
parameters of each route. The distribution was used to assign 10 grades for the source components according to nine percentiles to equalise exposure estimates across sources.

By using the same grading scale for all sources, the parameters of each source \((a, \beta, \gamma, \delta, \text{ and } \varepsilon)\) will give more weight to one source than another and these parameters were assigned by the experts. The five experts were asked to estimate the contribution of exposure from each source to the total exposure after assuming the maximum expected exposure from all sources except for falling in the bath which was assumed as one fall only. The geometric mean of the middle three estimates was calculated and parameters of exposure from each source were extracted by assuming DIP source as a baseline \((\beta = 1.00)\). The weights of other exposure sources are presented in Table 3-15.

### Table 3-15: Weights of pesticide exposure sources in sheep dipping

<table>
<thead>
<tr>
<th>Exposure source</th>
<th>Parameters of sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handling the concentrate</td>
<td>(a = 1.05)</td>
</tr>
<tr>
<td>Dipping sheep in the bath</td>
<td>(\beta = 1.00)</td>
</tr>
<tr>
<td>Handling dipped sheep</td>
<td>(\gamma = 0.53)</td>
</tr>
<tr>
<td>Disposal of sheep dip</td>
<td>(\delta = 0.26)</td>
</tr>
<tr>
<td>Incidental exposure</td>
<td>(\varepsilon = 0.19)</td>
</tr>
</tbody>
</table>

#### 3.10 Discussion

In this chapter, a new conceptual model of pesticide exposure in sheep dipping was developed. This aggregative model included all sources, routes, and modifying factors that affect pesticide exposure in sheep dipping. A semi-quantitative exposure algorithm was then derived to be used for improved estimation of exposure in epidemiological studies to determine association between long-term pesticide exposure and ill-health (Chapter 6 and 8).

All five exposure sources included in this new conceptual model were also included in the SHAPE model\(^\text{29}\) but not included in the empirical model of Buchanan \textit{et al.} which included only two sources; handling the concentrate and dipping sheep\(^\text{99}\). However, the new model includes many more modifying factors compared to the SHAPE model in the estimation of pesticide exposure from each source; especially for the two main sources (\textit{i.e.} handling the concentrate and dipping activity)

The new model gives a little higher weight for exposure from handling the concentrate compared to that from dipping in the diluted dip. This was not the case in the previous models which assigned a very high relative weight for exposure from handling the
concentrate\textsuperscript{2,99}. This difference originates from the different values assigned by the experts for the relative weight of each source. The disagreement in handling the concentrate might be because some experts took into consideration the recent use of concentrate sachets which is supposed to reduce the absolute contribution of exposure from this source significantly. The experts were asked to estimate the effect of using concentrate sachets instead of the traditional containers when assigning scores for this specific variable not when estimating the relative weight of handling the concentrate. This idea should have been stressed on when the assignments were requested from the experts. However, the applied methodology of using the geometric mean of the three middle values resulted in attenuation of this difference, and the relative weight of handling the concentrate was not so much higher than the dipping activity.

The methodology of using the geometric mean was used since when it is not feasible to reach a consensus between the experts through discussions, like the situation in this study, the use of average estimates becomes a solution for considerable differences\textsuperscript{145}. Any further refinements for the new model might obtain better scores by achieving consensus between the experts and by more clarifications for the process of assigning the scores and weights (e.g. when to estimate the effect of using concentrate sachets).

The experts have assigned the weights of each source based on the maximum potential exposure from that source. This approach might be suitable for the normal sources (i.e. all sources except the incidental one) but its use with incidental exposure might be tricky since this exposure is hugely variable. Incidental exposure includes falling in the dipping bath and spilling the concentrate on body. Falling in bath for example, can increase the exposure many times compared to the exposure from dipping sheep in the diluted dip if not followed by prompt changing clothes. However, it might not affect the exposure too much if the farmer changes his clothes immediately, which is more likely. The same argument is also applied on spilling the concentrate (with or without immediate wash) and normal handling of concentrate.

Previous sheep dipping models have focused mainly on the dermal route of exposure\textsuperscript{29,99}, and even when the inhalation route was included, it was included as a constant\textsuperscript{7}. The aggregation of exposure through different routes is challenging since in order to estimate the contribution of exposure through each route to the total exposure, not only the intensity of exposure through each route is required but also the rates of uptake via these routes\textsuperscript{390}. The new conceptual model combined the exposure through
ingestion, inhalation, and dermal routes in one aggregative model. This was done by summing up exposures through different routes from each source then by summing up exposures from different sources. This was made possible by the experts who estimated an appropriate contribution of each route to the total exposure from each source taking into account the uptake rate. The fact that dermal route is the most important route of exposure in sheep dipping\textsuperscript{7,12,29,99} resulted in the consistency of the assignments of the dermal route between the experts. This consistency was not the case of the other two routes, but it is expected that their contribution to the total exposure is likely to be much less.

The aggregation can be performed differently by summing up the exposure by routes across all sources then summing up exposures through all routes or even without the final summing across routes. The advantage of this alternative approach of aggregation is that it leads to estimate the total exposure from each route. These exposure estimates of each route can be validated and calibrated by ambient exposure measurements that are appropriate for that route, whereas these measurements are not helpful when the aggregation is carried out across routes. In addition to that, if biological markers are used to validate the model, the comparison between exposures summed by route across different sources and these markers might give additional insight in the relative importance of exposure routes. This comparison can be used to calibrate the estimated contribution of each route to the total exposure in a way that takes into account both exposure intensity and uptake rate.

However, the performed approach was chosen instead of the alternative one because one of the main purposes of this new model is to include exposures through all routes in the final exposure estimate, thus the final aggregation across routes is required. It was assumed that it is easier and more appropriate to estimate the contribution of each route to the total exposure from each source separately than to estimate the contribution of each route to the total exposure from all sources together. Moreover, the aggregation according to sources makes the comparison between the contributions of different sources to the total exposure easier, since such comparison is important to decide whether the inclusion of these sources in the model is effective or not. This comparison will be performed in Chapter 5. In addition to that, not all farmers are involved in all sheep dipping activities and therefore, the probability of a farmer to be involved in these activities should be included in the probabilistic model developed from this conceptual model. If the aggregation is performed by route across different sources, the inclusion of
this probability would have been more complicated. This inclusion of probabilities will be also performed in Chapter 5. Furthermore, handling the concentrate has been suggested to be the major source of pesticide exposure in sheep dipping\textsuperscript{12,99} and it might be reasonable in epidemiological studies to investigate the association between this source especially and health effects, which is easier when the aggregation is performed according to sources over all routes. This PhD study chose this approach for the previous reasons but the alternative approach might be applied in any further work on the exposure model. However, it is important to realise that if the contributions of all routes and sources to total exposure have been estimated without bias then both approaches – aggregation across exposure routes and across sources – will give the same final estimates.

The use of expert judgment in assigning scores for the majority of modifying factors was a result of the very limited exposure measurements in monitoring studies. In a previous method for structured assessment of airborne concentration\textsuperscript{291} and in the DREAM method for semi-quantitative dermal exposure assessment\textsuperscript{282} experts assigned values for variable effects in equal steps on a logarithmic scale. This was justified by the log-normal distribution which exposures generally follow. In this new model, the effect of many modifying factors on exposure was expected to be very small (\textit{e.g.} the use of a linear bath compared to a circular one, or using a slipway in sheep entry compared to a walk in method). Therefore, the logarithmic scale was not appropriate to be followed by the experts in this new model and a nonparametric scale was used.

The conceptual model includes many modifying factors not described in previous epidemiological studies. These factors were given the score of one because no data were available to base any decision on and because the probabilistic model cannot be applied to them if their distributions are unavailable as described in Chapter 5. To generate closer estimates to the true exposure, monitoring studies can be performed and the unavailable factors can be assigned appropriate scores. However, these unavailable factors might not affect the usage of the new model in epidemiological studies since most of them are not easy to be recognised or recalled by the dippers. Modifying factors like personal hygiene and behaviour and atmospheric conditions are complex since they include many embedded variables. For example, atmospheric conditions include, in addition to the wind, air temperature and air humidity and these two variables affect contaminant volatility interchangeably\textsuperscript{292}. Therefore the final algorithm included only wind variable under the modifying factor of atmospheric conditions.
Since the new model was developed to be used as a generic model for sheep dipping processes, chemical-specific modifying factors were also given the score of one in the final algorithm. Literature suggests that generic exposure models might not work well with all pesticides and this might lead to exposure misclassification\textsuperscript{138,139}. However, the use of generic exposure model in sheep dipping tends to be valid because it was supposed that exposure (not uptake) is affected only by non-chemical factors that are non-specific for the pesticide\textsuperscript{94} and also pesticides used in sheep dips usually have the same physical properties\textsuperscript{13}. Furthermore, few pesticides have been used as sheep dips in last decades with diazinon being the main pesticide in the UK market in the last twenty years\textsuperscript{12,45,99,293}.

The new model was built on the basis of one session not on the basis of frequent sessions. Therefore the application of this model in a historical study needs a modification by adding frequency variables (\textit{i.e.} number of dipping days and years). Validation studies are needed to get confidence in the estimation results of the new model either for the individual components (sources and routes) or for the total exposure.

In conclusion, the new developed conceptual model will likely lead to more realistic estimates of pesticide exposure in sheep dipping. However, aggregation across routes rather than across sources as done in this work may be a valuable approach for further validation in future work. In both cases, this new model needs further refinements especially for the weights of exposure sources and routes.
4.1 Introduction

To build a new exposure assessment model in any field, different types of data are used to determine sources of exposure, exposure routes, pesticide transport processes and exposure modifying factors, and each of these aspects are given an actual weight in the exposure assessment model. Although a number of studies have tried to identify sources and routes of exposure and factors that affect exposure in sheep dipping, limited data is still available about the actual effects of these sources, routes and factors on the exposure\textsuperscript{12,29,99,155}.

Ideally, every model for exposure assessment should be validated to be relatively sure that it gives a credible estimate for the real exposure. Validation studies need the availability of different indicators of exposure which is usually possible only for a subset of subjects within the same study\textsuperscript{127} or the validation will depend on other studies in which these indicators are available\textsuperscript{138,139}. These indicators could measure pesticide exposure or uptake. Both the measurement of pesticide exposure through three routes (skin, ingestion and inhalation) at the same time and combining the three measurements after that are complex\textsuperscript{104}. There are also difficulties in assessing the ingestion route\textsuperscript{99}. Therefore, a model which takes into account different routes of exposure is better to be validated depending on uptake indicators (\textit{e.g.} urinary metabolites) rather than direct exposure measurements\textsuperscript{104}.

Biological monitoring has been considered as one of the most accurate indicators of the actual absorbed dose of pesticides (uptake) and this monitoring could be performed by measuring pesticide metabolites in body fluids, urine or in other excreta\textsuperscript{136}. Acquavella \textit{et al.}\textsuperscript{138} and Coble \textit{et al.}\textsuperscript{139} have used biological monitoring to evaluate the algorithm developed by Dosemeci \textit{et al.}\textsuperscript{153} and used in the AHS study\textsuperscript{28}.

OP exposure can be biologically monitored either by measuring OP urinary metabolite levels or by monitoring the OP biological effects by measuring the reduction of plasma cholinesterase and AChE activity\textsuperscript{49}. Potential occupational exposure to OPs is generally low in farming activities, and therefore measuring OP urinary metabolite level is more practical since the depression of cholinesterase activity due to these activities is unlikely\textsuperscript{49,52}. 


The aim of this chapter was to evaluate the new sheep dipping exposure model developed and discussed in Chapter 3 by using exposure and OP urinary metabolite levels of sheep dippers who participated in the HSDS study. The evaluation was conducted by estimating OP exposure in sheep dipping sessions using the new model and then comparing the estimates with measured levels of OP urine metabolites.

4.2 Materials and methods

The HSDS study was described in Chapter 2. The farmers in the HSDS used different methods to treat their sheep; however only data from those farmers who dipped was used in this evaluation study because the model is specific for sheep dipping. The evaluation depended on the levels of OP urine metabolites in the samples collected in the second visit which supposed to be immediately after the first dipping day, therefore only farmers who used an OP sheep dip and gave a sample in the second visit were included in this study.

4.2.1 Analysis of OP urinary metabolites

The most frequent metabolites of OPs approved in the UK are DEP, DETP, DEDTP, DMP, DMTP and DMDTP\(^\text{48}\) (described in detail in Section 1.3.1.1.1). All of these metabolites are measured in the original HSDS study. During the study period, the only OP product licensed for sheep dipping in the UK was diazinon\(^\text{293,294}\). Diazinon is metabolised to DEP and DETP\(^\text{13}\) and therefore only the results of these two metabolites were analysed. In this work, DEP and DETP were added together to form a new variable (SUM).

Urine samples were collected three times; before treatment, as soon as possible after the start of treatment, and then about two or three weeks after the second visit. The traditional approach is to evaluate exposure estimates based on the difference in metabolite levels between pre and post-dipping samples. However, the first urine samples were not taken at the same time prior to the treatment for each farmer and may have been taken potentially after another use of pesticide. Therefore, the decision was made not to use the difference between sample 1 and 2, and only the values of sample 2 were used in this evaluation study.

Furthermore, ideally, the urine sample should have been collected at a specific time after the dipping had taken place. However, this was not done in the HSDS study in which the urine samples were collected at different times and the only available time is
the sampling day while the number of hours between dipping and sampling is not available. Unfortunately, these shortcomings in the HSDS data prevent the use of a pharmacokinetic model in this study.

4.2.2 Exposure estimates

The new semi-quantitative model has five different sources and for two of them, namely handling sheep after dipping and disposal of sheep dip, no information was collected in the HSDS and so they were not included in the model. The other three components, namely handling the concentrate (CON), dipping sheep in the bath (DIP) and incidental exposure (INC) were included in the model and were estimated according to the models in Section 3.8. The total exposure (TOTAL) was derived according to the following equation:

\[ \text{Eq. 4.1: } \text{TOTAL} = \alpha \times \text{CON} + \beta \times \text{DIP} + \epsilon \times \text{INC} \]

Where: \( \alpha, \beta, \) and \( \epsilon \) = Parameters.

None of the farmers mentioned getting wet through entering the dipping bath, therefore exposure through "fall in bath" which is part of INC was set at zero for all farmers. As not all the variables in the sheep dipping model were collected in the HSDS all these uncollected variables were set as constants according to the most frequent result found in sheep dipping literature (See Section 5.2.3 for details). The question about using PPE did not differentiate between its use during different activities (e.g. handling the concentrate or dipping sheep) so the answer to that question was assumed to apply to all activities. Appendix 5 lists the model constants for uncollected variables and the rules for handling missing information.

Four exposure estimates were calculated for the analysis; TOTAL (i.e. total exposure), DIP (i.e. exposure from dipping sheep in the bath only), CON (i.e. exposure from handling the concentrate only), and SHEEP. SHEEP, the number of dipped sheep, is a simple surrogate added to determine the difference, if any, between sophisticated models and simple surrogates. OP metabolites may be excreted through urine more than 24 hours after the exposure\textsuperscript{52}, therefore all of the four exposure estimates were computed twice; one for the exposure in the same day of sample 2 (Same day) and one for the exposure in the previous day (Previous day).
4.2.3 Statistical analysis

Different methods were used to determine associations between exposure estimates and diazinon urinary metabolite levels. Spearman correlation coefficients were used to study the correlation between exposure estimates and urinary metabolites since urinary metabolite levels and exposure estimates were not normally distributed. Urinary metabolites were categorised into both detected and undetected categories and logistic regression was used to assess the association with exposure estimates, whereas multinomial logistic regression was used when the metabolites were categorised into three ordinal groups. All logistic regression results were adjusted for age and number of days since last dip because it affects the metabolite level in the sample. Results were displayed in the form of odds ratio and 95% confidence interval (OR, 95%CI). Since only one farmer was a female no adjustment was carried out for sex. Both exposure estimates of sampling day and SUM metabolites were arranged in three relatively even groups according to their tertiles then inter-rater agreement test (kappa) was performed. This was not performed on DEP and DETP and neither on exposure estimates of the previous day since it was not possible to categorise them into three equal categories (many undetectable metabolite levels). Geometric means and standard deviations of urine metabolite levels were compared between three ordinal categories of exposure intensity of sampling day to investigate any trend. Trends were analyzed by regression analysis between the geometric means of metabolite levels and the medians of exposure categories.

4.3 Results

4.3.1 Descriptive analysis

Sixty eight out of 156 farmers who gave urine samples in the HSDS at the second visit had dipped sheep; 56 out of these 68 dippers used OPs, whereas 9 used pyrethroids and 3 used unknown products. Eleven dippers were excluded because the urine samples of nine of them were collected more than three days after the last dipping day and the other two farmers did not write down the number of sheep dipped in any day of treatment. At the end 45 dippers were included in the evaluation analysis.

The mean age of the farmers was 50 ± 11 years and all of them were men except one. No differences in age, sex, and number of dipped sheep were found between farmers included in the analysis and those 11 farmers who were not included. Figure 4-1 shows the frequency of number of days between sampling date and first and last dipping day.
More than half of urine samples (55.6%) were taken in the first day of treatment while only 3 samples were taken after 3 days of the first dipping day. The majority of farmers (77.8%) worked as plungers or as a plunger with other tasks during sheep dipping, 17.8% worked as a chucker, and 4.4% worked as a helper. Only 22.2% of the dippers did not handle the concentrate.

![Figure 4-1: Number of days between sampling and first dipping day and last dipping day](image)

As most samples were taken in the first dipping day, 77.8% of the farmers did not dip sheep in the previous day, whereas only 17.8% of the farmers did not dip any sheep in the same day of sampling or in the previous day. Details of the distributions of exposure estimates are shown in Table 4-1 while Figure 4-2 shows the distribution of TOTAL estimates. The exposure of the exposed dippers in the sampling day was relatively normally distributed, whilst exposure estimates of the previous day were scattered.

### Table 4-1: Pesticide exposure estimates

<table>
<thead>
<tr>
<th>Day</th>
<th>Model</th>
<th>Zero frequency (%)</th>
<th>Scores of estimated pesticide exposure *</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same day</td>
<td>SHEEP</td>
<td>12 (26.7)</td>
<td>455 ± 326</td>
<td>350</td>
<td>72 – 1430</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>12 (26.7)</td>
<td>8.0 ± 2.5</td>
<td>7.8</td>
<td>3.3 – 11.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>20 (44.4)</td>
<td>9.7 ± 2.5</td>
<td>11.1</td>
<td>3.5 – 11.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>12 (26.7)</td>
<td>13.1 ± 4.7</td>
<td>13.5</td>
<td>5.0 – 21.0</td>
<td></td>
</tr>
<tr>
<td>Previous day</td>
<td>SHEEP</td>
<td>35 (77.8)</td>
<td>303 ± 225</td>
<td>322</td>
<td>20 – 700</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>35 (77.8)</td>
<td>6.8 ± 3.3</td>
<td>8.1</td>
<td>1.2 – 10.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>37 (82.2)</td>
<td>10.2 ± 1.9</td>
<td>11.3</td>
<td>6.5 – 11.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>35 (77.8)</td>
<td>12.5 ± 5.4</td>
<td>13.5</td>
<td>1 – 17.5</td>
<td></td>
</tr>
</tbody>
</table>

*After excluding those with zero results*
Figure 4-2: Distribution of TOTAL exposure scores
(A) In the day of sampling, (B) In the previous day

OP urine metabolites were detected individually in about half of the samples. Table 4-2 presents the distribution of detected diazinon urinary metabolite levels while Figure 4-3 shows these distributions which are relatively log-normally distributed.

Figure 4-3: Distribution of detectable diazinon urinary metabolite levels
(A) DEP, (B) DETP, (C) SUM
Table 4-2: Detected urinary diazinon metabolite levels

<table>
<thead>
<tr>
<th>OP Metabolite</th>
<th>Detectable (%)</th>
<th>Metabolite levels (μmol/mol creatinine) a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>DEP</td>
<td>25 (55.6)</td>
<td>13.9 ± 9.2</td>
</tr>
<tr>
<td>DETP</td>
<td>26 (57.8)</td>
<td>39.8 ± 41.2</td>
</tr>
<tr>
<td>SUMb</td>
<td>34 (75.6)</td>
<td>40.6 ± 45.9</td>
</tr>
</tbody>
</table>

a Of urine samples containing detectable levels, b Total of both metabolites

4.3.2 Association between exposure estimates and diazinon urinary metabolites

Using Spearman correlation test, no significant correlations were found between diazinon urinary metabolites and sheep dipping exposure estimates either for the day of sampling or for the previous day (Table 4-3).

Table 4-3: Correlations between exposure estimates and diazinon metabolites

<table>
<thead>
<tr>
<th>Day</th>
<th>Model</th>
<th>Spearman Correlation coefficients (r) a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DEP</td>
</tr>
<tr>
<td>Same day</td>
<td>SHEEP</td>
<td>-0.15</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>-0.13</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>-0.07</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>-0.13</td>
</tr>
<tr>
<td>Previous day</td>
<td>SHEEP</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>0.10</td>
</tr>
</tbody>
</table>

a No statistically significant correlations were found

Similarly, logistic regression did not reveal any association between detecting individual urinary metabolites and exposure estimates either for the day of sampling or for the previous day (Table 4-4).

Table 4-4: Associations between exposure estimates and detecting diazinon metabolites

<table>
<thead>
<tr>
<th>Day</th>
<th>Estimation model</th>
<th>DEP (95%CI) a</th>
<th>DETP (95%CI) a</th>
<th>SUM (95%CI) a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same day</td>
<td>SHEEP</td>
<td>0.96 (0.78 – 1.18)</td>
<td>1.15 (0.91 – 1.46)</td>
<td>1.07 (0.82 – 1.40)</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>0.96 (0.76 – 1.21)</td>
<td>1.15 (0.90 – 1.47)</td>
<td>1.09 (0.83 – 1.43)</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>0.93 (0.81 – 1.08)</td>
<td>1.13 (0.97 – 1.32)</td>
<td>1.03 (0.87 – 1.21)</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>0.94 (0.82 – 1.07)</td>
<td>1.14 (0.99 – 1.32)</td>
<td>1.03 (0.89 – 1.21)</td>
</tr>
<tr>
<td>Previous day</td>
<td>SHEEP</td>
<td>1.36 (0.84 – 2.23)</td>
<td>0.99 (0.68 – 1.44)</td>
<td>1.18 (0.68 – 2.03)</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>1.14 (0.92 – 1.41)</td>
<td>1.04 (0.85 – 1.27)</td>
<td>1.10 (0.84 – 1.43)</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>1.13 (0.95 – 1.36)</td>
<td>1.02 (0.87 – 1.20)</td>
<td>1.08 (0.87 – 1.33)</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>1.09 (0.96 – 1.24)</td>
<td>1.02 (0.91 – 1.14)</td>
<td>1.06 (0.91 – 1.22)</td>
</tr>
</tbody>
</table>

a Adjusted for age and number of days since last dip
Using the lowest category of each diazinon urinary metabolites (DEP, DETP and SUM) as a reference to perform multinomial logistic regression, exposure estimates were not significantly associated with having medium or high values of urinary metabolites (Table 4-5).

Table 4-5: Association between exposure estimates and urinary diazinon metabolites

<table>
<thead>
<tr>
<th>Day</th>
<th>Exposure Model</th>
<th>Metabolite level</th>
<th>OR (95% CI) *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>DEP</td>
</tr>
<tr>
<td>Same day</td>
<td>SHEEP</td>
<td>Medium</td>
<td>1.01 (0.80 - 1.28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>0.89 (0.67 - 1.19)</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>Medium</td>
<td>1.08 (0.81 - 1.44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>0.85 (0.63 - 1.13)</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>Medium</td>
<td>0.91 (0.77 - 1.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>0.95 (0.80 - 1.14)</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>Medium</td>
<td>0.96 (0.82 - 1.12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>0.92 (0.78 - 1.08)</td>
</tr>
<tr>
<td>Previous day</td>
<td>SHEEP</td>
<td>Medium</td>
<td>1.49 (0.89 - 2.50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>1.20 (0.68 - 2.12)</td>
</tr>
<tr>
<td></td>
<td>DIP</td>
<td>Medium</td>
<td>1.18 (0.93 - 1.49)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>1.09 (0.84 - 1.40)</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>Medium</td>
<td>1.12 (0.92 - 1.38)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>1.13 (0.93 - 1.37)</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>Medium</td>
<td>1.10 (0.96 - 1.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>1.08 (0.94 - 1.24)</td>
</tr>
</tbody>
</table>

* The reference is the lowest category of urinary metabolites and the association is adjusted for age and number of days since last dip.

An inter-rater agreement analysis using Kappa test was performed to study the agreement between estimated exposures and SUM when all of them were grouped into three equal ordinal categories. Slight agreements were found between SUM and exposure estimates according to SHEEP and DIP in day the sampling (kappa =0.10) but they were not significant (Table 4-6).

Table 4-6: Inter-rater agreement between exposure estimates of sampling day and total urinary diazinon metabolites

<table>
<thead>
<tr>
<th>Model *</th>
<th>Kappa</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEEP</td>
<td>0.10</td>
<td>0.34</td>
</tr>
<tr>
<td>DIP</td>
<td>0.10</td>
<td>0.34</td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* 44.4% of CON results were zero in sampling day; three equal categories were not possible.
Table 4-7 presents the geometric means and geometric standard deviations of urinary metabolites when stratified by intensity of pesticide exposure. Positive trends were found for DETP and SUM with increasing exposures using all estimates in the day of sampling. The trend of SUM geometric means was significant with the CON model (P=0.04) and borderline significant with the DIP model (P=0.09). Positive trends were seen in DEP according to SHEEP, DIP and TOTAL estimates of the previous day but they were not significant. The same trends were also found in SUM according to DIP and TOTAL estimates but only the trend that was according to the DIP estimates was borderline significant (P=0.07). The trends of DEP geometric means were negative according to SHEEP, DIP and CON estimates; however only that which was according to the DIP estimates was borderline significant.

### Table 4-7: Geometric means of diazinon urinary metabolites by three exposure intensities

<table>
<thead>
<tr>
<th>Day</th>
<th>Exposure</th>
<th>Urinary metabolites (µmol/mol creatinine)</th>
<th>DEP</th>
<th>DETP</th>
<th>SUM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>GM (GSD)</td>
<td>P&lt;sub&gt;t&lt;/sub&gt;</td>
<td>GM (GSD)</td>
<td>P&lt;sub&gt;t&lt;/sub&gt;</td>
</tr>
<tr>
<td>Same day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLEEP</td>
<td>Low</td>
<td>15</td>
<td>5.1 (4.4)</td>
<td>0.10</td>
<td>5.3 (7.7)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>14</td>
<td>4.2 (3.9)</td>
<td></td>
<td>6.8 (5.0)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>16</td>
<td>3.2 (3.5)</td>
<td></td>
<td>7.1 (5.9)</td>
</tr>
<tr>
<td>DIP</td>
<td>Low</td>
<td>15</td>
<td>5.1 (4.4)</td>
<td>0.05</td>
<td>5.3 (7.7)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>15</td>
<td>3.9 (4.0)</td>
<td></td>
<td>6.0 (5.1)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>15</td>
<td>3.4 (3.4)</td>
<td></td>
<td>8.1 (5.8)</td>
</tr>
<tr>
<td>CON</td>
<td>Low</td>
<td>20</td>
<td>4.3 (3.7)</td>
<td>0.45</td>
<td>4.3 (6.0)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>10</td>
<td>4.3 (3.9)</td>
<td></td>
<td>6.8 (5.0)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>15</td>
<td>3.7 (4.3)</td>
<td></td>
<td>10.4 (6.5)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>Low</td>
<td>15</td>
<td>5.3 (3.8)</td>
<td>0.50</td>
<td>3.7 (6.1)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>15</td>
<td>3.3 (4.1)</td>
<td></td>
<td>8.2 (5.5)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>15</td>
<td>3.9 (3.9)</td>
<td></td>
<td>8.7 (6.2)</td>
</tr>
<tr>
<td>Previous day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLEEP</td>
<td>Low</td>
<td>35</td>
<td>3.8 (4.0)</td>
<td>0.55</td>
<td>6.3 (6.2)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>5</td>
<td>5.0 (4.4)</td>
<td></td>
<td>13.9 (5.4)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>5</td>
<td>5.1 (2.8)</td>
<td></td>
<td>3.2 (4.9)</td>
</tr>
<tr>
<td>DIP</td>
<td>Low</td>
<td>35</td>
<td>3.8 (4.0)</td>
<td>0.11</td>
<td>6.3 (6.2)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>5</td>
<td>4.6 (4.1)</td>
<td></td>
<td>5.6 (5.1)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>5</td>
<td>5.4 (3.1)</td>
<td></td>
<td>7.9 (7.5)</td>
</tr>
<tr>
<td>CON</td>
<td>Low</td>
<td>37</td>
<td>3.7 (4.0)</td>
<td>0.35</td>
<td>6.2 (6.1)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>4</td>
<td>6.6 (3.5)</td>
<td></td>
<td>16.5 (1.6)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>4</td>
<td>5.6 (3.7)</td>
<td></td>
<td>3.1 (9.7)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>Low</td>
<td>35</td>
<td>3.8 (4.0)</td>
<td>0.34</td>
<td>6.3 (6.2)</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>5</td>
<td>3.9 (3.7)</td>
<td></td>
<td>10.6 (4.0)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>5</td>
<td>6.5 (3.3)</td>
<td></td>
<td>4.2 (7.9)</td>
</tr>
</tbody>
</table>

* P<sub>t</sub>= p-for-trend
4.4 Discussion

This study aimed to evaluate the new sheep dipping model by using pesticides urinary metabolites as a reference. Pesticide exposure scores estimated by the new model were compared with the urinary metabolites based on the assumption that the increment in pesticide exposure should be associated with an increment in urinary metabolite levels. This evaluation study was applied to one pesticide, diazinon, which was licensed for use as a sheep dip in the UK.

Positive trends in geometric means were found in DETP and SUM (total of diazinon metabolites) when compared between three ordinal categories of exposure intensity in the day of sampling and some of them in the previous day. The trend of SUM according to CON exposure estimates was significant. Slight but not significant agreements were found between SUM and exposure estimates according to SHEEP and DIP on the sampling day. However, generally no significant correlations were found between estimated pesticide exposures and urinary metabolites. The use of the new model (TOTAL), its components (DIP and CON) or the surrogate (SHEEP) had no effect on the results.

The apparent poor association between the results of the new model and the OP metabolite levels may not suggest a poor model, but may have a number of possible other explanations; most notably that the HSDS study was not designed as an evaluation study for this model. Therefore its conditions (e.g. collected variables, timing of urine samples) were not completely appropriate for such a study. Although many modifying factors have been identified in the new model of sheep dipping, information on some of them were not collected in the HSDS. For instance, two main sources of exposure, namely the disposal of sheep dip and handling sheep after dipping were not addressed in this evaluation study, while also different variables about dipping activity, like bath type and the presence of splashing guards, were not collected. The probabilistic model developed from the new conceptual model showed that the contribution of these sources (i.e. disposal of sheep dip and handling dipped sheep) to the total exposure is not minimal (Chapter 5).

Pre-dipping urine samples were taken at different times prior to the dipping session. Since this time becomes critical if there is potential pesticide exposure from other sources, any differences in urine metabolites between the pre and post dipping session were ignored. Therefore, levels of urine metabolites found in the post-dipping samples
and used in this study may not simply have come from the last dipping session only. Furthermore, post-dipping samples in this study were collected in one, two or three days after the last dipping session. This number of days was adjusted for in the analysis but metabolite levels change every hour after exposure\textsuperscript{13,50}, which means that the measured metabolite levels might significantly vary due to the variation of sampling time not due to the variation of exposure. Additionally, OP metabolite excretion peaks at different times according to the exposure route. For example, DEP and DETP excretion peaked at 2 hours after the oral exposure to diazinon and 90\% of the metabolites were excreted within 14 hours, whilst after dermal exposure, the metabolites peaked after 12 hours and 60\% of the metabolites were excreted after 6 to 26 hours\textsuperscript{52}. Therefore, the collecting of 24-hour post-dipping urine is the optimal option for evaluation studies not a spot urine sample\textsuperscript{296}, but this 24-hour urine was not collected in the HSDS study since in a field situation it is not always practical.

Since the half-lives of DEP and DETP vary according to the route of exposure, it was suggested that a spot urine sample at the end of an 8 hours shift reflects about 10\% of dermal exposure in the previous hour, 80\% of exposure over the whole working day and 10\% of exposure from the previous day. For oral exposure the spot sample reflects 25\% of exposure in the previous hour and the rest reflects exposure of the remaining working day\textsuperscript{52}. If exposure was aggregated in the sheep dipping model according to the routes instead of aggregating according to exposure sources, these representative values of the spot urine sample would have been used to make the comparison with exposure estimates. Such approach will be used if the model modified in a future work. Moreover, percentages of diazinon excreted as urinary DAP vary significantly between dermal and oral routes (about 1\% and 60\% respectively)\textsuperscript{52}. Therefore, the modification of the model to be aggregated according to exposure routes would help in taking the differences in absorption, metabolism and excretion rates between routes into account when making the comparison with the urinary metabolites.

The proportions of DEP and DETP urinary metabolites after diazinon exposure vary according to the route of exposure and these proportions vary with time after exposure and therefore previous studies used the sum of DAP metabolites as an estimate of exposure\textsuperscript{49,99,155}. In the study of Grafitt \textit{et al.} the ratio of DETP to DEP excretion was about 7:1 at 2 hours after oral exposure and this ratio declined to be 1:1 at 8 hours after exposure, while the ratio ranged around 3.5:1 at 4 to 12 hours after dermal exposure and then decreased to reach 1:1 at about 20 hours after exposure\textsuperscript{52}. Moreover, DEP is
produced as a result of the oxidative metabolic pathway of diazinon while DETP is produced as a result of the hydrolysis pathway. Therefore, different proportions of excreted DEP and DETP in individuals might be discovered after same level of exposures because of the interindividual differences in metabolism. In addition to that, the analytical method itself might produce some conversion of DETP to DEP, which may to some extent explain differences between individuals but this conversion is very low and constant. Thus, the use of the sum of both metabolites is more appropriate than the use of a single marker in evaluating diazinon exposure estimates.

Moreover, although the dermal route is the most important route of pesticide exposure it was reported previously that only about 1% of a dermal dose of diazinon was excreted as urinary DEP and DETP. In addition to that, urinary metabolite levels measured in this study were generally low and a quarter of the samples had no detectable levels, which is consistent with previous studies. Such low levels might affect the correlation between predicted exposure and urinary metabolite levels.

The presence of DMP, DMTP and other OP urinary metabolites which are not related to diazinon exposure was also detected in many urine samples as reported in the HSDS study. The source of these metabolites was not identified and could be due to dietary exposure either to the pesticides or to the metabolites themselves. However, the presence of these metabolites might also indicate that dippers may have being exposed to other OPs coming from other sources different from sheep dipping. This is supported by the fact that 63% of farmers who used only avermectins and 75% of those who used only triazines in sheep treatment in the HSDS study had detectable levels of urinary OP and pyrethroid metabolites. Other OPs used in agricultural work like chlorpyrifos may increase DEP and DETP meaning that other OP exposure sources should be controlled or at least adjusted for in evaluation studies; both were not applicable in this study.

The difference between exposure and uptake is probably another reason of the poor association. The urinary metabolites are indicators of uptake and many factors can play a role in influencing differences between exposure and uptake. Physiological differences (e.g. surface area, skin thickness and condition), temperature and humidity are examples of these factors. In addition to that, levels of urinary metabolites may vary not only due to the variability in the uptake but also due to the variability in the rate of metabolism and excretion between individuals, let alone intraindividual variation which can be considerable and therefore needs repeated biological assessment.
Exposure estimation in this study has depended on self reported information about sheep dipping sessions. Better correlations have been found between intensity scores and urinary metabolites when field observers were used to assess exposure rather than the farmers themselves\(^\text{138}\). This suggests that evaluation studies of new models should better depend on the assessment of expert occupational hygienists instead of self-reported exposure.

On the other hand, the poor association could be attributed to different shortcomings in the new model. One of the main concerns in this model is the weight assigned to each source of exposure. These weights were assigned by experts, and this assignment depended on their knowledge of sheep dipping processes and practices. The positive trend of the metabolite geometric means according to the CON component was significant while the trends with the DIP component and the TOTAL model were not significant. This may indicate that the exposure during handling the concentrate is more important than the exposure during other activities which is consistent with previous studies\(^\text{12,99}\). Such a finding might suggest that the weight of the CON component (\(\alpha\)) should be increased. On the other hand, the occupational practices may have changed in the recent years which can affect the importance of each source in the total exposure. For instance, farmers tend these days to use sachets of concentrate instead of using big containers, and these sachets were designed to reduce contact with the concentrate, suggesting that if this practice becomes predominant, the weight of handling the concentrate in this model should be reduced when it is used to estimate pesticide exposure in recent sheep dipping sessions.

Another main concern in this model is the use of PPE. Using PPE can reduce exposure substantially and can nearly eliminate the dermal exposure if used properly\(^\text{99,151}\). However, if the PPE is not used correctly or has become old it may increase exposure to pesticides\(^\text{181}\). Since it is difficult for farmers to assess whether their use of PPE is proper or not, the question about the use of PPE in the model was limited to “Did you use (yes/no)” for each type of PPE.

The new model is generic for all type of pesticides. Many studies have found that some pesticide exposure models are valid for few kinds of applied pesticides and generalizing the models over all pesticides will result in some errors\(^\text{123,139,298}\). Generic models are more applicable in epidemiological studies where different kinds of pesticides will be found; however the use of diazinon as the only approved pesticide for dipping sheep in
the UK for about ten years may make it important to develop a specific model for
diazinon.

In conclusion, additional improvements in the new sheep dipping model, especially in
the weight of handling the concentrate and on the variable of PPE use, may lead to
better exposure estimations. However, in this evaluation study weak correlations were
found between exposure estimates and urinary pesticide metabolite data available from
the HSDS study. Most likely, this seems to be because of various shortcomings in the
available dataset that prohibit valid comparison with the derived exposure estimates. As
such, the question about the validity of this model will need be answered through future
dedicated and controlled studies
5.1 Introduction

The use of any model includes the possibility of two types of uncertainty; namely parameter (variable) uncertainty and modelling uncertainty\textsuperscript{299}. The first relates to inaccurate or incomplete measurements whilst the second relates either to the way of combining different variables or to the decisions taken by the analysts. Contextual uncertainty, which is related to the boundaries and the definitions used in the assessment, have also been reported among other types of uncertainties\textsuperscript{300}.

Contextual uncertainty can be reduced by proper discussion about the definitions, reporting them and using them consistently. Modelling uncertainty usually emerges from lacking and contradictory knowledge and can be reduced by more research. However, modelling uncertainty can also be dealt with by the use of different conceptual models, exploring their pedigree and how much these models sufficiently represent the range of plausible models\textsuperscript{301}.

Probabilistic analysis which employs Monte Carlo simulation has been used to handle variable uncertainty\textsuperscript{302}. A probabilistic model utilises “the full range of potential observations and combines these to accurately simulate the potential consumer, environmental or worker exposure”\textsuperscript{303}. Thus to extract a probabilistic model from any deterministic model, the distributions of all model variables should be obtained, the model should be modified to include the uncertainty of its components, and an appropriate technique should be used to simulate the output. Monte Carlo Analysis is a technique developed in the 1940s which uses statistical sampling techniques to attain a distribution of the model’s output, while simulation is the repetitive process of random application of a model’s algorithm according to the input variable distributions\textsuperscript{304}.

Probabilistic models can be used to decrease the degree of determinism in the exposure assessment and to be closer to real exposure scenarios by simultaneously simulating all different exposure conditions and integrating all sources of parameter uncertainty\textsuperscript{305}. The distribution of the exposure model output will estimate the probability of the real exposure to be more or less than the deterministic estimate\textsuperscript{306}. Whereas probabilistic exposure modelling has been used in environmental epidemiology\textsuperscript{307-311}, its use in occupational settings remains limited\textsuperscript{312-314}. Probabilistic models in pesticides have been
mainly used to help regulators in making their decisions regarding consumer and worker exposure to pesticides in order to have more realistic risk assessments\textsuperscript{303,315}.

The aim of this study is to develop a probabilistic model for pesticide exposure in sheep dipping based on the conceptual model described in Chapter 3, to obtain the distributions of the exposure estimates and to determine the contribution of each source to the total exposure. This probabilistic model will help also in exploring the effect of unavailable data on exposure determinants in exposure assessment by applying the probabilistic model to different exposure scenarios and comparing the results of deterministic and probabilistic approaches. Ultimately, the probabilistic model developed in this chapter will be used in Chapter 8 among other methodologies to study associations between long-term pesticide exposure and several adverse health effects.

5.2 Development of the probabilistic model

5.2.1 Development steps

Figure 5-1 shows the development steps of this model. The new conceptual sheep dipping algorithm was transformed into a probabilistic model, and the distributions of all model variables were extracted from the literature. Monte Carlo simulation was used based on variable distributions to predict the distribution of the exposure estimates during one sheep dipping session. Using MS Excel software (2003) 10,000 samples of semi-quantitative exposure intensity scores were generated. Excel software was used to perform Monte Carlo simulation as described by Vertex42.com\textsuperscript{316}. Each variable was allocated a cell in the Excel sheet. The software picked one value for each variable from its distribution found in the literature and scored it according to the scores assigned by the experts (Section 3.9). Then the model was applied to the results of all variables to get the first exposure estimate. This process was repeated 10,000 times and the results formed the distribution of the overall exposure.

Monte Carlo simulation was performed three times (Figure 5-1). The first was performed on the individual route components of the model (\textit{i.e.} CON\textsubscript{der}, CON\textsubscript{ing}, CON\textsubscript{inh}, DIP\textsubscript{der}, etc.). The results were used to assign 10 grades for the route components according to nine percentiles (See Section 3.9.4). The second was performed on the source component (\textit{i.e.} CON, DIP, AFT, DIS, and INC). The results were also used to assign 10 grades for the source components according to nine percentiles. The final simulation was performed for the whole model and results of the
total exposure estimates obtained. The percentiles of the route exposures and source exposures resulted from the first two sets of simulations were used also in any further use of the new exposure algorithm (e.g. for SHAW farmers or for the exposure scenarios).

5.2.2 Modification of the conceptual algorithm

The probabilities of getting exposed from different sources (e.g. handling the concentrate or handling the dipped sheep) were added to the conceptual algorithm to make it suitable for a probabilistic model. No probability variable for dipping activity

**Figure 5-1: Methodology for developing the probabilistic exposure model of sheep dipping**
(DIP) was added since all farmers were considered to be involved in this activity at least as helpers. The final algorithms used in the probabilistic model were as follows:

Eq. 5.1: \( \text{EXPOSURE} = \alpha \times \text{CONPRO} + \beta \times \text{DIP} + \gamma \times \text{AFTPRO} + \delta \times \text{DISPRO} + \varepsilon \times \text{INCPRO} \)

Where:
\( \alpha, \beta, \gamma, \delta \text{ and } \varepsilon \) = Parameters;
\( \text{CONPRO} \) = Exposure from handling the concentrate taking into account its probability;
\( \text{DIP} \) = Exposure from dipping sheep in the bath;
\( \text{AFTPRO} \) = Exposure from handling dipped sheep taking into account its probability;
\( \text{DISPRO} \) = Exposure from disposal of sheep dip taking into account its probability;
\( \text{INCPRO} \) = Exposure from incidental exposure taking into account its probability.

DIP was calculated using Eq. 3.2.2 while other exposures are calculated as follows:

Eq. 5.1.1: \( \text{CONPRO} = \alpha_{\text{der}} \times \text{CONPRO}_{\text{der}} + \alpha_{\text{ing}} \times \text{CONPRO}_{\text{ing}} + \alpha_{\text{inh}} \times \text{CONPRO}_{\text{inh}} \)

Eq. 5.1.1.1: \( \text{CONPRO}_{\text{der}} = \text{PRO}_{\text{con}} \times \text{CON}_{\text{der}} \) (calculated by Eq. 3.2.1.1)

Eq. 5.1.1.2: \( \text{CONPRO}_{\text{ing}} = \text{PRO}_{\text{con}} \times \text{CON}_{\text{ing}} \) (calculated by Eq. 3.2.1.2)

Eq. 5.1.1.3: \( \text{CONPRO}_{\text{inh}} = \text{PRO}_{\text{con}} \times \text{CON}_{\text{inh}} \) (calculated by Eq. 3.2.1.3)

Where: \( \text{PRO}_{\text{con}} \) was the probability of handling the concentrate.

Eq. 5.1.2: \( \text{AFTPRO} = \gamma_{\text{der}} \times \text{AFTPRO}_{\text{der}} + \gamma_{\text{ing}} \times \text{AFTPRO}_{\text{ing}} + \gamma_{\text{inh}} \times \text{AFTPRO}_{\text{inh}} \)

Eq. 5.1.2.1: \( \text{AFTPRO}_{\text{der}} = \text{PRO}_{\text{aft}} \times \text{AFT}_{\text{der}} \) (calculated by Eq. 3.2.3.1)

Eq. 5.1.2.2: \( \text{AFTPRO}_{\text{ing}} = \text{PRO}_{\text{aft}} \times \text{AFT}_{\text{ing}} \) (calculated by Eq. 3.2.3.2)

Eq. 5.1.2.3: \( \text{AFTPRO}_{\text{inh}} = \text{PRO}_{\text{aft}} \times \text{AFT}_{\text{inh}} \) (calculated by Eq. 3.2.3.3)

Where: \( \text{PRO}_{\text{aft}} \) was the probability of contacting dipped sheep.

Eq. 5.1.3: \( \text{DISPRO} = \delta_{\text{der}} \times \text{DISPRO}_{\text{der}} + \delta_{\text{ing}} \times \text{DISPRO}_{\text{ing}} + \delta_{\text{inh}} \times \text{DISPRO}_{\text{inh}} \)

Eq. 5.1.3.1: \( \text{DISPRO}_{\text{der}} = \text{PRO}_{\text{dis}} \times \text{DIS}_{\text{der}} \) (calculated by Eq. 3.2.4.1)

Eq. 5.1.3.2: \( \text{DISPRO}_{\text{ing}} = \text{PRO}_{\text{dis}} \times \text{DIS}_{\text{ing}} \) (calculated by Eq. 3.2.4.2)

Eq. 5.1.3.3: \( \text{DISPRO}_{\text{inh}} = \text{PRO}_{\text{dis}} \times \text{DIS}_{\text{inh}} \) (calculated by Eq. 3.2.4.3)

Where: \( \text{PRO}_{\text{dis}} \) was the probability of taking part in disposal of sheep dip.

Eq. 5.1.4: \( \text{INCPROB} = \varepsilon_{\text{der}} \times \text{INCPROB}_{\text{der}} + \varepsilon_{\text{ing}} \times \text{INCPROB}_{\text{ing}} \)

Eq. 5.1.4.1: \( \text{INCPROB}_{\text{der}} = \text{PRO}_{\text{fall}} \times \text{FALL} \times \text{LEVEL} \times \text{PHB} \)

\[ + \text{PROB}_{\text{spil}} \times \text{SPIL} \times \text{AMOUNT} \times \text{CONC}_{\text{con}} \times \text{PPE} \times \text{PHB} \]

Eq. 5.1.4.2: \( \text{INCPROB}_{\text{ing}} = \text{PRO}_{\text{fall}} \times \text{FALL} \times \text{PHB} \)

\[ + \text{PROB}_{\text{spil}} \times \text{SPIL} \times \text{AMOUNT} \times \text{CONC}_{\text{con}} \times \text{PPE} \times \text{PHB} \]
Where:
PROfall = Probability of falling in the dip bath;
PROspil = Probability of spilling the concentrate on body;
FALL = Number of falls;
LEVEL = Level of immersion;
PHB = Personal hygiene and behaviour;
SPIL = Frequency of spillage of the concentrate on a part of the body;
AMOUNT = Average amount of concentrate spills;
CONCcon = Concentration of the pesticide in the container;
PPE = Personal protective equipment.

5.2.3 Distribution of model variables

To develop a probabilistic model, the distribution of all its variables should be available. Therefore, the distributions of model variables were derived from the available data in the literature. Essentially eight studies which focused on sheep dipping practice were available\textsuperscript{12,29,58,97,104,155,264,281}. The abstracts of these eight studies are presented in Appendix 6. The probabilities of being involved in different dipping activities were also derived since they were included in the probabilistic model. These studies have not discussed all variables used in the model and as the aim of these studies differed, the variables and the nature of variables found in those studies varied (\textit{e.g.} reporting the variable in one dipping session or over a period of time).

Figure 5-2 shows the methodology of obtaining the distribution of each variable. The raw data of each of the five continuous variables (\textit{i.e.} volume of the concentrate dip, duration of the session, number of sheep dipped, dip rate and volume of sheep dip) found in different studies were combined together to get the final distribution of each variable. To get the final distributions of the dichotomous and categorical variables different methods were used. The raw data of three variables (namely, number of dippers, farmer's task and atmospheric conditions) in different studies were combined together to obtain the distribution of each variable. The data for three variables (namely, probability of getting involved of dip disposal, probability of falling in the bath and frequency of handling concentrate) were not available but it was possible to get a theoretical distribution for these variables depending on other variables. The distribution of five variables (namely, probability of handling the concentrate, probability of handling dipped sheep, probability of spilling concentrate, type of container and size of container) relied on a few chosen studies (although those variables were sometimes
mentioned in other studies), as the chosen studies had collected the variable in a more appropriate way than the other studies. The remaining nine variables (i.e. how concentrate was mixed with bath, type of submerge tool, bath location, bath type, sheep entry, splash guard, method of sheep dip disposal, PPE and personal hygiene) were collected in previous studies in different ways (e.g. different categories, or different periods of time) and therefore it was not possible to combine all the studies together mathematically. Judgment guided by literature (i.e. by the distributions of the variable in the available studies) was used to decide the distribution of these nine variables that was used in the probabilistic model.

Figure 5-2: Methodology for obtaining the distribution of each variable used in the probabilistic model

Appendix 7 presents the available data for each variable and how the distributions of each variable in different studies were combined in one distribution to be used in the probabilistic model. Table 5-1 summarises the distributions of the variables of the
A probabilistic model. Only variables that have been described in the literature and used in the probabilistic model are presented in this table.

**Table 5-1: Summary of distributions used in the probabilistic model**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Distribution or probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of handling the concentrate</td>
<td>PRO\textsubscript{con}</td>
<td>For plunger For chucker For helper For plunger/chucker For chucker/helper For all Tasks</td>
<td>70% 30% 5% 95% 10% 100%</td>
</tr>
<tr>
<td>Probability of handling dipped sheep</td>
<td>PRO\textsubscript{dip}</td>
<td>Dichotomous variable</td>
<td>28.9%</td>
</tr>
<tr>
<td>Probability of taking part in disposal of sheep dip</td>
<td>PRO\textsubscript{dis}</td>
<td>Dichotomous variable</td>
<td>50%</td>
</tr>
<tr>
<td>Probability of falling in bath</td>
<td>PRO\textsubscript{fall}</td>
<td>For plunger For chucker For helper For plunger/chucker For chucker/helper For all Tasks</td>
<td>1% 0.05% 0% 1.5% 0.05% 1.5%</td>
</tr>
<tr>
<td>Probability of spilling concentrate</td>
<td>PRO\textsubscript{spil}</td>
<td>Probability among those who handled concentrate (dichotomous variable)</td>
<td>47%</td>
</tr>
<tr>
<td>Frequency of handling the concentrate</td>
<td>FREQ</td>
<td>Discrete variable (lognormally distributed)</td>
<td>Mean±SD\textsubscript{ln}: 1.95±0.71, GM±GSD:7.03±2.03, Range: 1 – 34.1</td>
</tr>
<tr>
<td>Volume of the concentrate used</td>
<td>COVOL</td>
<td>Continuous variable (normally distributed)</td>
<td>Mean±SD: 4126±2380, Tertiles: 2500 and 5000, Range: 450 – 9700 ml</td>
</tr>
<tr>
<td>Type of container</td>
<td>TYP</td>
<td>Container with a pouring mechanism Container without a pouring mechanism Sachets</td>
<td>73% 17% 10%</td>
</tr>
<tr>
<td>Size of container</td>
<td>SIZ</td>
<td>5 litres 10 litres 20 litres</td>
<td>80% 5% 15%</td>
</tr>
<tr>
<td>How concentrate was mixed with bath</td>
<td>MIX</td>
<td>Pouring directly in the bath Using a jug Using automatic unit</td>
<td>28% 55% 17%</td>
</tr>
<tr>
<td>Duration of the session</td>
<td>DUR</td>
<td>Continuous variable (normally distributed)</td>
<td>Mean±SD: 261±130, Tertiles: 180 and 330, Range: 30 – 540 minutes</td>
</tr>
<tr>
<td>Number of dipped sheep</td>
<td>FLOCK</td>
<td>Discrete variable (normally distributed after square root transformation)</td>
<td>Mean\textsubscript{sr}=SD\textsubscript{sr}: 20.16±8.35, Range: 1-2000 sheep</td>
</tr>
<tr>
<td>Dip rate</td>
<td>RATE</td>
<td>Discrete variable (normally distributed)</td>
<td>Mean±SD: 205±99, Tertiles: 153 and 216, Range: 49 – 457 sheep/hour</td>
</tr>
</tbody>
</table>

\[ a \text{ Mean}_{\text{ln}} = \text{the mean of the log transformed values, SD}_{\text{ln}} = \text{the standard deviation of the log transformed values, GM} = \text{geometric mean, and GSD} = \text{geometric standard deviation.} \]

\[ b \text{ Mean}_{\text{sr}} = \text{the mean of the square root transformed values and SD}_{\text{sr}} = \text{the standard deviation of the square root transformed values.} \]
Table 5-1: Summary of distributions used in the probabilistic model (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Variable abbreviation</th>
<th>Category</th>
<th>Distribution or probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of dippers</td>
<td>NUM</td>
<td>One</td>
<td>4.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two or three</td>
<td>79.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Four</td>
<td>13.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Five</td>
<td>2.5%</td>
</tr>
<tr>
<td>Task</td>
<td>TASK</td>
<td>Plunger</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chucker</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Helper</td>
<td>24.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plunger/chucker</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chucker/helper</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All tasks</td>
<td>0.5%</td>
</tr>
<tr>
<td>Submerging tool</td>
<td>TOOL</td>
<td>Metal tool</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feet</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hands</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>4%</td>
</tr>
<tr>
<td>Bath location</td>
<td>LOC</td>
<td>Outside and exposed</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outside and sheltered</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td>10%</td>
</tr>
<tr>
<td>Bath type</td>
<td>BATH</td>
<td>Linear</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Circular</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mobile</td>
<td>5%</td>
</tr>
<tr>
<td>Sheep entry</td>
<td>ENTRY</td>
<td>Walk in method (Slope or ramp)</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slipway (tilt)</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td>50%</td>
</tr>
<tr>
<td>Splash guard</td>
<td>GUARD</td>
<td>Presence (dichotomous variable)</td>
<td>20%</td>
</tr>
<tr>
<td>Method of the disposal</td>
<td>METHOD</td>
<td>Drain</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mechanical</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td>35%</td>
</tr>
<tr>
<td>Volume of sheep dip</td>
<td>VOL</td>
<td>Continuous variable (normally distributed)</td>
<td>Mean±SD: 1934±807, Tertiles: 1630, 2000, Range: 755-4500 litre</td>
</tr>
<tr>
<td>Atmospheric conditions (wind)</td>
<td>ATM</td>
<td>Still</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breezy</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gusting</td>
<td>5%</td>
</tr>
<tr>
<td>Personal protective equipment during handling the concentrate</td>
<td>PPE_{con}</td>
<td>Gloves</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof boots</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof trousers/leggings</td>
<td>60% (67% if apron was not worn)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof apron/overall</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof coat</td>
<td>41%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Face protection (visor)</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Head protection (hat)</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Respirator</td>
<td>0.5%</td>
</tr>
<tr>
<td>Personal protective equipment during dipping, during handling dipped sheep and during the disposal of sheep dip</td>
<td>PPE_{dip}, PPE_{ae}, PPE_{dis}</td>
<td>Gloves</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof boots</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof trousers/leggings</td>
<td>75% (83% if apron was not worn)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof apron/overall</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waterproof coat</td>
<td>41%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Face protection (visor)</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Head protection (hat)</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Respirator</td>
<td>0.5%</td>
</tr>
<tr>
<td>Personal hygiene and behaviour (washing off concentrate spills)</td>
<td>PHB_{spil}</td>
<td>At the end of the session</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before meal break</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediately after spillage</td>
<td>50%</td>
</tr>
<tr>
<td>Personal hygiene and behaviour (washing off dip)</td>
<td>PHB_{dip}</td>
<td>Occasionally or at end of the day</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regularly:</td>
<td>15%</td>
</tr>
</tbody>
</table>
5.3 Results of probabilistic model

Figure 5-3 shows the distributions of exposure estimates through each route from handling the concentrate (CONPRO) and dipping sheep in the bath (DIP). Exposure estimates from CONPRO and DIP through all routes were lognormally distributed if zero results were omitted and the median was zero in all routes of CONPRO source. The ranges of all routes of CONPRO and DIP sources were wide and the ranges of DIP estimates were wider than those of CONPRO estimates due to some very high estimates. The highest estimate was found for the exposure from the DIP source through the dermal route (maximum of DIP\text{der} = 4083 whereas the 90\textsuperscript{th} percentile = 122).

Figure 5-4 shows the distributions of exposure estimates through each route from the disposal of the sheep dip (DISPRO), handling dipped sheep (AFTPRO), and from incidental exposure (INCPRO). Estimates of exposure from DISPRO through the dermal route were approximately lognormally distributed if zero results were omitted while the estimates of exposure through other routes and from AFTPRO and INCPRO were dispersed with narrow ranges. These narrow ranges were due to the limited variables included in the equations (majority of variables were set as 1 since they were not reported in the literature) while the absence of any continuous variable resulted in the dispersed estimates. The median was zero in all routes of the three sources. The exposure from AFTPRO through ingestion (AFTPRO\text{ing}) had only three values; 0 (70.2%), 0.6 (0.8%) and 1 (29%) while exposure through inhalation (AFT\text{inh}) had only four values; 0 (70.2%), 0.4 (0.1%), 0.7 (0.8%) and 1 (28.9%) (not presented in the figures). These distinct values of exposure estimates resulted from the distinct values of the only available variable in their models (i.e. the use of visors or respirators).

The distributions of pesticide exposure scores from each source and the distribution of the total exposure are presented in Figure 5-5. The distributions of the exposure from CONPRO and DIP sources were relatively uniform, though DIP estimates accumulated around different values. The reason of the nature of this distribution is that all route estimates were equalised before aggregation as explained in Section 3.9.4. Exposure estimates from each route were transformed to grades from 1 to 10 according to its percentile in its distribution (Figure 5-4) before aggregating the three routes together and therefore the log-normal distributions turned into relatively uniform ones. Estimates of exposure from DISPRO and INCPRO scores were lognormally distributed if zero exposures were omitted while the scores of the AFT source were dispersed for the same reason mentioned earlier. The total exposure scores (EXPOSURE) were lognormally distributed with a range of (1-30.11) and a median of 9.
Figure 5-3: Distribution of exposure scores from CON and DIP sources

(A) CONPRO\textsubscript{der}  
Range= 0-782, Mean±SD= 19±47  
Median= 0, 90\textsuperscript{th} Percentile= 55

(B) CONPRO\textsubscript{ing}  
Range= 0-958, Mean±SD= 30±67  
Median= 0, 90\textsuperscript{th} Percentile= 93

(C) CONPRO\textsubscript{inh}  
Range= 0-229, Mean±SD= 9±17  
Median= 0, 90\textsuperscript{th} Percentile= 26

(D) DIP\textsubscript{der}  
Range= 0.003-4083, Mean±SD= 55±153  
Median= 16, 90\textsuperscript{th} Percentile= 122

(E) DIP\textsubscript{ing}  
Range= 0.004-1937, Mean±SD= 40±58  
Median= 16, 90\textsuperscript{th} Percentile= 94

(F) DIP\textsubscript{inh}  
Range= 0.004-534, Mean±SD= 31±43  
Median= 16, 90\textsuperscript{th} Percentile= 75

157
Figure 5-4: Distribution of exposure scores from DIS, AFT and INC sources

(A) DISPRO_{der}  
Range= 0-10.9, Mean±SD= 1.2±1.7  
Median= 0, 90\(^{th}\) Percentile= 3.1

(B) DISPRO_{ing}  
Range= 0-7.6, Mean±SD= 1.5±1.9  
Median= 0, 90\(^{th}\) Percentile= 4.6

(C) DISPRO_{inh}  
Range= 0-6.2, Mean±SD= 1.2±1.5  
Median= 0, 90\(^{th}\) Percentile= 3.2

(D) AFTPRO_{der}  
Range= 0-1, Mean±SD= 0.17±0.29  
Median= 0, 90\(^{th}\) Percentile= 0.77

(E) INCPro_{der}  
Range= 0-1.6, Mean±SD= 0.05±0.15  
Median= 0, 90\(^{th}\) Percentile= 0.2

(F) INCPro_{ing}  
Range= 0-2, Mean±SD= 0.11±0.27  
Median= 0, 90\(^{th}\) Percentile= 0.7
Figure 5-5: Distribution of exposure scores from each source and total exposure

(A) CONPRO
Range = 0-12.1, Mean±SD = 3.0±4.0
Median = 0, 90th Percentile = 9.8

(B) DIP
Range = 0-12.2, Mean±SD = 1.4±2.0
Median = 0, 90th Percentile = 3.8

(C) AFTPRO
Range = 0-11.7, Mean±SD = 6.5±3.3
Median = 6.7, 90th Percentile = 11.1

(D) DISPRO
Range = 0-12.2, Mean±SD = 1.4±2.0
Median = 0, 90th Percentile = 3.8

(E) INCPO
Range = 0-1.85, Mean±SD = 0.07±0.18
Median = 0, 90th Percentile = 0.21

(F) EXPOSURE
Range = 0-30.11, Mean±SD = 9.91±5.8
Median = 9, 90th Percentile = 18.58

(A) CONPRO, (B) DIP, (C) AFTPRO, (D) DISPRO, (E) INCPO, (F) EXPOSURE
Figure 5-6 shows the ratio of the exposure from each source to the total exposure. For handling the concentrate, this ratio ranged from 0 to 85% of the total exposure and it was zero in about 55% of the simulations, less than 0.37 in 75% and less than 0.54 in 95% of the simulations. The contribution of exposure from dipping sheep in the diluted dip ranged from 0.06 to 1 with a median of 0.59. The DIP exposure was the only exposure (the ratio was 1) in 20% of the simulations. Exposure from other sources together (AFT, DIS, and INC) contributed from 0 to 0.88 of the total exposure with a median of 0.15. This contribution was less than 0.32 in 75% and less than 0.62 in 95% of the simulations.

![Diagram](image.png)

**Figure 5-6: Ratio of pesticide exposure from each source to the total exposure**

### 5.4 Application of probabilistic models to different exposure scenarios

In epidemiological studies, information about all exposure factors is not always available and researchers sometimes depend on a few available variables to estimate the exposure. This ignorance of other exposure factors might lead to important exposure misclassification. The developed probabilistic model was applied in different exposure scenarios to compare deterministic estimates depending on available variables with the probabilistic exposure estimates which take into account the probabilities of unavailable variables of exposure.
5.4.1 Illustration of differences between probabilistic and deterministic approaches for three dipping tasks in the same dipping session

In this scenario, exposure estimation was performed for three virtual dippers working in the same dipping session assuming that the only available information was information on task performed (i.e. plunger, chucker, and helper). Since the three dippers were working in the same session, all variables related to the farm and dipping session (number of sheep dipped, bath type, etc.) did not affect the difference between the exposures of the three dippers and the difference came from the variation of personal exposure variables such as the use of PPE and being involved in dipping activities.

Two exposure estimates were performed for each dipper; one was deterministic and the other was probabilistic. The conceptual algorithm (Section 3.8) was used to obtain deterministic estimates for the three dippers. However since the only available information is their task all other variables were omitted by setting all variables of exposure from dipping sheep in the bath (DIP) except TASK to be scored 1 and exposures from all sources except DIP to be scored 0.

In the probabilistic estimation, all variables related to the farm and dipping session were the same between the three dippers since they were working in the same session. Therefore, these variables set to be scored 1 since they did not affect the difference between the final exposures. Personal exposure variables were not available so these variables were determined in a probabilistic way. Monte Carlo simulations generated 10,000 samples of exposure scores using the probabilistic model (Section 5.2.2).

Figure 5-7 shows the results of both estimation methods. Deterministic exposure scores for a plunger, chucker and helper in the same dipping session were 3.51, 2.40, and 1.17, respectively. Probabilistic simulation showed a considerable overlap between the distributions of the three dippers scores. The (5th, 95th) percentiles of the scores of the plunger, chucker, and helper were (2, 9.91), (1, 7.82), and (1, 5.76) respectively. The median of the chucker and the helper simulation scores were close to the deterministic estimates (2.52 and 1.26 respectively) while the median of the plunger scores (5.51) was about 1.5 times the deterministic estimate. About 40% of the chucker simulations and about 20% of the helper simulations were more than the plunger deterministic score, whereas about 30% of the helper simulations were more than the deterministic score of the chucker.
**Figure 5-7: Exposure estimates of three different dipping tasks in the same session.**

Boxplots show the probabilistic estimates and the stars present the deterministic estimates

### 5.4.2 Illustration of differences between probabilistic and deterministic approaches for farmers in the SHAW study

In the second scenario, exposure estimations were performed for four actual farmers interviewed in the second phase of the SHAW study. Two plungers, one chucker, and one helper were selected from SHAW phase 2 farmers. Two plungers were taken to compare the results of two similar tasks. The sampling was random from the dippers of each task. The data of the four dippers are presented in Table 5-2.

Again both deterministic and probabilistic estimates were calculated. The conceptual algorithm (Section 3.8) was used to obtain deterministic estimates for the four farmers. In the deterministic estimation, the scores of all variables that were not collected in the SHAW study were set based on the most prevalent category reported for each variable (explained in detail is Section 6.2.4.2). In the probabilistic estimation, all variables collected in SHAW were held constant as they were recorded in the SHAW data whilst uncollected ones were determined in a probabilistic way. Monte Carlo simulations generated 10,000 samples of exposure scores of the probabilistic model (Section 5.2.2).
Table 5-2: Exposure data of four dippers interviewed in the SHAW study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Information collected in SHAW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Farmer 1</td>
</tr>
<tr>
<td>Task</td>
<td>Plunger</td>
</tr>
<tr>
<td>Submerging tool</td>
<td>Metal tool</td>
</tr>
<tr>
<td>Number of dipped sheep</td>
<td>1,000</td>
</tr>
<tr>
<td>Bath type</td>
<td>Linear</td>
</tr>
<tr>
<td>Bath location</td>
<td>Outside</td>
</tr>
<tr>
<td>Sheep entry</td>
<td>Manually</td>
</tr>
<tr>
<td>Splashguards</td>
<td>No</td>
</tr>
<tr>
<td>Number of dippers</td>
<td>3</td>
</tr>
<tr>
<td>Handling concentrate</td>
<td>Yes</td>
</tr>
<tr>
<td>Spill concentrate</td>
<td>Yes</td>
</tr>
<tr>
<td>Washing the spills</td>
<td>At the end</td>
</tr>
<tr>
<td>Handling dipped sheep</td>
<td>No</td>
</tr>
<tr>
<td>Disposal of sheep dip</td>
<td>Yes</td>
</tr>
<tr>
<td>Fall in dipping bath</td>
<td>No</td>
</tr>
<tr>
<td>PPE during handling the concentrate</td>
<td>Boots, apron &amp; leggings</td>
</tr>
<tr>
<td>PPE during dipping the sheep</td>
<td>Boots, apron &amp; leggings</td>
</tr>
</tbody>
</table>

Figure 5-8 shows the results of the two types of estimations. Deterministic scores of the four SHAW farmers were 13.61, 7.65, 12.15, and 9.66 respectively. Generally the probabilistic estimates resulted in higher estimations. The (5th, 95th) percentiles of the scores of the four farmers were (14.55, 23.48), (7.79, 17.52), (10.48, 22.21) and (7.14, 18.49) respectively. Similar to the deterministic estimates, the median of Farmer 1 simulations remained the highest (21.14), then the median of Farmer 3 (17.2), then the median of Farmer 4 (12.8) and finally the median of Farmer 2 (12.35). This means that the deterministic scores show a comparable ranking compared to medians or other quartiles of the probabilistic distributions.

The deterministic estimate of Farmer 1 is only a little higher than that of Farmer 3 but the figure shows that the 1st quartile of Farmer 1 probabilistic estimates was slightly lower than the 3rd quartile of Farmer 2. However, the considerable overlap that has been found between the ranges of the probabilistic estimates of the two farmers means that the probability of Farmer 1 exposure being equal or lower than Farmer 2 exposure is not very low. On the contrary, the difference between Farmer 2 and Farmer 4 deterministic scores was higher than that between Farmer 1 and Farmer 3 but the distributions of the scores of both farmers 2 and 4 were relatively identical. This indicates that the expected difference between the exposures of Farmer 2 and Farmer 4 is more likely to be lower than what is shown by the deterministic estimation.
Discussion

In this chapter, a probabilistic model for pesticide exposure in sheep dipping was developed from the conceptual model developed in Chapter 3 and was used to obtain the distribution of exposure estimates from each exposure source and route and the distribution of the total exposure. Although the contribution of AFT, DIS, and INC sources together to the total exposure was generally less than DIP source, it was nearly equal to the contribution of CON source. The utilisation of the probabilistic model in different scenarios showed that probabilistic estimates which take into account all conceptual variables draw a more comprehensive image of exposures than deterministic estimates which depend on available variables only. However, the use of the results of this probabilistic model as a gold reference is questionable due to the limitations in the input data discussed below.

The main purpose of the probabilistic models of pesticide exposure is to incorporate uncertainties in the model variables into the deterministic model to produce a distribution of expected estimates. The new probabilistic model for sheep dipping treatment illustrated this distribution but it helped as well in obtaining the distributions of exposure through each single route and then through each source. These distributions
helped in using the same grading scale (grades from 1-10 according to 9 percentiles) for the exposure through each route and source for the purpose of aggregating all these components in one model. The use of the new conceptual model to get deterministic exposure estimates in any epidemiological study will depend on the grading system obtained from the probabilistic model results.

The results of exposure from handling the concentrate and from dipping sheep in the bath compared to the exposure from other sources indicate that when more modifying factors are included in the component model, the results of that component might tend to take the logarithmic distribution. This consists with the assumption of Cherrie et al. that occupational exposures generally follow a lognormal distribution.

The comparison between the contribution of exposure from AFT, DIS, and INC sources to the total exposure and the contribution of CON shows that exposure from the first three sources should not be neglected. Models which neglect these three sources such as the model of Buchanan et al., might lead to a significant underestimation of the total exposure.

Researchers have used multiple imputation and other methods to handle the problem of missing data of both exposures and outcomes in epidemiological studies. However, these methods are not helpful when the data is not collected at all in the study. This study suggests that probabilistic models, which are usually used for regulatory risk assessment, might help to include uncertainty of uncollected variables in exposure estimation in epidemiological studies. This inclusion might result in a more precise point estimates than those resulted by deterministic approaches. Considering the probabilistic model as a gold reference, although it is questionable as mentioned earlier, the application of this new approach to two different scenarios showed that although the deterministic method gave relatively good estimates for predicted exposures, the probability that this method classifies the exposures erroneously is not low.

The scenario of three different dipping tasks in the same dipping session shows that the deterministic approach ordered the exposures properly but it underestimated the exposure of the plunger. The good estimations of the deterministic approach in this scenario might be due to the exposure difference between the three dippers being related only to personal factors since all the factors related to the environment were equalised and only the dipping activity was actually included. However, it should be recognised that the overlap between the distributions of the three exposure distributions means that
in the real situations the probability that the deterministic estimates ordered the exposures incorrectly cannot be neglected. This result indicates that the validity of an exposure model which depends mainly on dipper’s task is questionable. The second scenario showed also good performance for the deterministic approach especially with farmers who had the same task. The estimates of those farmers who have different tasks indicated that when a deterministic approach shows that the exposure of one dipper is more than the exposure of another, the reality might be that the exposure of the second dipper is more likely to be equal or even more than the exposure of the first.

In the application of the probabilistic model, 10,000 iterations were used. This number of iterations was used because it was found that increasing the number of iterations improves the convergence in the output in a previous study. The increment of iterations from 1000 to 10,000 in that study resulted in decreasing the coefficient of variation to less than the half but resulted at the same time in higher exposures which came from the combination of rare events. Such high predicted exposures will not affect the final estimates in our model because before calculating the final estimate the results of the components (routes and sources) were assigned grades from 1 to 10 according to percentiles.

Probabilistic models in general show that significant uncertainty is associated with the use of deterministic estimates and give more informed estimations for the exposure, but at the same time they increase the complexity of both exposure estimation and risk assessment. A trial of using this new probabilistic model in the assessment of pesticide health effects is presented in Chapter 8. It has been suggested for regulatory risk assessments to use the 75th percentile as a surrogate of the resulting distribution of estimates when working with long-term effects providing the use of large database for data input. If small databases were used the 90th percentile is preferable to be taken as a surrogate value.

The main concern of this study is the validity of the input data. The distributions of the model variables were extracted from different studies covering a long period of time. This is not the best approach to get the distributions if it is expected that the distribution of some variables has changed over the time. For example, concentrate sachets were not used before 2000, while it became more frequent after 2000. However, it is very difficult to get a specific distribution for each variable in each year or even decade since
little information is available. Thus the only feasible approach was the use of one distribution for all years.

The probabilistic model has practically excluded all those variables not described in the literature since no distributions were available for input. This prevented the model from estimating the effects of uncertainties in those variables. Further research about the unavailable distributions or even the use of theoretical distributions might help in the improvement of the model results.

To conclude, this study indicates that even the use of well-derived deterministic estimates might lead to exposure misclassification. Despite the concern about the validity of the input data, this study produced examples of how the use of the probabilistic model could help in including unavailable variables of exposure and show where the deterministic results fit within the total distribution of the exposure estimates. Consequently this approach might result in a reduction in exposure misclassification which is an important step towards consistent findings in the research of neuropsychiatric health effects of long-term pesticide exposure.
Chapter 6: Occupational pesticide exposure in the SHAW study

6.1 Introduction

Farmers are exposed to pesticides mainly when they apply pesticides to crops and other plants or when they apply pesticides to animals\(^4\). Sheep dipping is one of the main pesticide applications in the UK because sheep farming is an important industry in the UK\(^5\) and several British studies have focused on this application since it has been associated with acute and chronic neurological effects among farmers\(^7,11\). OP pesticides have been the main ingredients of sheep dips in the UK since the 1970s\(^12\) and have been also one of the main insecticides used in agriculture throughout the world in the last three decades of the last century\(^8\).

The effects of long-term low-level exposure to pesticides including OPs are still uncertain\(^18,23\) and the difficulty of retrospective assessment of long-term exposure has been suggested to be one of the main reasons of this uncertainty\(^24,25\). Studies of pesticide health effects have depended on different methods to estimate long-term pesticide exposure ranging from using simple surrogates like numbers of years of exposure\(^319\), frequency of use, and the acreage of the land\(^320\) and ending with sophisticated models\(^29,153\). To obtain a better understanding of health effects of long-term pesticide exposure, reducing exposure misclassification by developing better techniques to assess long-term pesticide exposure among farmers is a great need\(^138\).

This chapter aims to describe the occupational practices of the SHAW farmers related to pesticide exposure and how their occupational pesticide exposure can be estimated using different methodologies. Sheep dipping practice and exposure to OP pesticides specifically will have a special attention. The exposure estimates obtained in this chapter will be used in Chapter 8 to investigate the impact of using different methodologies on the association between long-term pesticide exposure and neuropsychiatric illnesses.

6.2 Materials and methods

The SHAW study was described in detail in Chapter 2 and the data of the SHAW phase 2 farmers has been investigated in this chapter. Although the analysis has included only phase 2 farmers, phase 1 data were used to obtain simple surrogates of occupational...
pesticide exposure for these farmers. Farmers in phase 2 of the SHAW study were asked about using pesticides in five farming sectors, namely sheep, cattle, other livestock, crops and grains, and other pesticide use.

6.2.1 Collection of additional data

During data entry, it was found that there was substantial amount of missing information on pesticide applications (e.g. application years and number of treated animals). Therefore the farmers were contacted again to ask them further questions to gather this missing information if it affected the ability to assess their pesticide exposure according to the utilised methodologies described later. This further contact helped also in sorting out inconsistencies found in their answers. All farmers were contacted by telephone. Ethical approval for this amendment of the original study was approved by the West Midlands Research Ethics Committee (05/MRE07/19).

The questions in the sections on cattle and other livestock were about using all veterinary medicines including pesticides (Appendix 2, Q3.1 and Q4.1) which made it impossible to differentiate between pesticide exposure and exposure to veterinary medicines. Contacting farmers for the second time provided new data about pesticide usage specifically and therefore all farmers who reported using pesticides to treat cattle or other livestock were contacted this second time even if there was no missing information elsewhere.

A new pesticide exposure spreadsheet (Appendix 8) was developed for farmers in the cattle sector to collect information on treating cattle with pesticides for warble fly, flies, lice and other OP cattle treatment. To make the telephone call in this secondary contact with farmers as short and precise as possible, no information on wormers was collected although the use of wormers is very common treatment in the cattle sector. Cattle farmers were asked to categorise applied pesticides into one of five categories: definitely not OP, probably not OP, do not know, probably OP, and definitely OP.

6.2.2 Handling of pesticide exposure data

All data were coded, cleaned and entered and then sheep farmers’ data were entered for each year from 1942 (first year found in the data) to 2007 (last year found) in order to calculate the exposure for each year separately. However, the final year included in the analysis was the year 2005 because farmers were interviewed in phase 2 during 2006 and 2007 and those farmers interviewed in 2006 might have not applied any pesticides in that year.
Any obvious inconsistencies were checked and corrected where needed. Rules for data entry and to deal with missing information of farmers not reached by telephone and data that farmers did not know were determined by the PhD student, and then after discussions they were agreed by two members of the SHAW research team.

As examples of these rules, the age of 10 was considered as the first year of work included in the exposure (it was assumed that children under 10 in the UK will not take part in a serious job). Therefore, the start year of farmers who started working in farm younger than 10 was changed according to this rule. If the farmer used a contractor or was not involved personally in the treatment in specific years, those years were not included in the exposure. All rules for handling pesticide exposure data are detailed in Appendix 9.

6.2.3 Outline of pesticide exposure estimation methodology

Two estimations of personal pesticide exposure were performed in all farming sectors, namely for exposure to all pesticides and to OPs specifically. There was a special focus on pesticide exposure from sheep dipping and more detailed information was collected on this practice since it’s one of the main sources of OP exposure in the UK. In all farm sectors, pesticide exposure was estimated using simple surrogates (e.g. number of dipping years) and more developed models (e.g. the new conceptual model of sheep dipping). Different surrogates and models were used to estimate the same exposure to evaluate if the estimation method would affect the associations between pesticide exposure and ill-health among farmers (Chapter 8).

In the sheep sector, the developed models were used exclusively to estimate pesticide exposure from dipping treatment. However, there are another three methods mentioned in the SHAW questionnaire (pour-on, showering and injection), and therefore another model was used to estimate pesticide exposure through all treatment methods in the sheep sector. Figure 6-1 outlines the process of estimating pesticide exposure.

6.2.3.1 Estimation of long-term OP exposure

For simple surrogates, pesticides used in all farming sectors were assumed to be free of OPs before 1971 as OPs were mainly used after that year\(^{13}\) and therefore all surrogates for general exposure were modified for the exposure after the year 1970. On the other hand, to perform the OP exposure estimation using the models developed in this section, a new variable was added to all models of general pesticides, namely OPPROB.
OPPROB is the probability that the pesticides used in a specific year contained an OP. The way of estimating this probability varied between farming sectors. Section 6.2.6 will describe in detail how this probability was obtained.

**Figure 6-1: Estimation of pesticide exposure in sheep and other farming sectors**

All abbreviations are models used to estimate pesticide exposure in the relevant farming sector.

### 6.2.4 Estimation of pesticide exposure in sheep farming

The SHAW farmers reported treating sheep using different methods, namely dipping, pouring-on, showering, injecting, and oral treatment. Pesticide exposure from sheep treatment was estimated by both using simple surrogates and more sophisticated models. Information collected on sheep dipping was very detailed compared to
information collected on other treatments. Therefore, three different estimation models were used to estimate exposure from dipping specifically while another model was developed to estimate exposure from all sheep treatment methods collectively. The first dipping model (NEW) was the newly developed model for pesticide exposure in sheep dipping described in Chapter 3. The remaining two (SHAPE and TASK) were developed models found in the published UK sheep dipping studies\textsuperscript{7,11,12,29,58,97,99,155,281}. These two models were selected from three models found in the literature but the third model\textsuperscript{7} was not used since it was very similar to one of the two used models\textsuperscript{29} and less information was available on its weighting factors.

6.2.4.1 Simple surrogates of exposure in sheep farming

Six surrogates were used to estimate general pesticide exposure in sheep farming; four of these surrogates were taken from the phase 1 questionnaire and two were taken from the phase 2 questionnaire (Table 6-1). The ever/never surrogates (EVSH, EVDIP, and EVCONSH) were simple use of answers for questions C2.1 and C2.2 (working years with sheep), C3.10 (ever dipped sheep) and C4.3 (ever handled concentrate to treat sheep) in the phase 1 questionnaire while other surrogates were derived from answers for questions C2.1, C2.2 in the phase 1 questionnaires and questions 2.1.1 (years of different treatments on sheep) and 2.1.2 (flock size and number of dipping days) in phase 2 questionnaire (Appendices 1 and 2).

The same surrogates were modified so as to estimate OP exposure specifically. The modification was to only include years after 1970. Ever dipped sheep (EVDIP) and ever handled concentrate to treat sheep (EVCONSH) were not used as surrogates for OP exposure since phase 1 data did not indicate whether the relevant activity occurred before 1970 or after (Table 6-1).

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Surrogate</th>
<th>Definition</th>
<th>Type</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>EVSH</td>
<td>Ever having sheep</td>
<td>Dichotomous</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>EVDIP</td>
<td>Ever dipped sheep</td>
<td>Dichotomous</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>EVCONSH</td>
<td>Ever handled the concentrate to treat sheep</td>
<td>Dichotomous</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>YRSH</td>
<td>Number of years having sheep</td>
<td>Numerical</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>YRDIP</td>
<td>Number of dipping years using any pesticides</td>
<td>Numerical</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>DYDIP</td>
<td>Number of dipping days using any pesticides</td>
<td>Numerical</td>
<td>2</td>
</tr>
<tr>
<td>OP</td>
<td>OPEVSH</td>
<td>Ever having sheep after 1970</td>
<td>Dichotomous</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>OPYRSH</td>
<td>Number of years having sheep after 1970</td>
<td>Numerical</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>OPYRDIP</td>
<td>Number of dipping years using all pesticides after 1970</td>
<td>Numerical</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>OPDYDIP</td>
<td>Number of dipping days using all pesticides after 1970</td>
<td>Numerical</td>
<td>2</td>
</tr>
</tbody>
</table>
6.2.4.2 The new conceptual model for sheep dipping

The new conceptual algorithm developed in Section 3.8 was used to estimate long-term pesticide exposure from sheep dipping. However, as not all the variables in this algorithm are available in the SHAW study, this algorithm was modified according to the available data. Two main modifications were applied. The first was adding variables (INVOL) to reflect whether the farmer had been involved in the activities of handling the concentrate, handling sheep after dipping, and in the disposal of sheep dip. A variable (OCC) was also added to the equation of incidental exposure to reflect whether incidental exposure had occurred. The second modification was to combine all variables not available in the SHAW study database into one new variable (REST) specific for each equation as shown in equations Eq.3.1.6.1 to Eq.3.1.6.16.

The modified new conceptual model was as follows:

**Eq. 6.1:** \( EXP = \alpha \times CON + \beta \times DIP + \gamma \times AFT + \delta \times DIS + \varepsilon \times INC \)

Where: \( EXP \) = pesticide exposure intensity in one dipping day, \( CON \) = exposure from handling the concentrate, \( DIP \) = exposure from dipping sheep in the bath, \( AFT \) = exposure from handling dipped sheep, \( DIS \) = exposure from the disposal of sheep dip, \( INC \) = exposure from incidental exposure, and \( \alpha, \beta, \gamma, \delta \) and \( \varepsilon \) = parameters.

These five individual exposures were calculated using the following equations:

**Eq.6.1.1:** \( CON = INVOL_{con} \times (\alpha_{der} \times CON_{der} + \alpha_{ing} \times CON_{ing} + \alpha_{inh} \times CON_{inh}) \)

Eq.6.1.1.1: \( CON_{der} = FREQ \times PPE \times REST_{con,der} \)
Eq.6.1.1.2: \( CON_{ing} = FREQ \times PPE \times REST_{con,ing} \)
Eq.6.1.1.3: \( CON_{inh} = FREQ \times LOC \times PPE \times REST_{con,inh} \)

**Eq.6.1.2:** \( DIP = \beta_{der} \times DIP_{der} + \beta_{ing} \times DIP_{ing} + \beta_{inh} \times DIP_{inh} \)

Eq.6.1.2.1: \( DIP_{der} = TASK \times NUM \times FLOCK \times BATH \times LOC \times TOOL \times GUARD \times ENTRY \times PPE \times REST_{dip,der} \)
Eq.6.1.2.2: \( DIP_{ing} = TASK \times NUM \times FLOCK \times BATH \times LOC \times TOOL \times GUARD \times ENTRY \times PPE \times REST_{dip,ing} \)
Eq.6.1.2.3: \( DIP_{inh} = TASK \times NUM \times FLOCK \times BATH \times LOC \times TOOL \times ENTRY \times PPE \times REST_{dip,inh} \)

**Eq.6.1.3:** \( AFT = INVOL_{aft} \times (\gamma_{der} \times AFT_{der} + \gamma_{ing} \times AFT_{ing} + \gamma_{inh} \times AFT_{inh}) \)
Eq. 6.1.3.1: \( \text{AFT}_{\text{der}} = \text{PPE} \times \text{REST}_{\text{aft.der}} \)

Eq. 6.1.3.2: \( \text{AFT}_{\text{ing}} = \text{PPE} \times \text{REST}_{\text{aft.ing}} \)

Eq. 6.1.3.3: \( \text{AFT}_{\text{inh}} = \text{PPE} \times \text{REST}_{\text{aft.inh}} \)

Eq. 6.1.4: \( \text{DIS} = \text{INVOL}_{\text{dis}} \times (\delta_{\text{der}} \times \text{DIS}_{\text{der}} + \delta_{\text{ing}} \times \text{DIS}_{\text{ing}} + \delta_{\text{inh}} \times \text{DIS}_{\text{inh}}) \)

Eq. 6.1.4.1: \( \text{DIS}_{\text{der}} = \text{LOC} \times \text{PPE} \times \text{REST}_{\text{dis.der}} \)

Eq. 6.1.4.2: \( \text{DIS}_{\text{ing}} = \text{LOC} \times \text{PPE} \times \text{REST}_{\text{dis.ing}} \)

Eq. 6.1.4.3: \( \text{DIS}_{\text{inh}} = \text{LOC} \times \text{PPE} \times \text{REST}_{\text{dis.inh}} \)

Eq. 6.1.5: \( \text{INC} = \varepsilon_{\text{der}} \times \text{INC}_{\text{der}} + \varepsilon_{\text{ing}} \times \text{INC}_{\text{ing}} \)

Eq. 6.1.5.1: \( \text{INC}_{\text{der}} = \text{OCC}_{\text{fall}} \times \text{REST}_{\text{inc.der1}} + \text{OCC}_{\text{spill}} \times \text{PHB} \times \text{PPE} \times \text{REST}_{\text{inc.der2}} \)

Eq. 6.1.5.2: \( \text{INC}_{\text{ing}} = \text{OCC}_{\text{fall}} \times \text{REST}_{\text{inc.ing1}} + \text{OCC}_{\text{spill}} \times \text{PHB} \times \text{PPE} \times \text{REST}_{\text{inc.ing2}} \)

Where: \( \text{INVOL} \) = involvement in different activities, \( \text{FREQ} \) = frequency of handling the concentrate, \( \text{PPE} \) = personal protective equipment, \( \text{REST} \) = combination of unavailable variables, \( \text{LOC} \) = bath location, \( \text{TASK} \) = task, \( \text{NUM} \) = number of dippers, \( \text{FLOCK} \) = number of dipped sheep, \( \text{BATH} \) = bath type, \( \text{LOC} \) = bath location, \( \text{TOOL} \) = submerging tool, \( \text{GUARD} \) = splash guard, \( \text{ENTRY} \) = sheep entry, \( \text{OCC}_{\text{fall}} \) = occurrence of falling in the bath, \( \text{OCC}_{\text{spill}} \) = occurrence of spilling the concentrate on the body, and \( \text{PHB} \) = personal hygiene and behaviour.

The variable REST in each equation was calculated as follows:

Eq. 6.1.6.1: \( \text{REST}_{\text{con.der}} = \text{COVOL} \times \text{TYP} \times \text{MIX} \times \text{SIZ} \times \text{DUR} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.2: \( \text{REST}_{\text{con.ing}} = \text{COVOL} \times \text{TYP} \times \text{MIX} \times \text{SIZ} \times \text{DUR} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.3: \( \text{REST}_{\text{con.inh}} = \text{COVOL} \times \text{TYP} \times \text{MIX} \times \text{ATM} \)

Eq. 6.1.6.4: \( \text{REST}_{\text{dip.der}} = \text{DUR} \times \text{RATE} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.5: \( \text{REST}_{\text{dip.ing}} = \text{DUR} \times \text{RATE} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.6: \( \text{REST}_{\text{dip.inh}} = \text{DUR} \times \text{RATE} \times \text{SUR} \times \text{ATM} \)

Eq. 6.1.6.7: \( \text{REST}_{\text{aft.der}} = \text{NAT} \times \text{FLOAFT} \times \text{DURAFT} \times \text{LENGTH} \times \text{GATHER} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.8: \( \text{REST}_{\text{aft.ing}} = \text{NAT} \times \text{FLOAFT} \times \text{DURAFT} \times \text{LENGTH} \times \text{GATHER} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.9: \( \text{REST}_{\text{aft.inh}} = \text{NAT} \times \text{FLOAFT} \times \text{DURAFT} \times \text{LENGTH} \times \text{GATHER} \times \text{ATM} \)
Eq. 6.1.6.10: \( \text{REST}_{\text{dis, der}} = \text{METHOD} \times \text{VOL} \times \text{DURDIS} \times \text{OLD} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.11: \( \text{REST}_{\text{dis, ing}} = \text{METHOD} \times \text{VOL} \times \text{DURDIS} \times \text{OLD} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.12: \( \text{REST}_{\text{dis, inh}} = \text{METHOD} \times \text{VOL} \times \text{DURDIS} \times \text{OLD} \times \text{PHB} \times \text{ATM} \)

Eq. 6.1.6.13: \( \text{REST}_{\text{inc, der1}} = \text{FALL} \times \text{LEVEL} \times \text{PHB} \)

Eq. 6.1.6.14: \( \text{REST}_{\text{inc, der2}} = \text{SPIL} \times \text{AMOUNT} \)

Eq. 6.1.6.15: \( \text{REST}_{\text{inc, ing1}} = \text{FALL} \times \text{PHB} \)

Eq. 6.1.6.16: \( \text{REST}_{\text{inc, ing2}} = \text{SPIL} \times \text{AMOUNT} \)

Where: \( \text{COVOL} \) = Volume of the concentrate used, \( \text{TYP} \) = Type of container, \( \text{MIX} \) = How mixed with bath, \( \text{SIZ} \) = Size of container, \( \text{DUR} \) = Duration of the session, \( \text{PHB} \) = Personal hygiene and behaviour, \( \text{ATM} \) = Atmospheric conditions like temperature and wind, \( \text{DUR} \) = Duration of the session, \( \text{RATE} \) = Dip rate, \( \text{SUR} \) = Area of bath surface, \( \text{NAT} \) = Nature of the handling, \( \text{FLOAFT} \) = Number of dipped sheep handled, \( \text{DURAFT} \) = Duration between dipping and handling, \( \text{LENGTH} \) = length of fleece, \( \text{GATHER} \) = Place for gathering sheep after dipping, \( \text{PPE} \) = Personal protective equipment, \( \text{METHOD} \) = Method of the disposal, \( \text{VOL} \) = Volume of sheep dip, \( \text{DURDIS} \) = Duration of disposal process, \( \text{OLD} \) = How old was the sheep dip, \( \text{FALL} \) = Number of falls into sheep dip, \( \text{LEVEL} \) = Level of immersion, \( \text{SPIL} \) = Frequency of spillage of the concentrate on a part of the body, and \( \text{AMOUNT} \) = Average amount of concentrate spills.

REST variables were used as deterministic variables and they were calculated according to the most prevalent category in each variable (Section 05.2.3). Appendix 10 presents the values of REST variables. For example the score of \( \text{REST}_{\text{con, der}} \) was set to 7.524 according to Eq.3.1.6.1. This was based on the following input values. Scores of \( \text{COVOL} \) and \( \text{DUR} \) were assigned based on the middle tertiles (scores were 2 and 1.8 respectively). The score of \( \text{TYP} \) was 1 according to the most prevalent type (container with a pouring mechanism), whereas that of \( \text{MIX} \) was 1.9 according to the most prevalent mixing method (using a jug), and \( \text{SIZ} \) was 1 according to the most prevalent size (5 litres), and \( \text{ATM} \) was 1.1 according to the most prevalent weather (Breezy). The score of \( \text{PHB} \) was 1 since this variable was not found in the literature review.

Hence \( \text{REST}_{\text{con, der}} = 2 \times 1 \times 1.9 \times 1.8 \times 1 \times 1.1 = 7.524 \)
EXP estimates the exposure intensity in one dipping day in a specific year; therefore the estimated cumulative exposure was calculated using the following equation:

**Eq. 6.2:** \[ \text{NEW} = \sum_{y=1}^{Y} (\text{EXP}_y \times \text{DPY}_y) \]

Where: NEW = cumulative pesticide exposure from sheep dipping, \( y = \) year, \( \text{EXP}_y = \) exposure intensity in one dipping day in year \( y \), and \( \text{DPY}_y = \) average number of dipping days in year \( y \).

The modified model of DIP (Eq.6.1.2) was more thorough than other components since most of its variables were available in the SHAW study, on the other hand CON (Eq.6.1.1) and AFT (Eq.6.1.3) depended on a crude answer in phase 2 about whether the farmer had ever handled the concentrate to treat sheep or ever been in contact with sheep within 24 hours after dipping. Therefore a NEWDIP model was derived from DIP to estimate the cumulative exposure from only the dipping source (Eq.6.3).

**Eq. 6.3:** \[ \text{NEWDIP} = \sum_{y=1}^{Y} (\text{DIP}_y \times \text{DPY}_y) \]

Where: NEWDIP = cumulative pesticide exposure from dipping source only, \( \text{DIP}_y = \) exposure intensity from dipping source in one day in year \( y \).

In order to estimate OP exposure specifically, the OPPROB variable was integrated into the NEW sheep dipping models and the resulted models were as follows:

**Eq. 6.4:** \[ \text{OPNEW} = \sum_{y=1}^{Y} (\text{EXP}_y \times \text{DPY}_y \times \text{OPPROB}_y) \]

**Eq. 6.5:** \[ \text{OPNEWDIP} = \sum_{y=1}^{Y} (\text{DIP}_y \times \text{DPY}_y \times \text{OPPROB}_y) \]

Where: OPNEW = cumulative OP exposure from sheep dipping, OPNEWDIP = cumulative OP exposure from dipping source only, and \( \text{OPPROB}_y = \) the probability of the pesticides used in a specific year containing an OP.
6.2.4.3 The SHAPE model for sheep dipping

Cherrie and Robertson\textsuperscript{134} developed an exposure metric to assess dermal exposure by incorporating three factors together: the concentration of the chemical in the skin contamination layer (\(C_{sk}\)), the duration of exposure (\(t\)) and the area of skin contaminated (\(S_{sk}\)). Dermal exposure (\(E_{sk}\)) was calculated by this metric:

Eq. 6.6: \(E_{sk} = C_{sk} \times t \times S_{sk}\)

The SHAPE study\textsuperscript{29} used this metric to establish models for pesticide exposure in different farming sectors and the most developed one was that for sheep dipping. In SHAPE, six different sources in the process of sheep dipping were identified. Using Eq.6.6 the exposure from these sources was assessed.

The cumulative pesticide exposure through sheep dipping was then calculated using the following equation:

Eq. 6.7: \(E_{sk} = E_{sk,dip} + E_{sk,conc} + E_{sk,splash} + E_{sk,handling} + E_{sk,fall} + E_{sk,lean}\)

This equation consists of six additive terms: exposure to dilute dip (\(E_{sk,dip}\)), exposure to concentrated dip on the hands (\(E_{sk,conc}\)), exposure to concentrated dip splashed onto the body (\(E_{sk,splash}\)), exposure to dip residue while handling sheep post dipping (\(E_{sk,handling}\)), exposure through falling into the dip (\(E_{sk,fall}\)), and exposure through cleaning the dip bath at the end of the work (\(E_{sk,lean}\)). The components of these six exposures were as follows:

Eq.6.7.1: Cumulative exposure to dilute dip (i.e. from dipping sheep in the bath)

\[
E_{sk,dip} = C_{sk,dip} \cdot t_{dip} \sum_{n=1}^{5} \delta_{sk,n} \cdot S_{sk,n} \cdot (1 - P_{clo,n} \cdot A_{clo,n} \cdot \eta_{clo,n})
\]

Eq. 6.7.2: Cumulative exposure to concentrated dip on hands

\[
E_{sk,conc} = C_{sk,conc} \cdot t_{conc} \cdot \delta_{sk,conc} \cdot S_{sk,hns} \cdot (1 - P_{glv,n} \cdot A_{glv,n} \cdot \eta_{glv})
\]

Eq. 6.7.3: Cumulative exposure to concentrated dip splashed on the body

\[
E_{sk,splash} = C_{sk,conc} \cdot t_{splash} \sum_{n=1}^{5} \delta_{sk,splash} \cdot S_{sk,n} \cdot (1 - P_{clo,n} \cdot A_{clo,n} \cdot \eta_{clo,n})
\]

Eq. 6.7.4: Cumulative exposure to dip residue while handling sheep post dipping

\[
E_{sk,handling} = (C_{sk,dip} \cdot t_{wet/hns} + C_{sk,residue} \cdot t_{dry/hns}) \sum_{n=1}^{5} \delta_{sk,handling} \cdot S_{sk,n} \cdot (1 - P_{clo,n} \cdot A_{clo,n} \cdot \eta_{clo,n})
\]
Eq. 6.7.5: Cumulative exposure to dip from falling into dip bath

\[ E_{sk,fall} = C_{sk,dip} \cdot t_{beforewash} \cdot S_{sk,total} \cdot N_{falls} \]

Eq. 6.7.6: Cumulative exposure to dip through cleaning dip bath

\[ E_{sk,clean} = C_{sk,dip} \cdot t_{clean} \cdot S_{sk,total} \cdot (1 - A_{clo,n} \cdot \eta_{clo,n}) \cdot N_{clean} \]

Where:
- \( C_{sk} \) = the concentration of the chemical in the skin contamination layer from the concentrate (\( C_{sk,conc} \)) and from the dilute (\( C_{sk,dip} \));
- \( t \) = the duration of exposure from dipping (\( t_{dip} \)), from concentrated dip on hands (\( t_{conc} \)), from concentrated dip splashed on the body (\( t_{splash} \)), from handling sheep post dipping (\( t_{wethns} \)), from falling into dip bath (\( t_{beforewash} \)), and from cleaning dip bath (\( t_{clean} \));
- \( n \) = five body areas (arms and upper torso, legs and lower torso, hands, feet, and head);
- \( S_{sk} \) = specific body area;
- \( \delta \) = the fraction of the skin area that could potentially be contaminated during the task;
- \( P \) = the proportion of time PPE was reported to have been used;
- \( A \) = the proportion of the relevant body area covered with clothing or gloves as a fraction of the whole of that body part;
- \( \eta \) = the effectiveness of the clothing or gloves at reducing exposure, expressed as a percentage;
- \( N_{falls} \) and \( N_{clean} \) = the total number of falls into the dip bath and the total number of occasions the person cleaned the dip bath, respectively.

By using the details of this exposure estimation algorithm and model weighting factors presented in appendix 11, the following equations were applied:

Eq. 6.8: \[ E_{sk} = E_{sk,dip} + E_{sk,conc} + E_{sk,splash} + E_{sk,handling} + E_{sk,fall} + E_{sk,clean} \]

Eq.6.8.1: Cumulative exposure to dilute dip

\[ E_{sk,dip} = d \times y \times (h + 1) \times \Delta_{dip} \times 8 \times \sum_{n=1}^{5} \delta_{sk,n} \times S_{sk,n} \times (1 - P_{clo,n} \times A_{clo,n} \times \eta_{clo,n}) \]

Eq.6.8.2: Cumulative exposure to pesticide concentrate on hands

\[ E_{sk,conc} = 0.625 \times d \times y \times \Delta_{conc} \times (1 - 0.95 \times P_{glv}) \]

Eq.6.8.3: Cumulative exposure to pesticide concentrate splashed on the body

\[ E_{sk,splash} = 500 \times y \times SR \times \sum_{n=1}^{5} \delta_{sk,splash} \times S_{sk,n} \times (1 - P_{clo,n} \times A_{clo,n} \times \eta_{clo,n}) \]
Eq.6.8.4: Cumulative exposure to dip residue while handling sheep post dipping

\[ E_{sk,\text{handling}} = d \times y \times (h + 1)(\Delta_{\text{wethand}} + 8 + \Delta_{\text{dryhand}} + 80) \times \sum_{i=1}^{2} \delta_{i,\text{handling}} \times S_{d,i} \times (1 - P_{\text{clo,}i} \times A_{\text{clo,}i} \times \eta_{\text{clo,}i}) \]

Eq.6.8.5: Cumulative exposure to dip from falling into dip bath

\[ E_{sk,\text{fall}} = 0.19 \times N_{\text{falls}} \]

Eq.6.9.6: Cumulative exposure to dip through cleaning dip bath

\[ E_{sk,\text{clean}} = 0.2204 \times N_{\text{clean}} \]

Where:

d = dipping days/year; y = dipping year; h = dipping hours/day;
SR = number of times per year the dipper splashed concentrate on himself;
\( \Delta_{\text{dip}} \) = proportion of time spent in chucking and plunging;
\( \Delta_{\text{conc}} \) = frequency of adding the concentrate to the bath;
\( \Delta_{\text{wethand}} \) = proportion of time spent as a wet helper;
\( \Delta_{\text{dryhand}} \) = proportion of time spent as a dry helper.

The available variables in the SHAW study differ from those available in SHAPE (e.g. number of dipping hours per day is not available in SHAW). Therefore some modifications were necessary to this model so that it was applicable for the SHAW study. All modifications and assumptions are presented in Appendix 12.

Cumulative pesticide exposure through sheep dipping among sheep farmers in SHAW phase 2 was estimated using Eq.6.9. However, in the SHAW study information is available on a yearly basis and therefore the model was changed to the following form:

**Eq. 6.9: SHAPE = \sum_{y=1}^{Y} E_{sk,y}**

Where: SHAPE is cumulative pesticide exposure from sheep dipping, \( y = \) year, and \( E_{sk,y} \) is pesticide exposure in year \( y \).

The OPPROB variable was integrated into the SHAPE model as follows:

**Eq. 6.10: OP SHAPE = \sum_{y=1}^{Y} (E_{sk,y} \times OPPROB_{y})**

Where: OP SHAPE = cumulative OP exposure from sheep dipping and OPPROB\(_{y} \) = the probability of the pesticides used in a specific year containing an OP.
6.2.4.4 The TASK model for sheep dipping

Buchanan *et al.* derived an empirical model of OP exposure (described in Section 1.3.4.6.1) and the cumulative exposure was estimated using this equation:

Eq. 6.11: EXP=3.6×CONC + 0.2×SPLASH

Eq.6.11.1: SPLASH = \[ \sum_{j=1}^{J} \text{ND}_{j} \left( \%\text{PLNG}_{j} \times 66 + \%\text{CHCK}_{j} \times 44 + \%\text{HELP}_{j} \times 10 \right) \]

Where \%\text{PLNG}_{j}, \%\text{CHCK}_{j} and \%\text{HELP}_{j} are the estimated percentage of time spent working as a plunger, chucker, and helper respectively in dipping job j, and \text{ND}_{j} is the number of dipping days spent in job j.

Eq.6.11.2 : CONC = \[ \sum_{j=1}^{J} \text{ND}_{j} \left( \%\text{HAND}_{j} \times 8 \right) \]

Where \%\text{HAND}_{j} is the estimated percentage of occasions spent as principal concentrate handler in job j.

In the SHAW study, information had been collected according to the years not the jobs, so (\[ \sum_{j=1}^{J} \text{ND}_{j} \]) was modified to the number of dipping days in all years. Moreover, the estimated number of occasions spent as principal concentrate handler was not collected, so the estimated percentage of time spent working as a plunger was used instead of it because it has previously been reported that the plunger was the principal concentrate handler in most cases. Hence, the modified model used in the SHAW study was as follows:

Eq. 6.12: TASK =3.6×CONC + 0.2×SPLASH

Eq.6.12.1: SPLASH = \text{ND} \left( \%\text{PLNG} \times 66 + \%\text{CHCK} \times 44 + \%\text{HELP} \times 10 \right)

Eq.6.12.2: CONC = \text{ND} \times 8

Where: TASK = the cumulative pesticide exposure from sheep dipping; ND = number of dipping days; \%\text{PLNG}, \%\text{CHCK} and \%\text{HELP} = the estimated percentage of time in all years spent working as a plunger, chucker, and helper respectively.

Since the variable of dipper’s task was not collected as a percentage of time, rules were applied to calculate these percentages as detailed in Appendix 13. The TASK model was not used for OP exposure specifically since the estimated percentage of time spent working in each task was calculated for all years of dipping regardless of the probability of using OP pesticides.
6.2.4.5 A model for pesticide exposure in sheep farming

The previous three models were specific for dipping treatment; however there were another three methods mentioned in the SHAW questionnaire (pour-on, showering and injection). Therefore another new model was developed to estimate pesticide exposure from all sheep treatment methods collectively. This model was developed based on the common variables between methods available in the SHAW phase 2 data. For all treatments the following variables were available, namely the average number of days treating in each year, average number of sheep treated each day, PPE used in the treatment, handling the concentrate, spilling the concentrate and time of washing the spill, and handling the treated animals.

Three main exposure sources were taken into account in the developed exposure model. These were treating sheep with pesticides, handling pesticide concentrate, and handling treated sheep. Total exposure was the sum of the exposure from these three sources. The following exposure model was used to estimate general pesticide exposure from all sheep treatments:

**Eq. 6.13:** \( \text{EXP} = \alpha \times \text{TRE} + \beta \times \text{CON} + \gamma \times \text{AFT} \)

Where:
- \( \text{EXP} \) = cumulative pesticide exposure in sheep farming;
- \( \alpha, \beta, \) and \( \gamma \) = parameters;
- \( \text{TRE} \) = exposure from treating sheep with pesticides;
- \( \text{CON} \) = exposure from handling the concentrate to treat sheep;
- \( \text{AFT} \) = exposure from handling treated sheep.

The exposure from these three sources was calculated using following equations:

**Eq.6.13.1:** \( \text{TRE} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \times \text{METH}_{m} \)

**Eq.6.13.2:** \( \text{CON} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \times \text{SPILPROB} \times \text{ATA}_{ms} \times \text{DPY}_{ms} \times \text{PPE}_{ms} \times \text{WASH} \)

**Eq.6.13.3:** \( \text{AFT} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \)
Where:
ATA = average number of animals treated in each day;
DPY = number of treatment days per year;
PPE = personal protective equipment;
METH = score of treatment method;
SPILPROB = probability of spilling concentrate;
WASH = duration between spillage and washing out;
m = method of treatment;
y = year of treatment;
s = year of concentrate spillage.

The same PPE scores of the new conceptual model of sheep dipping (Section 3.9.2) were used for the model of all treatments. PPE\textsubscript{der} were used for all PPE scores. The PPE scores of showering and spray were assumed to be the same as of those of dipping whilst the PPE scores of injecting, oral and pouring-on were assumed to be the same as of those of handling the concentrate. The probability of spilling concentrate (SPILPROB) was assumed to be once every 100 animals. The values of the parameters and the weighting scores of the remaining variables are presented in Table 6-2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Values</th>
<th>Source of values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
<td>(\alpha) (TRE)</td>
<td>1</td>
<td>The values of these parameters were taken from the new conceptual model after adjusting (\beta) since the source of handling the concentrate (CON) in this model includes concentrate spills as well</td>
</tr>
<tr>
<td>Parameters</td>
<td>(\beta) (CON)</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Parameters</td>
<td>(\gamma) (AFT)</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>Dip</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>Shower and spray</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>Pour on</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>Injection and oral treatment</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>WASH</td>
<td>Never wash after spillage</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>WASH</td>
<td>At the end of the session</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>WASH</td>
<td>Other intervals and missing</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>WASH</td>
<td>Immediately after spillage</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

Oral treatment was ignored because the questions were about treatment for external parasites while nearly all of oral treatments in SHAW were wormers. Moreover, the exact years of when this type of treatment was used and its frequency of use were not available and exposure was assumed to be limited.

For exposure from handling the concentrate (CON), only pour-on, showering, spray and dip methods are included in the estimated exposure. If the farmer stated that he did not
handle either the concentrate or treated animals the exposure in the related source will be zero. For handling treated sheep, the type of PPE used was assumed to be the same as that used during the treatment itself.

The previous exposure model used for general pesticides was modified by adding an OPPROB variable to be used for OP exposure estimation. The modified model was as follows:

Eq. 6.14: \( \text{OPEXP} = \alpha \times \text{OPTRE} + \beta \times \text{OPCON} + \gamma \times \text{OPAFT} \)

Where:
OPEXP = cumulative OP exposure in sheep farming;  
OPTRE = exposure from treating sheep with OP pesticides;  
OPCON = exposure from handling the OP concentrate to treat sheep;  
OPAFT = exposure from handling animals treated with OP.

The exposure from these three sources was calculated using following equations:

Eq.6.14.1: \( \text{OPTRE} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \times \text{METH}_{m} \times \text{OPPROB}_{my} \)

Eq.6.14.2: \( \text{OPCON} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \times \text{OPPROB}_{my} \)  
+ \( \sum_{m=1}^{M} \sum_{s=1}^{S} \text{SPAIPROB} \times \text{ATA}_{ms} \times \text{DPY}_{ms} \times \text{PPE}_{ms} \times \text{WASH} \times \text{OPPROB}_{my} \)

Eq.6.14.3: \( \text{OPAFT} = \sum_{m=1}^{M} \sum_{y=1}^{Y} \text{ATA}_{my} \times \text{DPY}_{my} \times \text{PPE}_{my} \times \text{OPPROB}_{my} \)

Where: OPPROB = probability of the pesticides used in a specific year to contain OP. The same scores and rules that were applied for general pesticides were also applied in the OP models.

6.2.5 Pesticide exposure estimation in other farming sectors

Pesticide exposure was estimated using simple surrogates and more sophisticated models in each farming sector. Exposure assessment models for treatment methods in different farming sectors were developed using the available information in the SHAW phase 2 data. The models of animal treatments (cattle and other livestock) were the same of that of sheep treatments with a slight modification.
6.2.5.1 Simple surrogates of exposure in other farming sectors

10 surrogates of pesticide exposure in other farming sectors were identified from phase 1. The ever/never surrogates (EVCAT, EVLIV, EVCRP, EVCONCAT, EVCONCRP, EVWAR, and EVAPPCRP) were simple use of answers for questions C2.1, C2.2, C3.1, C3.13, C4.1, and C4.3 while other surrogates were derived from answers for questions C2.1, C2.2 (Appendix 1). The same surrogates were modified so as to estimate OP exposure in other farming sectors. The modification was to include only years after 1970 (Table 6-3).

Four activities were not used as surrogates for OP exposure since phase 1 data did not indicate whether they occurred before 1970 or after. Those activities were ever handled the concentrate to treat cattle (EVCONCAT), ever applied treatment for warble fly (EVWAR), ever handled the concentrate to treat crops or grains (EVCONCRP), and ever applied insecticides to crops or grains (EVAPPCRP).

Table 6-3: Simple surrogates of pesticide exposure from other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Surrogate a</th>
<th>Definition</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EVCAT</td>
<td>Ever having cattle</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVCONCAT</td>
<td>Ever handled the concentrate to treat cattle</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVWAR</td>
<td>Ever applied treatment for warble fly</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRCAT</td>
<td>Number of years having cattle</td>
<td>Numerical</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVCAT</td>
<td>Ever having cattle after 1970</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRCAT</td>
<td>Number of years having cattle after 1970</td>
<td>Numerical</td>
</tr>
<tr>
<td>Other</td>
<td>General</td>
<td>EVLIV</td>
<td>Ever having other livestock</td>
<td>Dichotomous</td>
</tr>
<tr>
<td>Livestock</td>
<td></td>
<td>YRLIV</td>
<td>Number of years having other livestock</td>
<td>Numerical</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVLIV</td>
<td>Ever having other livestock after 1970</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRLIV</td>
<td>Number of years having other livestock after 1970</td>
<td>Numerical</td>
</tr>
<tr>
<td>Crops And</td>
<td>General</td>
<td>EVCRP</td>
<td>Ever having crops or grains</td>
<td>Dichotomous</td>
</tr>
<tr>
<td>Grain</td>
<td></td>
<td>EVCONCRP</td>
<td>Ever handled the concentrate to treat crops or grains</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVAPPCRP</td>
<td>Ever applied insecticides to crops or grains</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRCRP</td>
<td>Number of years having crops or grains</td>
<td>Numerical</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVCRP</td>
<td>Ever having crops or grains after 1970</td>
<td>Dichotomous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRCRP</td>
<td>Number of years having crops or grains after 1970</td>
<td>Numerical</td>
</tr>
</tbody>
</table>

* Based on phase 1 data

6.2.5.2 A model for other animal treatments

SHAW farmers reported treating a range of animals with pesticides in addition to sheep including cattle, pigs, poultry, horses and goats. Common treatment methods for these animals were dipping, pouring-on, showering, injecting, spraying and oral treatment. For all animals the following variables were available in the SHAW study, namely herd size in each year, method of treatment, average number of days treating in each year, average number of animals treated each day, PPE used in the treatment, handling the
concentrate during the treatment, spilling the concentrate and time of washing the spill, and handling the treated animals.

The same exposure model developed to assess general pesticide exposure and OP exposure in sheep farming (Section 6.2.4.5) was used to assess exposure in cattle and other livestock sectors. However, in cattle sector, farmers were asked about treatments according to reasons of treatment not according to methods, therefore the model was used after replacing all m (i.e. method of treatment) in Eq.6.13.1, Eq.6.13.2, Eq.6.13.3, Eq.6.14.1, Eq.6.14.2 and Eq.6.14.3 with r, where r is the reason of treatment. The METH variable in Eq.6.13.1 and Eq.6.14.1 was also replaced by REAS variable where REAS is the score of reason of treatment.

Exposure from applying wormers was calculated according to the following assumptions: ATA equals the herd size, DPY equals 1, and y is number of years of having cattle. For exposure from handling the concentrate (CON), only treatment for warble fly, lice and flies were taken into account, while for exposure from handling treated cattle (AFT) only warble fly and lice treatments were taken into account since the other two treatments are not applied to cattle topically.

The same scores of treatment methods used in Table 6-2 were used for the reasons of treatment. The scores of warble and lice treatments were 1.4, the score of fly treatment was 1.2, while the score of wormers was 0.2 instead of 0.4 to reduce the effect of assuming that wormers were applied to the whole herd in all years. These scores were applied based on the assumption that warble fly and lice treatments are applied mostly by pouring-on, fly treatment mostly by spraying, and wormers mostly by injections or orally111.

Pesticide exposure from all livestock treatments except sheep and cattle was combined into two exposure estimates (EXP\textsubscript{livestock} for general pesticides and OPEXP\textsubscript{livestock} for OP pesticides) simply by adding the results of all livestock together:

\begin{align*}
\text{Eq. 6.15: } \text{EXP}_{\text{livestock}} &= \text{EXP}_{\text{pigs}} + \text{EXP}_{\text{poultry}} + \text{EXP}_{\text{horses}} + \text{EXP}_{\text{goats}} \\
\text{Eq. 6.16: } \text{OPEXP}_{\text{livestock}} &= \text{OPEXP}_{\text{pigs}} + \text{OPEXP}_{\text{poultry}} + \text{OPEXP}_{\text{horses}} + \text{OPEXP}_{\text{goats}}
\end{align*}

6.2.5.3 A model for treating crops and grains

In the crops and grains sector, the following variables were available in the SHAW database: the type of treated crop, the area of treated crop, the type of pesticide
(herbicides, insecticides, fungicides, and other), whether pesticides contained OPs or not, the frequency of treatment, the average number of days/year and hours/day spent applying pesticides to crops, the application methods (tractor, hand-held sprayer, aerial application, and other), and handling the concentrate to treat crops or grains.

Only two main exposure sources, namely pesticide application to crops and grains and handling the concentrate before the application, were used to estimate pesticide exposure. Information on other sources of pesticide exposure in the crop sector like field entry after pesticide application were not available in the SHAW study. The following models were then used to estimate the exposure in this sector:

Eq. 6.17: \(\text{EXP}_{1\text{crops}} = \text{APP}_{1\text{crops}} + \text{CON}_{\text{crops}}\)

Eq.6.17.1: \(\text{APP}_{1\text{crops}} = \sum_{y=1}^{Y} \text{METH}_{1y} \times \text{ARE}_{ym1} + \text{METH}_{2y} \times \text{ARE}_{ym2} + \ldots\)

Eq.6.17.2: \(\text{CON}_{\text{crops}} = \sum_{y=1}^{Y} \text{AREA}_{y}\)

Eq. 6.18: \(\text{EXP}_{2\text{crops}} = \text{APP}_{2\text{crops}} + \text{CON}_{\text{crops}}\)

Eq.6.18.1: \(\text{APP}_{2\text{crops}} = \sum_{y=1}^{Y} \text{METH}_{1y} \times \text{HPY}_{ym1} + \text{METH}_{2y} \times \text{HPY}_{ym2} + \ldots\)

Eq.6.18.2: \(\text{CON}_{\text{crops}} = \sum_{y=1}^{Y} \text{AREA}_{y}\)

Where:
\(\text{EXP}_{1\text{crops}}\) and \(\text{EXP}_{2\text{crops}}\) = cumulative pesticide exposure in crops and grain sector;
\(\text{APP}_{1\text{crops}}\) and \(\text{APP}_{2\text{crops}}\) = exposure through pesticide application to crops and grains;
\(\text{CON}_{\text{crops}}\) = exposure through handling the concentrate to treat crops and grains;
\(\text{METH}\) = score of treatment method;
\(\text{ARE}_{m}\) = total area treated using that method;
\(\text{AREA}\) = total area treated;
\(\text{HPY}_{m}\) = number of treating hours in that year using that method;
\(y\) = year;
\(m\): treatment method.

The following method scores were taken from AHS study\textsuperscript{153}: boom or tractor = 3, hand spray = 9, airblast = 9, sprayer and gas fumer = 9, drip feed = 1, seed treatment = 1, and tractor and Hand spray = 6 (average of the two methods).
The same exposure models that were used for general pesticides were also used for OP exposure after adding the OPPROB variable.

Eq. 6.19: \( \text{OPEXP}_{1\text{crops}} = \text{OPAPP}_{1\text{crops}} + \text{OPCON}_{crops} \)

Eq. 6.19.1: \( \text{OPAPP}_{1\text{crops}} = \sum_{y=1}^{Y} \text{METH}_{1y} \times \text{Area}_{ym1} \times \text{OPPROB}_{ym1} \)

\[ \text{METH}_{2y} \times \text{Area}_{ym2} \times \text{OPPROB}_{ym1} + \ldots \]

Eq. 6.19.2: \( \text{OPCON}_{crops} = \sum_{y=1}^{Y} \text{AREA}_y \times \text{OPPROB}_y \)

Eq. 6.20: \( \text{OPEXP}_{2\text{crops}} = \text{OPAPP}_{2\text{crops}} + \text{OPCON}_{crops} \)

Eq. 6.20.1: \( \text{OPAPP}_{2\text{crops}} = \sum_{y=1}^{Y} \text{METH}_{1y} \times \text{HPY}_{ym1} \times \text{OPPROB}_{ym1} + \)

\[ \text{METH}_{2y} \times \text{HPY}_{ym2} \times \text{OPPROB}_{ym1} + \ldots \]

Eq. 6.20.2: \( \text{OPCON}_{crops} = \sum_{y=1}^{Y} \text{AREA}_y \times \text{OPPROB}_y \)

Where:
- \( \text{OPEXP}_{1\text{crops}} \) and \( \text{OPEXP}_{2\text{crops}} \) = cumulative OP exposure in crops and grain sector;
- \( \text{OPAPP}_{1\text{crops}} \) and \( \text{OPAPP}_{2\text{crops}} \) = exposure through OP application to crops and grains;
- \( \text{OPCON}_{crops} \) = exposure through handling OP concentrate to treat crops and grains;
- \( \text{OPPROB} \) = probability of utilised pesticides containing an OP.

6.2.5.4 A model for other pesticide use

Two other exposure sources were addressed in the SHAW questionnaire: application of pesticides to grain in storage and using pesticides for any other purpose. The exposure from these two sources was estimated using the following simple equation:

Eq. 6.21: \( \text{EXP}_{\text{other}} = \text{GRAIN} + \text{OTHER} \)

Where:
- \( \text{EXP}_{\text{other}} \) = pesticide exposure from other use;
- \( \text{GRAIN} \) = exposure from application of pesticides to grain in storage;
- \( \text{OTHER} \) = exposure from using pesticides for any other purpose.

Both of these variables are dichotomous (0/1). Therefore, pesticide exposure in this sector can take the score of 0, 1, or 2.

The generic model was modified for the OP estimation:
Eq. 6.22: \[ \text{OPEXP}_{\text{other}} = \text{OPGRAIN} + \text{OPOTHER} \]

Where:
\[
\text{OPEXP}_{\text{other}} = \text{OP exposure from other use};
\]
\[
\text{OPGRAIN} = \text{exposure from application of OP to grain storage};
\]
\[
\text{OPOTHER} = \text{exposure from using OP for any other use}.
\]

Both of these variables are 0/1 variables. Therefore general exposure in this sector can take the score of 0, 1, or 2. For OPOTHER when the product was unknown it was assumed to be free of OP. For OPGRAIN since the SHAW questionnaire did not include a question whether the fumigant was OP or not, two estimates were applied, the first considered all fumigants are OP and the second considered all fumigants were not OPs.

6.2.6 Estimation of OP probability (OPPROB)

OPPROB is the probability of utilised pesticides in any farming sector containing an OP in a specific year. This probability was estimated by the PhD student as described in the following sections, and then after discussions they were agreed by two members of the SHAW research team.

6.2.6.1 Sheep treatments

For sheep models, two databases were used to obtain OPPROB. The first database was obtained from the VMD and because its last update was in 2002, the VMD annual report was used for the last three years 2003-2005\(^293\). The second database was that used in the SCOPE study \(^{321,322}\). As mentioned all pesticides have been assumed to be free of OP before 1970; however the first year in the available sources was 1972 so probability data was obtained starting from that year.

When farmers gave the specific name of the applied product, OPPROB was 0 if that product was not OP and 1 if that product was OP according to the available pesticide databases. However, the SHAW farmers provided the general trade name of the dip in most cases. The probability of a general trade name being an OP pesticide in a certain year was then calculated by the ratio of the number of the products holding that general trade name and containing an OP in that year divided by the total number of products holding that name in that year. For instance, a farmer told that he used “Coopers” in 1972, and there were 6 products in that year holding the name “Coopers”. Of these, 5 products contained OP, so the probability of “Coopers” containing an OP in 1972 was \(5/6 = 0.83\). All assumptions used for applied pesticides are detailed in Appendix 14.
6.2.6.2 Cattle and other livestock

While detailed information about sheep dips after 1971 was available, such information was not available about pesticides used for treating cattle or other livestock. Therefore more general assumptions were used to estimate OPPROB in these sectors. Since there was no specific year after which we had detailed information about the use of OP in cattle treatments (i.e. similar to 1971 of sheep dips) and since OP pesticides were introduced in the cattle sector as early as 1960$^{83,115}$, this year was used as a start year and all pesticides used to treat cattle were assumed free of OP before 1960. The majority of farmers who had other livestock also had cattle; therefore 1960 was also used for other livestock to define when OPs were first used. Appendix 14 presents the rules of determining OPPROB in other livestock and cattle farming sectors.

6.2.6.3 Crops and grains

Crop farmers were asked in the phase 2 questionnaire whether the utilised pesticides contained OPs or not but the farmers did not know the answer for about two thirds of the crops. Moreover, the reported “yes” or “no” answers were not always consistent with the answers of a subsequent question about the trademarks of the utilised pesticides. This inconsistency was expected since various types of pesticides with too many trademarks were used by most of those farmers. Therefore an alternative method was used to estimate the probability of the pesticides used containing an OP.

The Pesticide Usage Survey (PUS) collects quantitative and qualitative data on pesticide use in agricultural and horticultural crops$^{44}$. These data have been collected since 1965 by the Food and Environment Research Agency in England and Wales, while in Scotland the survey is conducted by the Science and Advice for Scottish Agriculture and in Northern Ireland by the Agri-Food & Biosciences Institute.

The PUS gather data on pesticides applied to cereals and other arable crops, vegetables, glasshouse crops, soft and top fruit, mushrooms, and other agricultural and horticultural crops. The surveys give accurate data about pesticide usage like the range of chemicals used, the amount of active ingredients applied; the total treated area, and proportion of crops treated. The frequency of data collection varies between crops; for example arable crops are usually surveyed every two years while other crops are surveyed every 4 years$^{65}$.

From the collected data in the PUS, the total treated area was used as an indicator of OPPROB. The total area treated was summed twice, one when OP pesticides were
specifically used and the other for all types of pesticides. OPROB was equal to the ratio between the two figures.

The agricultural and horticultural crops were categorised into different groups in the previous PUSs. Therefore, the crop mentioned by the farmer in a specific year was matched with the most related category in the survey of that year to get the OP probability. The use of OPs on crops in the UK was very rare before 1965 and there is no available data about OP use before 1965\textsuperscript{13} and therefore that year was set as the start year of OP use in crops sector. When the data was not collected for the crops in a specific year, the data of the nearest year was used. This is why some probabilities are the same in consecutive years. Appendix 15 presents OPPROB for each type of crops from 1965 to 2005.

6.2.7 Statistical analysis

Exposure estimates are presented by summaries of the distributions and histograms. Most of developed exposure estimates were log-normally distributed therefore geometric means are also presented. All distributions and histograms are for the results after omitting zero exposures. Spearman correlation coefficients were mostly used to describe the correlations between different models and between models and surrogates. Kendall’s tau (\(\tau\)) was used to describe correlations with OPNY in all sectors since about half of the farmers have the same value of this variable. When the correlation between models and surrogates were studied, only farmers who had the relevant type of livestock or crops were included. When the correlation between general pesticides models and OP pesticides models were studied in a specific sector, only farmers who were exposed to pesticides in that sector were included.

6.3 Results

As described in detail in Chapter 2, 234 farmers were interviewed in phase 2 of the SHAW study. 219 farmers were contacted again in this PhD project to obtain further information on cattle treatment and get missing information. 6 had died and one had had a car accident and it was not possible to talk to him. The remaining 8 of phase 2 farmers had no missing information and no cattle or other livestock treatments and therefore they were not contacted. The results below are for all farmers interviewed in phase 2 taking into account the information collected in the second contact (\(i.e\). the telephone contact).
6.3.1 Description of farming practices

Of the 234 farmers, 198 farmers had been sheep farmers, 222 had been cattle farmers, 92 had been other livestock farmers and 140 had been crop farmers between 1942 and 2005. 191 farmers treated sheep with pesticides, 211 treated cattle with pesticides, 43 treated other livestock with pesticides, 121 applied pesticides to crops and grains, and 221 used pesticides for other purposes (Figure 6-2). A minority of farmers had ever applied pesticides in only one farming sector while about a third of the farmers had ever applied pesticides to sheep, cattle and crops and another third had ever applied pesticides to sheep and cattle. 5.6% of the farmers had ever applied pesticides in all farming sectors while 2 farmers had not applied pesticide in any sector (Table 6-4).

![Figure 6-2: Number of subjects who had ever been farmers in each farming sector between 1942-2005 and those who applied pesticides in that sector](image)

Table 6-4: Number of farmers who had ever applied pesticides in different farming sectors

<table>
<thead>
<tr>
<th>Applied pesticides to</th>
<th>Number of farmers</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep and cattle</td>
<td>79</td>
<td>33.8</td>
</tr>
<tr>
<td>Sheep, cattle and crops</td>
<td>74</td>
<td>31.6</td>
</tr>
<tr>
<td>Sheep, cattle and other livestock</td>
<td>17</td>
<td>7.3</td>
</tr>
<tr>
<td>Cattle and crops</td>
<td>15</td>
<td>6.4</td>
</tr>
<tr>
<td>All farming sectors</td>
<td>13</td>
<td>5.6</td>
</tr>
<tr>
<td>Crops</td>
<td>10</td>
<td>4.3</td>
</tr>
<tr>
<td>Cattle</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Cattle, other livestock and crops</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Sheep</td>
<td>4</td>
<td>1.7</td>
</tr>
<tr>
<td>Cattle and other livestock</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>Other livestock and crops</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Sheep and crops</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Sheep and other livestock</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Other livestock</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Nothing</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>234</td>
<td>100</td>
</tr>
</tbody>
</table>
6.3.1.1 Sheep farming practices

Of the 191 farmers who indicated in the phase 2 interview that they had personally been involved in treating sheep with pesticides, 188 farmers (98.4%) had dipped their sheep in the past, 94 (49.2%) had used pour-ons, 56 (29.3%) injections, and 13 (6.8%) had showered the sheep. 112 farmers (58.6%) had used multiple treatment methods, of which 65 had used two methods, 46 had used three methods and 1 had used all four methods. Table 6-5 details the methods used by these farmers.

Table 6-5: Treating methods used by sheep farmers

<table>
<thead>
<tr>
<th>Treating method</th>
<th>Farmers who ever used the method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>Dip only</td>
<td>76</td>
</tr>
<tr>
<td>Dip &amp; pour-on</td>
<td>46</td>
</tr>
<tr>
<td>Dip &amp; inject &amp; pour-on</td>
<td>41</td>
</tr>
<tr>
<td>Dip &amp; inject</td>
<td>14</td>
</tr>
<tr>
<td>Dip &amp; shower &amp; pour-on</td>
<td>5</td>
</tr>
<tr>
<td>Dip &amp; shower</td>
<td>5</td>
</tr>
<tr>
<td>Shower only</td>
<td>2</td>
</tr>
<tr>
<td>Dip &amp; shower &amp; inject &amp; pour-on</td>
<td>1</td>
</tr>
<tr>
<td>Pour-on only</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>191</td>
</tr>
</tbody>
</table>

Table 6-6 presents the distributions of cumulative flock size over a lifetime, the number of treating years and the number of treating days. The flock size ranged from 4 to 30000 with a median of 400 while the cumulative number of sheep for each farmer over a lifetime ranged from 150 to 163750 with a median of 15500.

Table 6-6: Cumulative number of flock size, treating years and treating days in sheep sector

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sheep farmers</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range</th>
<th>25th -75th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flock size</td>
<td>191</td>
<td>25463 ± 28235</td>
<td>15500</td>
<td>150 - 163750</td>
<td>6133 - 34250</td>
</tr>
<tr>
<td>Treating years</td>
<td>191</td>
<td>36.6 ± 17.2</td>
<td>42</td>
<td>1 - 62</td>
<td>25 - 49</td>
</tr>
<tr>
<td>Treating days</td>
<td>190</td>
<td>124 ± 131</td>
<td>93</td>
<td>2 - 940</td>
<td>47 - 150</td>
</tr>
</tbody>
</table>

Farmers who dipped their sheep had done so between 1942 and 2005 and the majority of them had dipped between 1960 and 1990, whereas the other three methods are of relatively recent use and have only been started to be used intensively since 1990 (Figure 6-3). The majority of sheep farmers had handled pesticide concentrate to treat sheep (92.7%), while a minority of sheep farmers had been in contact with sheep after being treated (28.7%).
Figure 6-3: Number of sheep farmers using different treating methods by year

(A) Dip, (B) Shower, (C) Injection, (D) Pour-on, (E) All methods
The median number of years that a farmer had treated sheep was 42 (range 1-62). The total number of days spent treating sheep in a lifetime ranged between 2 and 940 with a median of 93 days, while the annual number of treating days ranged between 1 and 21 with a median of 2 and a mode of 2 (Figure 6-4).

![Figure 6-4: Annual number of treating days in sheep sector](image)

Regarding PPE (Table 6-7), 75.7% had ever used PPE when handling the concentrate and 80% had ever used a type of PPE when applying pesticides to sheep. Boots were the most frequent equipment used by farmers when handling the concentrate and applying pesticides (92.5 and 94.2% respectively) followed by leggings (60.7 and 72.1%), aprons (45.1 and 53.2%) and gloves (35.3 and 26.3%). More than 60% of the gloves used were made of rubber and the rest were synthetic. Of those farmers who used gloves, 40% used gloves that went only up to the wrist, 34% to the mid-forearm, and 22% to the elbow.

<table>
<thead>
<tr>
<th>PPE</th>
<th>Ever used PPE during the process of any method *</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Handling concentrate</td>
<td>Applying pesticides</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number</td>
<td>% (n=173)</td>
<td>Number</td>
</tr>
<tr>
<td>Boots</td>
<td>160</td>
<td>92.5</td>
<td>179</td>
</tr>
<tr>
<td>Leggings</td>
<td>105</td>
<td>60.7</td>
<td>137</td>
</tr>
<tr>
<td>Apron</td>
<td>78</td>
<td>45.1</td>
<td>101</td>
</tr>
<tr>
<td>Gloves</td>
<td>61</td>
<td>35.3</td>
<td>50</td>
</tr>
<tr>
<td>Other</td>
<td>16</td>
<td>9.2</td>
<td>25</td>
</tr>
<tr>
<td>Face shield</td>
<td>7</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Respirator</td>
<td>1</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td>Never used PPE</td>
<td>42</td>
<td>24.3</td>
<td>38</td>
</tr>
</tbody>
</table>

* 17 farmers did not handle the concentrate and 1 farmer is missing.
To show any trends in the use of PPE overtime, the percentage of farmers who wore each type of PPE whilst handling the concentrate is shown in Figure 6-5. Wearing gloves increased over time while wearing aprons and leggings increased gradually till the mid 1990s, but then use fell. Wearing boots did not change until the mid 1990s when it also started decreasing. The percentage of farmers who did not use any type of PPE whilst handling the concentrate remained approximately constant until the mid 1990s and then started to rise. Similar trends were found for wearing PPE during applying pesticides (figures not shown).

Figure 6-5: Percentage of farmers who used different types of PPE during handling the concentrate to treat sheep

(A) gloves, (B) boots, (C) apron, (D) leggings, (E) none. The number of farmers is in Figure 6-3
Whilst dipping, 79.8% of the farmers had worked at some time as a plunger, 55.3% as a chucker, and 14.9% as a helper (Table 6-8). Most of the plungers always submerged the sheep with a special tool (64.4%), 19.4% always used their hands or feet, whereas the rest had used both a tool and their body to submerge the sheep. 63.4% of the dippers reported that they had been soaked to the skin on any part of their body at some point, although only 12.2% regularly entered the bath. 77.1% of the dippers had been involved in the disposal of sheep dip.

<table>
<thead>
<tr>
<th>Task</th>
<th>Ever work in the task a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>% (n=188)</td>
</tr>
<tr>
<td>Plunger</td>
<td>94</td>
</tr>
<tr>
<td>Chucked</td>
<td>45</td>
</tr>
<tr>
<td>Plunger &amp; Chucked</td>
<td>45</td>
</tr>
<tr>
<td>Helper</td>
<td>14</td>
</tr>
<tr>
<td>Plunger &amp; Chucked &amp; Helper</td>
<td>12</td>
</tr>
<tr>
<td>Chucked &amp; Helper</td>
<td>3</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
</tr>
</tbody>
</table>

a There are farmers who worked in different tasks throughout the years.

The majority of sheep dippers always used a straight dipping bath (73.9%), 4.8% always used a circular bath, while the rest used different types of dipping bath. 86.7% of dippers always used outside dipping baths, 2.7% always used covered dipping baths, while 2.1% always used baths inside buildings, whilst the remaining used baths at different locations. The majority of dipping baths did not ever have splash guards (66.5%) whereas 15.4% always had splash guards (Table 6-9).

<table>
<thead>
<tr>
<th>Description</th>
<th>Dipping bath</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>% (n=188)</td>
</tr>
<tr>
<td>Type</td>
<td></td>
</tr>
<tr>
<td>Straight</td>
<td>139</td>
</tr>
<tr>
<td>Circular</td>
<td>9</td>
</tr>
<tr>
<td>Different</td>
<td>40</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Outside</td>
<td>163</td>
</tr>
<tr>
<td>Outside and covered</td>
<td>5</td>
</tr>
<tr>
<td>Inside buildings</td>
<td>4</td>
</tr>
<tr>
<td>Different</td>
<td>16</td>
</tr>
<tr>
<td>Splash guard</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>125</td>
</tr>
<tr>
<td>Always</td>
<td>29</td>
</tr>
<tr>
<td>Different</td>
<td>34</td>
</tr>
</tbody>
</table>
About half of the dippers (52.7%) manipulated the sheep manually to enter the bath, 27.4% let them drop into the bath using a slide mechanism or a tilt, 2.2% let them walk into the bath using a ramp, and the remaining farmers used different methods. 45% of the farmers said that there were 3 dippers involved in the dipping process, 33.9% said that there were 2 dippers, 17.4% said that there were more than 3 dippers, while 3.7% reported that they were the only dipper.

6.3.1.2 Other farming practices

211 farmers reported treating cattle with pesticides and of them 94.8% handled the concentrate for these treatments and 60.7% were in contact with cattle after they had been treated. The herd size ranged from 1 to 1000 with a median of 81 while the cumulative number of cattle for each farmer ranged from 54 to 32100 with a median of 3410. Almost all cattle farmers had treated their cattle for warble fly (94.3%), two thirds had treated them for lice (67.8%) and half of them treated them for flies (49.3%). Table 6-10 shows the number of farmers using each type of treatment and the mean number of treating years.

Table 6-10: Cattle treatments applied by the SHAW farmers

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cattle farmers</th>
<th>Total number of years treating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number % (n=211) Mean ± SD Range</td>
<td></td>
</tr>
<tr>
<td>Warble fly</td>
<td>199 94.3</td>
<td>13.5 ± 10.9 1 – 49</td>
</tr>
<tr>
<td>Flies</td>
<td>104 49.3</td>
<td>28.6 ± 16.2 3 – 60</td>
</tr>
<tr>
<td>Lice</td>
<td>143 67.8</td>
<td>29.8 ± 14.7 2 – 59</td>
</tr>
</tbody>
</table>

Boots were the most frequent PPE used by farmers whilst handling pesticides concentrate for cattle treatment (78%) then gloves and aprons (35% and 22.5% respectively) while only 11.5% used leggings. A similar usage of PPE was found when pesticides were applied (Table 6-11).

Table 6-11: PPE used by cattle farmers when using pesticides

<table>
<thead>
<tr>
<th>PPE</th>
<th>Ever used PPE during the process of any treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Handling concentrate Applying pesticides</td>
</tr>
<tr>
<td></td>
<td>Number % (n=200) Number % (n=211)</td>
</tr>
<tr>
<td>Boots</td>
<td>156 78</td>
</tr>
<tr>
<td>Gloves</td>
<td>70 35</td>
</tr>
<tr>
<td>Apron</td>
<td>45 22.5</td>
</tr>
<tr>
<td>Legging</td>
<td>23 11.5</td>
</tr>
<tr>
<td>Face shield</td>
<td>2 1</td>
</tr>
<tr>
<td>Respirator</td>
<td>0 0</td>
</tr>
<tr>
<td>Never used PPE</td>
<td>31 15.5</td>
</tr>
</tbody>
</table>

* 11 farmers did not handle the concentrate.
In the other livestock sector, 43 farmers had treated livestock with pesticides; of them 22 had applied pesticides on pigs, 12 on poultry, 2 on horses, 1 on goats, 5 on pigs and poultry, and 1 on pigs, poultry and horses. Table 6-12 presents the number of farmers who used pesticides on other livestock and the number of treating years. 16 farmers applied pesticides only topically, 8 only orally, 5 used a spray method, and the remaining used different methods. The number of farmers who handled pesticide concentrate to treat other livestock was 29 (67.4%) and the number who handled the livestock within 24 hours of treatment was 12 (27.9%).

Table 6-12: Other livestock treatments applied by the SHAW farmers

<table>
<thead>
<tr>
<th>Livestock</th>
<th>Number of farmers</th>
<th>Total number of years treating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Pigs</td>
<td>28</td>
<td>23.5 ± 13.9</td>
</tr>
<tr>
<td>Poultry</td>
<td>18</td>
<td>20.9 ± 10.3</td>
</tr>
<tr>
<td>Horses</td>
<td>3</td>
<td>27.7 ± 11.8</td>
</tr>
<tr>
<td>Goats</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

About half of other livestock farmers used boots whilst handling pesticide concentrate for other livestock treatment (48.3%), 17.2% used gloves and 10.3% used aprons, while no farmer used leggings. The use of PPE during handling the concentrate and applying pesticides to other livestock is presented in Table 6-13.

Table 6-13: PPE used by other livestock farmers when using pesticides

<table>
<thead>
<tr>
<th>PPE</th>
<th>Ever used PPE during the process of any treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Handling concentrate</td>
</tr>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>Boots</td>
<td>14</td>
</tr>
<tr>
<td>Gloves</td>
<td>5</td>
</tr>
<tr>
<td>Apron</td>
<td>3</td>
</tr>
<tr>
<td>Leggings</td>
<td>0</td>
</tr>
<tr>
<td>Face shield</td>
<td>2</td>
</tr>
<tr>
<td>Respirator</td>
<td>0</td>
</tr>
<tr>
<td>Not ever used PPE</td>
<td>10</td>
</tr>
</tbody>
</table>

* 14 farmers did not handle the concentrate.

In the crops and grains sector, 119 farmers had used pesticides to treat crops or grains, and of them 113 had ever handled the concentrate to treat crops or grain. Another two only handled the concentrate whilst a contractor then applied the pesticide to the crops. Table 6-14 presents all types of crops and grains treated with pesticides. Barley was the most common crop treated by farmers (64.7%), then wheat (42%) and potatoes (29.4%).
Table 6-14: Type of crops and grains treated

<table>
<thead>
<tr>
<th>Crop and grain</th>
<th>Number of farmers</th>
<th>%  (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barley</td>
<td>77</td>
<td>64.7</td>
</tr>
<tr>
<td>Wheat</td>
<td>50</td>
<td>42.0</td>
</tr>
<tr>
<td>Potatoes</td>
<td>35</td>
<td>29.4</td>
</tr>
<tr>
<td>Beans</td>
<td>21</td>
<td>17.6</td>
</tr>
<tr>
<td>Oats</td>
<td>20</td>
<td>16.8</td>
</tr>
<tr>
<td>Sugar beet</td>
<td>19</td>
<td>16.0</td>
</tr>
<tr>
<td>Oil seed rape</td>
<td>18</td>
<td>15.1</td>
</tr>
<tr>
<td>Maize and corn</td>
<td>16</td>
<td>13.4</td>
</tr>
<tr>
<td>Turnips and swede</td>
<td>15</td>
<td>12.6</td>
</tr>
<tr>
<td>Arable and cereals</td>
<td>12</td>
<td>10.1</td>
</tr>
<tr>
<td>Peas</td>
<td>7</td>
<td>5.9</td>
</tr>
<tr>
<td>Flowers and pot plant</td>
<td>5</td>
<td>4.2</td>
</tr>
<tr>
<td>All crops</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Linseed</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Tomatoes</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Vegetables</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Cabbage and kale</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Lettuce</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Strawberries and raspberries</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Beet</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Chrysanthemums</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Fodder</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Apples</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Carrots</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Celery</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Cucumber</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Fruits</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Mustard</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Soya beans</td>
<td>1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* farmers might have more than one type of crops

The majority of farmers (85.7%) used only tractors to apply pesticides to crops and grains, 5.9% used only a hand-held sprayer, 6.7% used both methods. The remaining used other methods (Table 6-15). 109 farmers had a grain bin or another grain storage building on their farm, and of them 71 farmers applied pesticides to the building or the grain itself. The majority of farmers also used pesticides for uses other than on their livestock and crops (94%)

Table 6-15: Pesticide application methods in the crops sector

<table>
<thead>
<tr>
<th>Application method</th>
<th>Number of farmers</th>
<th>%  (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tractors</td>
<td>99</td>
<td>83.2</td>
</tr>
<tr>
<td>Hand-held sprayer</td>
<td>7</td>
<td>5.9</td>
</tr>
<tr>
<td>Tractor and hand-held sprayer</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>Tractor and airblast</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Tractor and seed treatment</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Hand-held sprayer and gas fume</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Drip feed</td>
<td>1</td>
<td>1.0</td>
</tr>
</tbody>
</table>
6.3.2 Estimates of pesticide exposure

6.3.2.1 Sheep farming

Of the 234 farmers, 198 farmers had been sheep farmers between 1942 and 2005 and 172 had been sheep farmers after 1970. 193 farmers (84.3%) had ever dipped sheep (missing data on 5 farmers) and 184 farmers (81.4%) had ever handled the concentrate to treat sheep (8 with missing data). Table 6-16 summarises the distributions of other surrogates (number of years having sheep, number of dipping years and number of dipping days).

Table 6-16: Pesticide exposure surrogates in sheep farming

<table>
<thead>
<tr>
<th>Surrogate</th>
<th>Zero frequency (%) (n=234)</th>
<th>Exposure score *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>YRSH</td>
<td>36 (15.4)</td>
<td>17 ± 1</td>
</tr>
<tr>
<td>YRDIP</td>
<td>46 (19.7)</td>
<td>16 ± 1</td>
</tr>
<tr>
<td>DYDIP</td>
<td>47 (20.1)</td>
<td>113 ± 2</td>
</tr>
<tr>
<td>OPYRSH</td>
<td>62 (26.5)</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>OPYRDIP</td>
<td>70 (29.9)</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>OPDYDIP</td>
<td>71 (30.3)</td>
<td>78 ± 2</td>
</tr>
</tbody>
</table>

* After excluding those with zero results

Figure 6-6 shows the distributions of scores of the pesticide exposure models for sheep dipping and for all treatments in sheep farming. The scores of all models were log-normally distributed. Generally the maximum scores of all OP estimates were about half of the maximum scores of the general pesticide estimates.

6.3.2.2 Cattle and other livestock farming

222 farmers had ever worked with cattle and 203 had ever worked with cattle after 1970. The number of farmers who had ever applied treatment for warble fly was 209 (90.1%, 2 with missing data) and the number of those who had ever handled the concentrate to treat cattle was 203 (89.9%, 8 missing). 92 farmers had ever worked with other livestock (39.3%) and 57 farmers had ever worked with other livestock after 1970 (24.4%).
Figure 6-6: Sheep dipping exposure model scores after excluding zero results
(A) NEW(Eq.6.2), (B) NEWDIP(Eq.6.3), (C) SHAPE(Eq.6.9), (D) EXPSH(Eq.6.13) (E) TASK(Eq.3.12), (F) OPNEW(Eq.6.4), (G) OPNEWDIP(Eq.6.5), (H) OPSHAPE(Eq.6.10), (I) OPEXSH(Eq.6.14)
Table 6-17 summarises the distributions of number of years having cattle and other livestock and number of years having cattle and other livestock after 1970. Most farmers had worked with cattle in most years either before 1970 or after.

The results of pesticide exposure models in cattle and other livestock sectors were log-normally distributed either for general pesticides or for OP pesticides (Figure 6-7). There were a few farmers with high exposure in the cattle sector either to general pesticides or to OP specifically whilst in other livestock sector high exposure was only found to OP pesticides. Generally the maximum scores of all OP estimates were about half of the maximum scores of the general pesticide estimates.

![Figure 6-7: Cattle farming exposure model scores after excluding zero results](image)

(A) $\text{EXP}_{\text{cat}}$ (Eq.6.13), (B) $\text{OPEXP}_{\text{cat}}$ (Eq.6.14), (C) $\text{EXP}_{\text{liv}}$ (Eq.6.15), (D) $\text{OPEXP}_{\text{liv}}$ (Eq.6.16)
Table 6-17: Pesticide exposure surrogates in cattle and other livestock sectors

<table>
<thead>
<tr>
<th>Surrogate</th>
<th>Zero frequency (%)</th>
<th>Exposure score a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=234)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>YRCAT</td>
<td>12 (5.1)</td>
<td>42 ± 15</td>
</tr>
<tr>
<td>OPYRCAT</td>
<td>31 (13.2)</td>
<td>28 ± 9</td>
</tr>
<tr>
<td>YRLIV</td>
<td>142 (60.7)</td>
<td>24 ± 16</td>
</tr>
<tr>
<td>OPYRLIV</td>
<td>177 (75.6)</td>
<td>18 ± 11</td>
</tr>
</tbody>
</table>

a After excluding those with zero results

6.3.2.3 Crops and grains farming

140 farmers had worked with any type of crops or grains and 122 farmers had worked after 1970. 162 farmers (70.1%) had ever applied insecticides to arable, fodder crops or grassland (3 missing data), while 106 farmers (57.0%) had ever handled the concentrate for the treatment of pests on arable (48 missing data). The distributions of other pesticide exposure surrogates in crop farming are presented in Table 6-18.

Table 6-18: Pesticide exposure surrogates in crops farming

<table>
<thead>
<tr>
<th>Surrogate</th>
<th>Zero frequency (%)</th>
<th>Exposure score a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=234)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>YRCRP</td>
<td>94 (40.2)</td>
<td>37 ± 15</td>
</tr>
<tr>
<td>OPYRCRP</td>
<td>112 (47.9)</td>
<td>26 ± 9</td>
</tr>
</tbody>
</table>

a After excluding those with zero results

Figure 6-8 shows the distributions of the results of pesticide exposure models in crops farming. The estimates were log-normally distributed with a very high OP exposure found in a few farmers.

6.3.2.4 Other pesticide use

The exposure to general pesticides from other use (EXPUSE) was estimated as zero for 13 farmers, one for 151 farmers, and two for 70 farmers. Considering all fumigants as non OP, only 7 farmers were assigned a score of one whereas the rest were assigned a score of zero. Considering all fumigants as OP, 159 farmers were scored zero, 72 farmers were given a score of 1, and 3 farmers were scored 2.
6.3.3 Correlations between surrogates of exposure and model scores

The correlations between different models and surrogates in sheep dipping were investigated to explore the effect of including different exposure variables in the models on exposure assessment and to explore the effect of using simple surrogates instead of developed models. Statistically significant correlations were found between scores of pesticide exposure models and surrogates for both general pesticides and OP pesticides (Table 6-19 and Table 6-20). The correlations were greatest between models themselves either for general pesticides or for OP pesticides ($r_s = 0.86 - 0.98$).

The correlations between model scores and pesticide exposure surrogates were highest in the case of number of dipping days (DYDIP and OPDYDIP) ($r_s = 0.81 - 0.96$), lower in the case of number of dipping years (YRDIP and OPYRDIP) ($r_s = 0.73 - 0.80$) and lowest with number of years having sheep ($r_s = 0.55 - 0.68$ for YRSH and $r = 0.42 - 0.54$ for OPYRSH).
Table 6-19: Correlations between scores of general pesticide exposure models and surrogates of sheep dipping

<table>
<thead>
<tr>
<th>Model</th>
<th>Spearman correlation coefficient (r) *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YRSH</td>
</tr>
<tr>
<td>YRSH</td>
<td>1.0</td>
</tr>
<tr>
<td>YRDIP</td>
<td>1.0</td>
</tr>
<tr>
<td>DYDIP</td>
<td></td>
</tr>
<tr>
<td>NEW</td>
<td></td>
</tr>
<tr>
<td>NEWDIP</td>
<td></td>
</tr>
<tr>
<td>SHAPE</td>
<td></td>
</tr>
<tr>
<td>TASK</td>
<td></td>
</tr>
</tbody>
</table>

* All correlations were significant at the 0.01 level. n=197 in all correlations with models (NEW, NEWDIP, SHAPE, and TASK) and n=198 in all correlations between surrogates (YRSH, YRDIP, and DYDIP).

Table 6-20: Correlations between scores of OP pesticide exposure models and surrogates of sheep dipping

<table>
<thead>
<tr>
<th>Model</th>
<th>Spearman correlation coefficient (r) *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OPRYRSH</td>
</tr>
<tr>
<td>OPRYRSH</td>
<td>1.0</td>
</tr>
<tr>
<td>OPRYRDIP</td>
<td>1.0</td>
</tr>
<tr>
<td>OPDYDIP</td>
<td></td>
</tr>
<tr>
<td>OPNEW</td>
<td></td>
</tr>
<tr>
<td>OPNEWDIP</td>
<td></td>
</tr>
<tr>
<td>OPSHAPE</td>
<td></td>
</tr>
</tbody>
</table>

* Except for the correlations with OPRYRSH where Kendall’s tau correlation coefficient (τ) was used. All correlations were significant at the 0.01. n=197 in all correlations with models and n=198 in all correlations between surrogates (OPRYRSH, OPRYRDIP, and OPDYDIP).

To discover the effect of using simple surrogates instead of using more developed models on exposure assessment in all farming sectors the correlation between the estimates of these two methods were determined. Table 6-21 presents the correlation coefficients between simple surrogates of exposure (YR) and model estimates (EXP) for both general pesticides and OP pesticides. The highest correlation was in the sheep sector (rs = 0.63). Generally the correlations were worse with OP exposure estimates compared to general pesticides and no significant correlation was found in the other livestock sector.
Table 6-21: Correlations between scores of exposure models and surrogates of pesticide exposure in all farming sectors (EXP and YR)

<table>
<thead>
<tr>
<th>Farm sector</th>
<th>Number of farmers</th>
<th>General pesticides (rs)^a</th>
<th>OP pesticides (τ)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>197</td>
<td>0.63</td>
<td>0.44</td>
</tr>
<tr>
<td>Cattle</td>
<td>222</td>
<td>0.32</td>
<td>0.23</td>
</tr>
<tr>
<td>Other livestock^c</td>
<td>32</td>
<td>0.47</td>
<td>0.04</td>
</tr>
<tr>
<td>Crops^c</td>
<td>101</td>
<td>0.39/0.43^d</td>
<td>0.40/0.37</td>
</tr>
</tbody>
</table>

^a rs: Spearman correlation coefficient. All correlations were significant at the 0.01 level
^b τ: Kendall’s tau correlation coefficient. All correlations were significant at the 0.01 level except other livestock. ^c With other livestock and crops only farmers with EXP > 0 were included since farmers with EXP=0 are 60.
^d Correlations between YR and EXP1/EXP2

The correlations between the model estimates of general pesticide exposure and OP exposure from sheep dipping were investigated to explore the effect of including OPPROB variable in the dipping models on exposure assessment. Figure 6-9 shows scatter plots of the correlations between general pesticide exposure scores and OP exposure scores of the sheep dipping models. Spearman coefficients of the correlations between general pesticide exposure estimates and OP exposure estimates were 0.84 for NEW and NEWDIP models and 0.80 for the SHAPE model.

Figure 6-9: Associations between scores of general pesticide exposure models and scores of OP exposure models in sheep dipping

rs = Spearman correlation coefficients. All correlations were significant at the 0.01 level.
(A) NEW and OPNEW, (B) NEWDIP and OPNEWDIP, (C) SHAPE and OPSHAPE
Correlations between general pesticide exposure estimates and OP exposure estimates were significant in all farming sectors (Figure 6-10). Spearman correlation coefficients in the sheep and cattle sectors were 0.78, 0.80 respectively, 0.67 in the other livestock sector, whilst the correlation was the highest in the crops sector ($r_s = 0.91$).

**Figure 6-10: Associations between scores of general pesticide exposure models and scores of OP exposure models in different sectors**

$r_s$ = Spearman correlation coefficients. All correlations were significant at the 0.01 level.

(A) sheep, (B) cattle, (C) other livestock, (D) crops (EXP1), (E) crops (EXP2)
6.4 Discussion

This aim of this chapter was to describe the occupational practices of the SHAW farmers related to pesticide exposure. Their occupational pesticide exposure in each farming sector was estimated using different simple surrogates and more developed exposure models with a special attention on sheep dipping practice and OP exposure. The exposure estimates obtained in this chapter will be used in Chapter 8 to investigate the impact of using different methodologies on the association between long-term pesticide exposure and ill-health among the SHAW farmers.

The majority of farmers had worked with cattle and sheep and dipping was the most common method of treating sheep while about half of farmers applied pesticides to crops or grains. A minority of farmers had only ever applied pesticides in one farming sector while about a half of them had ever applied pesticides in at least three different sectors. Exposure estimates using assessment models in all farming sectors were log-normally distributed (i.e. highly variable). This is consistent with the a priori assumption that the use of ever/never surrogates of exposure (e.g. ever had sheep or ever applied insecticide to arable) may lead to important exposure misclassification and may conceal any relationship with health outcomes. Furthermore, low correlations were found between the number of years being a farmer in a specific sector and pesticide exposure in that sector estimated by a developed model. In contrary, good correlations were found between the estimates of the three dipping models and good correlations were found as well between general pesticide exposure estimates and OP exposure estimates.

6.4.1 Farming practices

The majority of farmers had worked with cattle and sheep; this was probably due to the nature of the utilised databases of the farmers in the SHAW study (Sheep and Cattle Association and Shepherd’s Guides). The SHAW study was designed to focus on OP exposure, and since most sheep dips in last 40 years contained OP pesticides, the questions about the sheep dipping process were thorough. Therefore there was more information available on variables of pesticide exposure in sheep farming than for other farming sectors and the models of pesticide exposure estimates were more developed.

Dipping was found to be the most common method of treating sheep before the year 2000, which explains the interest of studies in this method although pesticide
exposure through pouring-on method was considered greater. There was a decreasing trend in the use of sheep dipping after 1990 due to the increase in the use of other methods such as pour-ons and injections. This is consistent with the figures of number of sheep treatments sold in the UK in 1990s as reported by the NOAH; more pour-on and injectable products have been available since 1990. However, it is also possible that these changes may be related to the age of the farmers. An older farmer may start to use less energy intensive methods such as pour-ons or injecting pesticides than dipping.

Almost all cattle farmers were involved in warble fly treatment, and this treatment was mainly with OPs between 1978 and 1982, which makes it important to take this treatment into account in any study of OP exposure among farmers. Other treatments (i.e. for lice and flies) were applied by fewer farmers and most of those treatments did not use OPs. However, these two treatments were applied for a much longer period of time (i.e. number of treating years) compared to warble fly treatment. The frequency of applying warble fly and lice treatments per year was to some extent stable (one or two treatments per year) but the frequency of fly treatment was much more variable which made it difficult for many farmers to decide the frequency of such treatments.

After sheep and cattle, pigs were the most frequent livestock on which pesticides were applied and it is reasonable to ask separately about pigs in any pesticide exposure questionnaire. The questions in the utilised questionnaire were not appropriate for applying pesticide to poultry since the questions assumed that the application is individual however the application to poultry usually happens to the nest or in food or drinking water.

About half of farmers applied pesticides to crops or grains. This number did not include any application on grass land since some farmers mentioned this application and others did not, although they had most likely applied weedkiller to grass land. That might be due to the nature of the question which asked about using pesticides to treat crops and grains while grass land was not mentioned. The most applicable solution was to include the application to grass land in other pesticide uses.

Although most farmers wore boots and about two thirds of them wore leggings when sheep were treated with pesticide, only one third of them had ever worn gloves. This shows that asking about the use of PPE in general is not sufficient to assess past pesticide exposure and that detailed information about the use of PPE needs to be collected. Whether PPE is worn correctly or not is also important but it is difficult to
assess using a self-reported occupational history. A trend of increasing use of gloves was found between 1942 and 2005, whereas the use of boots, aprons, and leggings decreased after 1995. The most probable explanation for this result is that these trends depend on the method of pesticide application since the question on the use of PPE was not specific for each method; i.e. farmers have increasingly tended to use gloves regardless of the application method, while they may tend not to use other types of PPE during injecting, showering or pouring-on pesticides for sheep treatment because these treatments that have been common in the recent years are less messier than sheep dipping. Farmers who used different types of PPE (especially leggings and aprons) during treating cattle or other livestock were fewer than those who used PPE during sheep treatment. A probable reason is that sheep dipping, which is the most frequent method of sheep treatment, is much messier than those methods used with cattle or other livestock.

### 6.4.2 Pesticide exposure estimates

Three models were used to estimate exposure from sheep dipping; one of which was modified from the new conceptual model while two were modified from previously used models (i.e. TASK and SHAPE)\(^{29,99}\). The new model was discussed in detail in the previous chapter; however it should be mentioned that many important variables were not available in the SHAW study such as type of concentrate container and how the concentrate was mixed with the bath. These variables can significantly affect the exposure during sheep dipping activities and the use of constants instead of these variables may lessen the power of this model. The very strong correlation between NEW model and NEWDIP model indicates that we may depend on the simpler one (i.e. NEWDIP) instead of the more complicated one. However, handling the concentrate is known to be the major source of pesticide exposure in sheep dipping\(^{12,99}\), therefore it is still important in any exposure-response analysis to use the NEW model estimates as they took handling the concentrate into account.

Parameters used in the TASK model were derived from one hygiene study and generalising them to be used in epidemiological studies may lead to a systematic bias. However, the processes of sheep dipping are generally similar in the UK\(^{12,104,155,281}\) and small differences between practices will not lead to important variation in the exposure. The TASK model was modified in this study to address the estimated percentage of time in all years the farmer spent working as a plunger (%PLUNG) as a surrogate of the CONC component instead of the estimated number of occasions spent as principal
concentrate handler (%HAND) since the latter was not available. Although %PLUNG is more valid because it is easier to recall, %HAND is more trustworthy to estimate the CONC component since plungers are not always the responsible for handling the concentrate. The developers of the TASK model excluded PPE usage since they did not find a significant effect of PPE on exposure. This finding might be due the low power of the study since only a few farmers used PPE during the sessions and at the same time it is not consistent with the results of another study.

The SHAPE model is to some extent similar to the NEW model because the development of the latter model has benefited from the former, which may explain the high correlation between the results of the two models. The SHAPE model ignored exposure through inhalation and ingestion and estimated only the dermal exposure based on the fact that dermal route is the main route of OP exposure. However, the modifications applied in this study for the SHAPE model to make it suitable for the data of SHAW might decrease its competence.

Results of the three sheep dipping models were highly correlated. This high correlation is most likely because these models estimated cumulative exposures which are to a large extent driven by number of dipping days. This interpretation is supported by the very good correlations found between model estimates and DYDIP which is also comparable to a previous study. To exclude the effect of the duration of exposure on the correlation, a comparison between the models on a few short-term scenarios might be performed in a future work. However, the high correlation between the models found in this study reinforces the assumption that the degree of misclassification is lower when dealing with lifetime cumulative exposure estimates than when dealing with a single session.

A good sample-size validation study may form the base of any comparison between the utilised sheep dipping models, otherwise it is expected that the models which include more exposure variables can give more valid estimates. However if the weighting factors of the exposure variables are not assigned rightfully, more variables would mean more estimation errors. Furthermore, even though the weighting factors of exposure variables are mostly independent of the utilised pesticide, the use of models developed especially to estimate OP exposure (such as TASK and SHAPE) to estimate other pesticide exposure might be inappropriate.
Pesticide exposure models for cattle, other livestock and crops were developed essentially according to the available information in the SHAW study. The model of animal treatments was similar in the general formula to the conceptual model of sheep dipping; however it was simpler and had fewer variables. Three exposure sources were addressed in the model, applying pesticides to animals, handling the concentrate, and handling treated animals. The estimation of the exposure intensity during application depended on two variables; ATA and PPE taking into account the application method. These are the only available variables for cattle and other livestock in the SHAW study; however there are no other expected variables that could be useful in a general exposure model for all animals and all methods. Scores of PPE and weights of exposure sources were taken from the sheep dipping conceptual model with few modifications. Such modifications may lead to some error.

The crops model was simpler than the animal one with very few variables included. Pesticide exposure through application was estimated depending on either the area treated or the number of treating hours taking into account the application method in both cases. The consideration of application method was important because it was found that when the farm is large in size more mechanized equipment is used\textsuperscript{151} which decreases exposure compared to using manual methods\textsuperscript{153}, and the same idea may be applied to the number of treating hours. It was preferred not to incorporate treated area and number of treating hours in one model since it was assumed that they may be highly intercorrelated. The CON component depended on the area of treated crop assuming that it is correlated with the amount of the pesticides handled. One of the shortcomings of the crop model that it did not include an important source of exposure reported in the literature which is the re-entry to the sprayed area since farmers will be exposed again to the applied pesticides if they re-enter the treated field early\textsuperscript{119}. This source had to be omitted from the model because it was not available. The usage of PPE and the type of protection used in tractor (e.g. enclosed cab and charcoal filter) were also not included in the model since there were no questions about that in the questionnaire. These variables are important in the exposure\textsuperscript{180} and any advanced models should take them into account.

Estimating OP exposure specifically depended in this study on the same models of the general pesticides after including the probability of each applied pesticide to contain an OP (OPPROB). To my knowledge the use of such an approach has not been used before in estimating specific pesticide exposures. The use of this approach might help in
epidemiological studies of pesticide health effects that depend on self-reported exposure since the farmer’s recall of the use of specific pesticides was found not accurate.\textsuperscript{118,126,132} However, the validity of OPPROB varied between farming sectors as described below and therefore its use in estimating OP exposure might lead to a systematic bias.

The correlations between general pesticide exposure estimates and OP exposure estimates were generally high in all farming sectors except other livestock where the correlation was moderate. In the sheep sector, this correlation was a little higher between the results of dipping models compared to the model of all treatments, indicating that using general dipping models instead of OP dipping models may not lead to large bias, especially when no credible information about the nature of the pesticides exists. However, OPPROB of the pesticides used in sheep sector may be more trustworthy than other sectors due to the reliable database utilised to obtain OPPROB for sheep dips and the relatively precise answers of farmers about product names. Therefore the usage of sheep OP models will most likely reduce the degree of OP exposure misclassification.

The correlations between general exposure estimates and OP estimates were also high in the cattle sector. In this sector OPPROB depended to a great degree on an expert judgment and the validity of OPPROB varies between reasons of treatment. OPPROB was more reliable in warble fly treatment than other treatments since the farmers were more confident about the nature of the pesticides. OP exposure estimates in other cattle treatments were dependent on the general exposure estimates as the majority of farmers did not know the type of products used and the same OPPROB was used for all those farmers. Hence, for an analysis of pesticide health effects general estimates can be used instead of OP estimates in cattle sectors for all treatments except warble fly treatment and because EXP model included this reason of treatment it might be still better to use the OPEXP model to estimate OP exposure in the cattle sector.

In the other livestock sector the correlation between general estimates and OP estimates was moderate. Despite the concern about the validity of OPPROB in this sector since it depended to a great degree on an expert judgment, the use of OP models might be preferred since farmers were able to recall the type of pesticide used fairly well.

Regarding crops and grains, the great number of pesticides used in this sector makes it very difficult for farmers to remember the names of pesticides or their types. Therefore
it may be better to depend on other sources of data to decide the type of pesticides used in the farm sector like registries of the seller or the provider although these data are not always available\textsuperscript{119,124}. In this study OPPROB in crops sector depended completely on the available database depending on the type of crops regardless of farmers’ answers about pesticide names or types. The correlation was high between general pesticide estimates and OP estimates most probably because the latter was dependent on the former. This dependence was mainly due to the great resemblance between types of crops among farmers and because most farmers gave the area of many crops together which made OPPROB more general. When there is such similarity between farmers in respect of types of crops, the use of general models instead of OP ones is plausible, otherwise the use of specific OP models might be more valid.

The correlation between model scores and continuous surrogates (\textit{i.e.} Number of years or number of days) varied between sectors and between surrogates. Correlations found between number of working years in each farming sector and general pesticide exposure estimates were between weak and moderate and the correlations were weaker with OP exposure estimates. The best correlation was in the sheep farming sector which was probably due to the systematic treatment in this sector compared to other sectors\textsuperscript{99}. However these weak correlations suggest that the use of the number of years as a surrogate for pesticide exposures, especially for OP exposures, is not reliable.

The correlations between the scores of sheep dipping models and number of dipping years (YRDIP and OPYRDIP) were lower than number of dipping days (DYDIP and OPDYDIP). The number of dipping days tends to be less prone to measurement error compared to other dipping model variables, which increases the power of any further exposure-outcome analysis\textsuperscript{99}. Therefore, DYDIP and OPDYDIP may form preferable surrogates for cumulative pesticide exposure from sheep dipping in epidemiological studies. However, the length of a dipping day and type of activities performed in that day can vary greatly\textsuperscript{178} which might lead to an important variation in pesticide exposure during one dipping day. This variation, even if it was relatively small, may aggregate over time leading to significant differences in exposure-response associations between both methods (\textit{i.e.} DYDIP or OPDYDIP and more developed models). Such associations will be investigated in Chapter 8. However, it should be mentioned that even if the degree of exposure misclassification was low, it might attenuate or even hide the association between pesticide exposure and health outcomes\textsuperscript{31} in the agricultural field where very weak associations (\textit{i.e.} small odds ratios) are expected\textsuperscript{31,325,326}. 

\textsuperscript{194}
Finally, the validation of the cumulative exposure assessment models developed in this chapter is not easy since biological markers are only practical for recent exposures and generalizing it over long-term exposure will lead to errors. Assuming OPPROB in all farming sectors is also another challenge in OP models and a further work is needed to assess this validity of this variable. Furthermore, occupational exposure history of the farmers in the SHAW study was self-reported. The validity of self-reported exposure history in agricultural studies will be investigated in the following chapter.
Chapter 7: Validation of self-reporting exposure among farmers

7.1 Introduction

Epidemiologic studies have relied on self-reported occupational history to estimate long-term exposures to different agents since self-reported history is often the only available resource of exposure data\textsuperscript{125,126}. The validity of self-reported occupational exposure have been investigated in many studies\textsuperscript{128-130,327,328} and it was found that this validity varies from study to study and from agent to agent within studies\textsuperscript{131}.

Fewer studies have investigated the accuracy of self-reported exposures by farmers and farmworkers with a special focus on pesticide use\textsuperscript{118,126,132}. Self-reported exposure was found to be accurate for the analysis of broad categories of pesticides in epidemiological studies, but not for analysing specific pesticides\textsuperscript{126}. The agreement between suppliers and farmers regarding herbicide and insecticide use was about 60\% for both of them\textsuperscript{118}. Iowa pesticide applicators (n=4,088) who took part in the AHS study were interviewed twice with a one year interval\textsuperscript{132}. The percentage agreement of ever/never use of specific pesticides and application practices was high (70\% -90\%) but was lower (50-60\%) for frequency, duration, and decade of first use of specific pesticides.

This chapter aimed to validate self-reported occupational exposure among farmers by investigating the accuracy of farmer answers on livestock populations and crop areas in different years by comparing it with data collected in the appropriate year. Since occupational exposure history in the SHAW study was self-reported, it was important to investigate its accuracy before performing any analysis on the association between estimated pesticide exposure and health outcomes.

7.2 Materials and Methods

This validation study was performed by comparing farmers’ answers in the SHAW study with the data collected by the June Survey of Agriculture and Horticulture in specific years.

7.2.1 June Survey of Agriculture and Horticulture (JSAH)

The June Survey of Agriculture and Horticulture (JSAH) started in England in 1866 and has been performed every year since\textsuperscript{329}. It was a full census until 1995 when it was
turned to a randomised sample survey with a full census every ten years; the most recent full censuses were held in 2000 and 2010. In the applied sampling frame, holdings are divided into strata based on their theoretical labour requirement and higher sampling rates are used in the larger strata.

This survey is run on 1st June every year by sending farmers a questionnaire to collect detailed information about arable and other horticultural crops, number of livestock, land usage and number of workers. Recently farmers can fill the questionnaire electronically via the Internet. The response to this survey is a legal requirement under the Agricultural Statistics Act 1979. Results from England, Scotland, Wales and Northern Ireland are collated by the Department of Health and Defra to produce UK level results.

### 7.2.2 Collection of JSAH data of SHAW farmers

Farmers who participated in phase 2 of SHAW were asked to give permission for the study team to access information in their County Parish Holding file which holds data from the JSAH. The County Parish Holding Number (CPHN) is related to the farm not to the farmer himself. Consent forms (Appendix 16) of those farmers who agreed to give their CPHN were sent to Defra to obtain collected data for specific years. Defra verified the signature of the farmer and checked if there were any partners in the farm and if so they requested their permission as well.

Computerised data was available since 1983 and five years were selected to represent the period (1983-2003): 1983, 1988, 1993, 1998, and 2003. Data for the year 2000 was also requested as year 2000 was a full census year while data of 2003 was not used in the analysis as its data had imputed figures for holdings not surveyed or not responded.

### 7.2.3 Data handling

Although only the farmers interviewed in the phase 2 of the SHAW study were included in this validation study, the data of those farmers in both phases were validated. In SHAW phase 1, farmers were asked about having sheep or cattle in every year from 1946 to 2003. The same question was also asked for four groups of agricultural crops (combinable crops, glasshouse Production, outdoor Vegetables or Potatoes, and top & soft fruit). The JSAH also contained information on each agricultural crop separately and therefore the individual crops in the JSAH were matched with crop categories in the SHAW phase 1 questionnaire as presented in Table 7-1.
Table 7-1: Matching between SHAW phase 1 data and JSAH data

<table>
<thead>
<tr>
<th>SHAW phase 1 questionnaire</th>
<th>JSAH questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combinable crops</td>
<td>Barley, corn, field beans and beans for stock feeding, flax, linseed, maize, oats, oilseed rape, peas harvested dry, rye, sugar beet, triticale, wheat, and all other crops used for stock feeding.</td>
</tr>
<tr>
<td>Outdoor Vegetables or Potatoes</td>
<td>Beetroot, broad, French and runner beans, broccoli, Brussels sprouts, cabbage, carrots, cauliflower, celery, fodder beat, hops, kale, lettuce, mangolds, mushroom, onion, parsnips, picked green and vining peas, potatoes, rape, savoy, Swedes, sweet corn, turnips, and all other vegetables.</td>
</tr>
<tr>
<td>Glasshouse Production</td>
<td>Cucumbers, tomatoes, lettuce under glass, sweet papers, other vegetables and herbs, strawberries and other fruits under glass, roses, carnations, chrysanth and other flowering plants.</td>
</tr>
<tr>
<td>Top &amp; soft fruit</td>
<td>Orchards, apples, pears, cherries, plums, open grown strawberries, raspberries, wine grapes, other small fruits, blackcurrants, gooseberries, blackberries, and other top fruit including nuts.</td>
</tr>
</tbody>
</table>

The information in SHAW phase 1 was in the form of yes/no answers, while it is numerically presented in the JSAH, hence the JSAH data was converted to yes/no answers by recording any number of livestock or having any area of crops as a ‘yes’. The questions in the SHAW phase 2 questionnaire were about applying pesticides to sheep, cattle, or agricultural crops not about just having those livestock or crops. Therefore the analysis included only farmers who said in the SHAW questionnaire that they had treated sheep or cattle or applied pesticides on specific crops.

Eight crops were frequently mentioned by farmers in the SHAW study, namely wheat, barley, maize and corn, sugar beet, beans, oilseed, and potatoes. However, the comparison of crop acreage was only performed on barley and wheat since the area of other crops was mostly not given individually.

7.2.4 Statistical methods

Cohen's kappa statistical measure was used to analyse the inter-rater agreement between yes/no categories in phase 1 and the JSAH. However, only one to three farmers had glasshouse production or fruit farm in either SHAW phase 1 or JSAH data, therefore these two farm types were not analysed. The kappa test was also performed when livestock numbers and crop acreages in both datasets (SHAW phase 2 and June survey) were categorised in 4 groups according to quartiles for sheep and cattle, in 3 groups according to tertiles for barley and into 2 groups according to the median for wheat. The
number of categories varied according to the number of farmers in each farm type and according to the frequency of zeroes in each type of farming. A Spearman correlation test was used to study the relationship between numbers in both datasets.

In the JSAH data farmers gave information about their farms for the same year of the survey and therefore the JSAH data were considered the gold standard. The associations between the degree of inaccuracy in SHAW data and the age and health status of the farmers when they were interviewed were examined. The SHAW farmers were categorised in two groups for each type of livestock or crops; one contained those farmers whose answers in phase 1 matched those in the JSAH and the other for farmers whose answers did not match. Independent-sample t-test was used to study any differences in age and memory between these two groups, while chi-square tests were used to study any differences in the prevalence of four phase 1 screen-identified neuropsychiatric illnesses (described in Section 2.1.1.1) between these two groups.

Further analysis was carried out using the numerical data (i.e. number of livestock and acreage of crops). The importance of the difference in numbers between the two datasets varies according to the numbers themselves. For example, a difference of 20 sheep between the two datasets of one subject was considered less important than the difference of 10 sheep for another subject if the number of sheep in the JSAH was 1000 for the first case and 100 for the second. Therefore, the analysed difference depended on the ratio of the numbers in the two datasets. Since the changes in both side of 1 are the same for this analysis (i.e. it is the same if the figure in the JSAH data was the same percentage less or higher than the figure of SHAW), the following equation was used to calculate a new variable (PERdiff):

\[
\text{PERdiff} = (1 - \frac{N_{\text{SHAW}}}{N_{\text{June}}}) \text{ if } N_{\text{SHAW}} < N_{\text{June}}, \\
\text{or } (1 - \frac{N_{\text{June}}}{N_{\text{SHAW}}}) \text{ if } N_{\text{SHAW}} > N_{\text{June}}
\]

Where: \(N_{\text{SHAW}}\) = livestock number or crop acreage in SHAW, \(N_{\text{June}}\) = livestock number or crop acreage in June survey.

PERdiff was created for sheep, cattle, barley and wheat farmers who had reported figures for the analysed type in both datasets (i.e. the number of livestock or acres is > zero) since the purpose of this analysis was to study the accuracy of those figures in the SHAW data. Spearman correlation coefficients were used to study the relationship between PERdiff and age and memory of farmers.
All the above analyses were repeated for the five years mentioned earlier, namely 1983, 1988, 1993, 1998 and 2000. Linear regression was used to obtain P-for-trend ($P_t$) of the kappa and Spearman correlation results over the five years by giving the values (1 to 5) to the years in order, while boxplots were used to examine any trend of PERdiff.

7.3 Results

7.3.1 Descriptive analysis

181 farmers agreed to give their CPHN (response rate 77.4%). No differences in sex, memory scores, and farming activities (i.e. being sheep farmers, cattle farmers, etc.) were found between those who gave their CPHN and those who did not. However, those who refused to give their CPHN were significantly older than those who agreed (mean±SD of age was 68.2±4.8 and 65.8±5.6 respectively).

Data from 43 of these farmers was not accessible due to a variety of reasons. No records were found in the JSAH for 13 farmers while the signature of another 13 farmers could not be verified. The data of 17 farmers was not accessible due to the lack of permission from other partners in the same holding. From those 138 farmers whose data was accessible, the records of 90 farmers were found for all requested years, while the records of 15 farmers were not found for all years (maybe because the farmer were not surveyed in the sampling years, they did not respond, or they had retired before the survey especially for the latest two years). The records of the remaining 33 farmers were not accessible in different years because of a lack of partners’ permission. Figure 7-1 shows number of farmers’ records which were accessible.

All farmers were included in the analysis of SHAW phase 1 data, while different numbers were included in the analysis of phase 2 data according to the type of livestock or crops they had in the studied years. Table 7-2 presents the number of farmers included in the analysis of phase 1 and phase 2 data.

Table 7-2: Number of farmers included in the analysis of phase 1 and phase 2 data

<table>
<thead>
<tr>
<th>Year</th>
<th>Phase 1</th>
<th>Type of farm in phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sheep</td>
</tr>
<tr>
<td>1983</td>
<td>134</td>
<td>105</td>
</tr>
<tr>
<td>1988</td>
<td>120</td>
<td>95</td>
</tr>
<tr>
<td>1993</td>
<td>116</td>
<td>91</td>
</tr>
<tr>
<td>1998</td>
<td>98</td>
<td>75</td>
</tr>
<tr>
<td>2000</td>
<td>95</td>
<td>73</td>
</tr>
</tbody>
</table>
### 7.3.2 Agreement between the two databases

The agreement between having sheep and cattle in specific years in SHAW phase 1 and the information in the JSAH is shown in Table 7-3. Kappa values ranged from 0.68 to 0.78 for sheep and 0.69 to 0.83 for cattle. Similar kappa values were also found for combinable crops (kappa = 0.71 - 0.77), while lower values were found for vegetables (kappa = 0.17 - 0.44). No trend was found in the agreement results in all farm types over the years.

#### Table 7-3: Agreements between SHAW Phase 1 data and JSAH data over time

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Kappa (SE)</th>
<th>1983 (n=134)</th>
<th>1988 (n=120)</th>
<th>1993 (n=116)</th>
<th>1998 (n=98)</th>
<th>2000 (n=95)</th>
<th>P&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td></td>
<td>0.70 (0.06)</td>
<td>0.78 (0.06)</td>
<td>0.76 (0.06)</td>
<td>0.69 (0.07)</td>
<td>0.68 (0.08)</td>
<td>0.44</td>
</tr>
<tr>
<td>Cattle</td>
<td></td>
<td>0.79 (0.07)</td>
<td>0.69 (0.08)</td>
<td>0.73 (0.07)</td>
<td>0.71 (0.07)</td>
<td>0.83 (0.06)</td>
<td>0.66</td>
</tr>
<tr>
<td>Combinable crops</td>
<td></td>
<td>0.71 (0.06)</td>
<td>0.72 (0.06)</td>
<td>0.72 (0.06)</td>
<td>0.77 (0.06)</td>
<td>0.73 (0.07)</td>
<td>0.28</td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td>0.44 (0.10)</td>
<td>0.17 (0.10)</td>
<td>0.23 (0.13)</td>
<td>0.38 (0.19)</td>
<td>0.27 (0.22)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

a Agreement about being a sheep, cattle, combinable crops, or vegetable farmer. All results were significant (P<0.05). b P: p-for-trend
Figure 7-2 shows the percentage of agreement between SHAW phase 1 data and the JSAH data with respect to sheep, cattle, combinable crops and vegetables. Observed differences within specific types were mainly because farmers did not mention having that type in SHAW while they had it according to the JSAH. Only two years in sheep sector showed the opposite, i.e. the difference was mainly because of farmers who mentioned having sheep although they did not have them according to the JSAH.

Correlations between the figures given by farmers in SHAW phase 2 (i.e. number of sheep and cattle and acres of barley and wheat) and the figures found in the JSAH are presented in Table 7-4. Spearman correlation coefficients ($r_s$) ranged from 0.70 to 0.81 for sheep and from 0.73 to 0.83 for cattle. The range of Spearman correlation coefficients found in barley acreages was 0.68 to 0.80, while low, non significant correlations were found for wheat. There was no trend for correlations over the years except for number of cattle where a significant positive trend was found ($P_t = 0.02$).
Table 7-4: Correlations between figures of the SHAW and the JSAH over time

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Spearman correlation coefficient ($r_s$) $^a$</th>
<th>$P_t$ $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>0.70</td>
<td>0.81</td>
</tr>
<tr>
<td>Cattle</td>
<td>0.73</td>
<td>0.73</td>
</tr>
<tr>
<td>Barley</td>
<td>0.80</td>
<td>0.65</td>
</tr>
<tr>
<td>Wheat</td>
<td>0.44</td>
<td>0.18</td>
</tr>
</tbody>
</table>

$^a$ Correlation between numbers of sheep and cattle and areas of barley and wheat. All correlations were significant ($P<0.05$) except those for wheat. $^b$ $P_t$: p-for-trend.

Table 7-5 presents the agreement between numbers of sheep and cattle and acres of barley and wheat found in SHAW phase 2 and the JSAH when the numbers were grouped in ordinal categories. Kappa values for sheep ranged from 0.43 to 0.57 whilst they were a little lower for cattle and barley (kappa = 0.39 - 0.52 and 0.36 - 0.53 respectively). No significant agreement was found for wheat acreage although it was categorised only in two categories. Although the agreements in year 1983 were generally lower than following years in sheep, cattle and barley, no significant trends were found. There was a negative trend in the kappa results of wheat throughout the years ($P_t = 0.02$), however the agreements themselves were not significant.

Table 7-5: Agreements between SHAW Phase 2 data and JSAH data over time

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Kappa (SE) $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>0.43 (0.06)</td>
</tr>
<tr>
<td>Cattle</td>
<td>0.39 (0.06)</td>
</tr>
<tr>
<td>Barley</td>
<td>0.36 (0.13)</td>
</tr>
<tr>
<td>Wheat</td>
<td>0.29 (0.23)</td>
</tr>
</tbody>
</table>

$^a$ Numbers of sheep and cattle were ordered into 4 categories, areas of barley into 3 categories, and areas of wheat into 2 categories. All correlations were significant ($P<0.05$) except those for wheat. $^b$ $P_t$: p-for-trend.

Using the same categories, the percentages of farmers who were in the same category in both databases, who were in a category lower in SHAW, and who were in a category higher in SHAW are displayed in Figure 7-3. No apparent trends were found in the percentages over the time for sheep, cattle and barley; however the agreement was lowest in the earliest year (1983) in all of them. In contrast, agreement decreased with time for wheat. Regarding disagreements between both datasets, the percentage of sheep farmers who were in a higher category in SHAW were less than the percentage of those
who were in a lower category in all years except for 1983 when the latter was slightly higher. The same pattern was found for cattle but the latter was also higher in 1988. No pattern was found for barley whereas for wheat the two percentages were equal in all years.

To discover any trend over years in the size of differences between numbers given by farmers in SHAW and numbers found in the JSAH, the distributions of PERdiff are presented in Figure 7-4. No obvious trends were found in PERdiff over the years except for a little decrease in the median of PERdiff in 2000 for sheep and in years 1998 and 2000 for cattle. The number of farmers in wheat sector was low (n = 7-14) so it was implausible to discuss any trend.
Figure 7-4: Distributions of PERdiff in different farm types over time

(A) Sheep, (B) Cattle, (C) Barley, (D) Wheat

7.3.3 Association between age, memory, and health status and agreements between SHAW and JSAH databases

To discover if the accuracy of the answers was affected by the farmer's age or by the memory of the farmer, age and memory were compared between farmers whose answers in the SHAW study matched the information in the JSAH and farmers whose answers did not match. Table 7-6 shows age of farmers in each group for each type in 1983 and Table 7-7 presents the memory, whilst the results of other years are presented in Appendix 17. No significant differences in age or memory were found between those two groups in all farm types in all years. The only exemption was in sheep in year 1983 and 2000 where the farmers of unmatched answers were younger than the farmers of matched answers.
Table 7-6: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Farmers</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>115</td>
<td>19</td>
<td>66.1 ± 5.7</td>
<td>63.1 ± 5.2</td>
</tr>
<tr>
<td>Cattle</td>
<td>125</td>
<td>9</td>
<td>65.7 ± 5.7</td>
<td>66.4 ± 5.4</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>114</td>
<td>20</td>
<td>66.0 ± 5.4</td>
<td>63.8 ± 6.8</td>
</tr>
<tr>
<td>Vegetables</td>
<td>113</td>
<td>21</td>
<td>65.6 ± 5.9</td>
<td>66.5 ± 4.3</td>
</tr>
</tbody>
</table>

Table 7-7: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Farmers</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>115</td>
<td>18</td>
<td>23.20 ± 1.92</td>
<td>23.55 ± 1.41</td>
</tr>
<tr>
<td>Cattle</td>
<td>124</td>
<td>9</td>
<td>23.26 ± 1.87</td>
<td>23.11 ± 1.90</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>114</td>
<td>19</td>
<td>23.32 ± 1.58</td>
<td>22.78 ± 3.08</td>
</tr>
<tr>
<td>Vegetables</td>
<td>112</td>
<td>21</td>
<td>23.17 ± 1.92</td>
<td>23.65 ± 1.46</td>
</tr>
</tbody>
</table>

Table 7-8 to Table 7-11 present the numbers of screen-identified cases of neuropsychiatric ill-health among the farmers whose answers in SHAW phase 1 matched the JSAH and among those who had different answers in year 1983. The results of all other years are in Appendix 18. No differences were found in the prevalence of ill-health between the two groups in all years except a borderline significant increase in the prevalence of screen-identified depression cases among the group of different answers compared to those of the same answers for combinable crops.

Table 7-8: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>13 (11.3)</td>
<td>2 (10.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>15 (12.0)</td>
<td>0 (0.0)</td>
<td>0.60</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>10 (8.8)</td>
<td>5 (25.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Vegetables</td>
<td>14 (12.4)</td>
<td>1 (4.8)</td>
<td>0.47</td>
</tr>
</tbody>
</table>
Table 7-9: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>13 (11.3)</td>
<td>1 (5.3)</td>
<td>0.69</td>
</tr>
<tr>
<td>Cattle</td>
<td>13 (10.4)</td>
<td>1 (11.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>10 (8.8)</td>
<td>4 (20)</td>
<td>0.23</td>
</tr>
<tr>
<td>Vegetables</td>
<td>13 (11.5)</td>
<td>1 (4.8)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Table 7-10: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>11 (9.6)</td>
<td>2 (10.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>11 (8.8)</td>
<td>2 (22.2)</td>
<td>0.21</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>11 (9.6)</td>
<td>2 (10)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables</td>
<td>11 (9.7)</td>
<td>2 (9.5)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 7-11: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1983

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>18 (15.7)</td>
<td>3 (15.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>20 (16.0)</td>
<td>1 (11.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>18 (15.8)</td>
<td>3 (15.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables</td>
<td>19 (16.8)</td>
<td>2 (9.5)</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Spearman correlation coefficients were determined between age and memory and the accuracy of livestock numbers or crop acreages given by the farmers. As shown in Table 7-12, there was a positive correlation between the difference and age of farmer in cattle in 1998 and 2000 ($r_s = 0.39$ and $0.36$ respectively). On the contrary negative correlations were found in barley in 1993 ($r_s = -0.65$) and in wheat in 1998 ($r_s = -0.84$); however the number of wheat farmers was only seven in 1998. No other correlations were found.
### Table 7-12: Correlation between age and PERdiff over time

<table>
<thead>
<tr>
<th>Year</th>
<th>Sheep</th>
<th>Cattle</th>
<th>Barley</th>
<th>Wheat</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>-0.12</td>
<td>-0.07</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>1988</td>
<td>-0.15</td>
<td>0.13</td>
<td>0.16</td>
<td>-0.07</td>
</tr>
<tr>
<td>1993</td>
<td>-0.06</td>
<td>0.15</td>
<td>-0.65*</td>
<td>-0.57</td>
</tr>
<tr>
<td>1998</td>
<td>-0.04</td>
<td>0.39</td>
<td>0.15</td>
<td>-0.84</td>
</tr>
<tr>
<td>2000</td>
<td>0.12</td>
<td>0.36</td>
<td>0.06</td>
<td>-0.53</td>
</tr>
</tbody>
</table>

*a Correlations with asterisks are significant (P<0.05)

Table 7-13 shows the correlations between PERdiff and the memory of the farmers. A negative correlation was found with Barley in year 2000 ($r_s = -0.66$) whereas the correlation was positive with wheat in the same year ($r_s = 0.81$). No correlations were found for sheep or cattle.

### Table 7-13: Correlation between memory scores and PERdiff over time

<table>
<thead>
<tr>
<th>Year</th>
<th>Sheep</th>
<th>Cattle</th>
<th>Barley</th>
<th>Wheat</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>-0.11</td>
<td>-0.03</td>
<td>0.19</td>
<td>-0.18</td>
</tr>
<tr>
<td>1988</td>
<td>-0.08</td>
<td>-0.02</td>
<td>0.09</td>
<td>0.52*</td>
</tr>
<tr>
<td>1993</td>
<td>-0.03</td>
<td>0.12</td>
<td>-0.23</td>
<td>0.44</td>
</tr>
<tr>
<td>1998</td>
<td>-0.13</td>
<td>-0.13</td>
<td>-0.45</td>
<td>0.37</td>
</tr>
<tr>
<td>2000</td>
<td>-0.06</td>
<td>-0.12</td>
<td>-0.66*</td>
<td>0.81*</td>
</tr>
</tbody>
</table>

*a Correlations with asterisks are significant (P<0.05)

### 7.4 Discussion

The aim of this chapter was to assess the validity of self-reported occupational history among farmers. This study indicates that the accuracy of self-reported exposure is apparently reliable to rank farmers’ exposures in epidemiologic studies in farming activities. The recall of farmers was accurate in livestock sectors and varied in the crop sectors. The recall of having sheep, cattle, and combinable crops was substantial but was not that good for vegetables. The recall of sheep flock size, cattle herd size, and barley acreage was also good while the recall of wheat acreage was not valid. Generally, farmer’s recall was affected neither by farmer’s age and memory nor by being a screen-positive case of neuropsychiatric illnesses.
Although researchers have examined the validity of self-reported use of pesticides among farmers\textsuperscript{118,126,132}, there is lack of studies that examined the validity of self-reported exposure variables like livestock herd size or crop acreages. The importance of examining such validity comes from that these variables (\textit{i.e.} livestock herd size or crop acreages) affect the exposure to pesticides and sometimes they were used as surrogates of long-term exposures\textsuperscript{8,320}. Furthermore, these factors were included in the exposure models developed in Chapter 6 which were used to study the association between pesticide exposure and neuropsychiatric illnesses in Chapter 8.

The data of the JSAH is self-reported data as well; however this data was collected in each year for the same year of data collection. Therefore, it was assumed to be reasonably accurate and was therefore considered as the "gold standard" in the analysis. When there is no true gold standard for occupational history, self-reported data available from the same year offers practically useable and accurate data to be used in the assessment of the validity of self-reported retrospective occupational history\textsuperscript{126}.

The recall of having sheep, cattle, and combinable crops was substantial and the recall of sheep flock size, cattle herd size, and barley acreage was also good. Recall of having vegetables was, however, not that good while recall of wheat acreage was not accurate. Agreements might be considered higher if the “percent agreement test” was used instead; however this study used the kappa test because it has been shown to be more robust because it takes into account agreement by chance\textsuperscript{131}. The results of this study suggest that farmers are better able to recall having a specific type of livestock or crops than the number or the acreage of that type. This is consistent with the studies which found that farmers can recall the use of a specific pesticide more than recalling specific details of its use\textsuperscript{126,132}.

The disagreement in having a type of farm in specific years between SHAW and JSAH databases, when found, was mainly because farmers did not report having that type in SHAW although they had reported it in JSAH. A probable reason for this disagreement is what can be called “contextual uncertainty”\textsuperscript{300}. A farmer who had only 3 cattle for three years might answer “no” in SHAW questionnaire to the question about being a cattle farmer in those years, although he reported the exact number to Defra in the JSAH. Therefore, it is important to define all relevant words in the questionnaire pretty clear\textsuperscript{330}. For instance, instead of asking about being a cattle farmer in a period of time the question might be whether the farmer had any number of cattle, even one, during
that period of time. The same reason might be behind the low agreement in reported vegetable farming between the two databases. The question in SHAW phase 1 questionnaire was about “outdoor vegetables and potatoes”; these vegetables should have been defined. Furthermore, in this study the individual agricultural crop mentioned in JSAH was matched with crop categories in the SHAW phase 1 questionnaire. This action of matching crops had been performed mentally by the farmer when he responded to the question in the SHAW phase 1 questionnaire but may have been different from the matching in this chapter or between farmers.

The number of sheep or cattle may be more recognised than number of acres covered with each crop, which may explain the lack of recall of wheat acreage and the low accuracy of recalling barley acreage compared to the recall of number of sheep and cattle. Furthermore, many farmers in phase 2 of SHAW provided the acreage of many crops together, indicating that it is difficult to recognise the acreage of each crop individually. This is similar to what has been reported in other studies that farmers are more likely to remember the use of pesticides in groups (e.g. insecticides, herbicides) than to remember the use of each pesticide\textsuperscript{126,132}.

A key life events calendar was used in SHAW phase 2 to enhance the memory of the farmer. The event history calendar and icon calendar based questionnaires have been used with farmers and found useful to improve the farmer’s recall of the lifetime farming activities\textsuperscript{26,125}. The accuracy of self-reported data in SHAW phase 2 might be partially due to the use of the calendar. Completion of the JSAH questionnaire by the farmers may also have improved their recall in the SHAW study. However, the response to the JSAH happened in a range of (6-23) years prior to the SHAW study, and the persistence of any appreciable memory booster effect is unlikely after such period of time\textsuperscript{126}. In addition to that, it is not known if the farmers responded to the JSAH by themselves or someone else from their farm did that.

A subject’s recall is reported to be better if the subject was personally involved in the selection of the agents or the activity required to be recalled\textsuperscript{131}. For instance, farmers who personally applied pesticides on crops were more accurate in recalling the utilised pesticides than farmworkers who harvested the crops\textsuperscript{118,331,332}. In this manner farmer’s recall of number of livestock or acres of specific crops depend on whether the farmer personally was involved in that farm sector. Therefore, it is helpful in all exposure questionnaires in agricultural studies to have a separate section to ask the farmers to
order the farming sectors in which they were mostly involved. Moreover, subject’s recall was found to be decreased as the number of assignments held by the subject increases\textsuperscript{328,333-335}. Therefore, further work may differentiate between the farmers who worked only in one farming sector and those who worked in different sectors.

Although the accuracy of answers regarding the number of livestock and acreages of crops of 1983 was generally lower than that in later years, the accuracy of answers about the type of farm, number of livestock and acreages of crops did not vary over the years. This suggests that the accuracy of self-reported data did not change if the farmer was asked about recent years or about decades ago. However, the small decrease in the results of 1983 might deserve further work in which earlier data available in paper format only is accessed.

Recall bias, which is the influence of reporting by disease status, has been always an important concern with self-reported exposure\textsuperscript{131}. However, most studies that compared the reports of cases and controls did not find significant differences in the accuracy of their exposure assessments\textsuperscript{118,336-338} let alone that recall bias is not expected in variables such investigated in this study (\textit{i.e.} having types of farms and number of livestock and acreages of crops).

A minor further limitation of this study was that some farmers in SHAW phase 2 reported that the number of sheep or cattle increased/decreased from x to z in duration of time without giving a specific number for each year in between. In those cases a gradual linear increase or decrease in this time period was assumed. This assumption might underestimate or overestimate the real number. However, generally for epidemiologic analysis the exact number is not important and this level of recall accuracy is probably adequate when it is enough to order the exposure, but it might limit investigating more specific associations between pesticide exposure and health effects\textsuperscript{126}.

The participation rate in this study was good but there is some concern about the generalisation of the results because the farmers who gave permission to access their data in JSAH were younger than those who did not. However, the fact that there was no difference in memory scores between the two groups reduces the likelihood of external invalidity. Moreover, this study found that generally farmer’s recall was not affected by farmer’s age and memory.
Another arguable matter is the representation of the good recall of the variables examined in this study (i.e. number of livestock and acreage of crops) of other variables in farming life, specifically other determinants of pesticide exposure. It can be argued that farmers are questioned frequently about number of livestock and acreage of crops in, for example, a census or when they want to buy pesticides. In addition to that these variables are very close to the core of farming business and they affect the farmers’ income, which might make the recall of such variables easier than the recall of other determinants like the amount or the type of pesticides. On the other hand, the recall of number of livestock or acreage of a crop is more difficult than the recall of other determinants like application types or application frequency since these are relatively stable over time compared to livestock numbers or crop acreages. Therefore, it seems that the good recall found in this study for some variables possibly reflects recall in farming occupation in general.

In conclusion, this study indicates that the accuracy of self-reported exposure is reliable for epidemiologic studies in farming activities which interest in ranking farmers’ exposures more than in obtaining the absolute exposures. However, the decreased accuracy in specific farming sectors suggests the use of tools to enhance the recall in these sectors.
8.1 Introduction

Farmers are exposed to pesticides mainly when they apply pesticides to animals or when they apply pesticides to crops and other plants\(^4\). Sheep dipping is one of the main pesticide applications in the UK\(^6\) and OPs have been the main ingredients of sheep dips in the UK since 1970s\(^12\). As a result most current sheep farmers were exposed to the OP compounds in the past\(^13\) and therefore several British studies have focused on this application to study the acute and chronic neuropsychiatric effects among farmers\(^7\)-\(^11\).

The neuropsychiatric effects of short-term high exposure to many pesticides especially OPs have been well described (\textit{e.g.} fatigue, headache, tremor, blurry vision, confusion, depression of respiration and ultimately coma and death)\(^15\)-\(^17\), while the effects of long-term exposure are still controversial\(^13\),\(^18\),\(^22\). Changes in mood and affect have been linked with long-term pesticide exposure\(^18\),\(^196\) and suicide is a noticeable problem among farming communities\(^203\). Symptoms of depression and amnesia were prevalent among UK sheep dippers who used OP dips\(^186\), while another survey found no association between past use of sheep dips and current anxiety or depression\(^11\).

Although negative results of nerve conduction velocity and vibration sensitivity were found among people who had been exposed chronically to pesticides, available evidence indicate that this exposure has little effect on the peripheral nervous system\(^18\),\(^196\). The review of Le Couteur \textit{et al.}, found that 12 out of 20 case-control studies had found a relationship between pesticide exposure and PD\(^229\) and a more comprehensive review concluded that the epidemiological data indicate a consistent relationship that appeared to be stronger for exposure to herbicides and insecticides\(^222\). Long-term pesticide exposure have also been linked with cognitive dysfunctions\(^8\),\(^249\),\(^250\), Alzheimer disease and vascular dementia\(^256\),\(^257\), whilst an environmental study found no linkage with Alzheimer disease\(^260\).

The inconsistent neuropsychiatric effects of long-term pesticide exposure might result from the relatively weak association between pesticide exposure and health effects and the difficulties in estimating long-term exposure\(^18\),\(^25\),\(^26\). Exposure misclassification has been suggested to be the reason behind most of the differences in disease risk estimates associated with pesticide exposure\(^263\).
The use of more sophisticated assessment methodologies is hypothesised to reveal any possible association between pesticide exposure and health effects more than the use of simple methodologies. Therefore, the application of the new developed exposure models to the SHAW study is used in this chapter to investigate the association between long-term pesticide exposure and screen-identified depression, neuropathy, Parkinsonism and dementia. Different assessment methodologies are used for pesticide exposure and for health effects to explore the impact of the assessment methodology on the association results.

8.2 Materials and methods

This association study depended on the SHAW study described in detail in Chapter 2. The SHAW study consisted of two phases. In phase 1 of the SHAW study, farmers were asked to complete a health and work history questionnaire, while in phase 2 a sample of phase 1 farmers were interviewed to obtain additional detailed information on their occupational exposures and health status. Although the data of phase 1 was used, the association analysis was only performed on the farmers who were interviewed in the second phase.

8.2.1 Definitions of the health effects

Potential cases of depression, neuropathy, Parkinsonism, and dementia were screen-identified according to different definitions which depended on the data of the two phases. Farmers’ answers on the phase 1 questionnaire were used to identify the screen-positive farmers of the four illnesses in phase 1 according to definitions described in Section 2.1.1.1. These definitions are called phase 1 definitions.

Screen-positive farmers who were identified in phase 1 and a random selection of other screen-negative farmers were administered questionnaires appropriate for the putative ill-health under investigation. Phase 2 ill-health classifications were based upon previously published scoring schemes or approaches. These definitions are called phase 2 definitions.

Table 8-1 presents the number of screen-positive and screen-negative subjects according to phase 1 and phase 2 definitions. 32 of phase 2 farmers (14.3%) were screen-positive as potential cases of depression in phase 1. 28 and 27 farmers (12.5% and 12.1%) were screen-positive as potential cases of neuropathy and Parkinsonism respectively while 19.2% were identified as potential cases of dementia. Numbers of screen-positive and screen-negative farmers according to phase 2 definitions varied according to how many subjects were nested for each illness. The memory scores of farmers ranged from 14 to
27 with a median of 23 and the mean±SD of 22.9±2.1. The 1st and 3rd quartiles (Q1,Q3) were 22 and 24 respectively.

### Table 8-1: Number of screen-positive and screen-negative subjects for each illness according to SHAW phase 1 and phase 2 definitions

<table>
<thead>
<tr>
<th>Ill-health</th>
<th>Definition</th>
<th>Number of screen-positive/number of screen-negative (%screen-positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Phase 1</td>
<td>32/192 (14.3)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>7/59 (10.6)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Phase 1</td>
<td>28/196 (12.5)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>41/48 (46.1)</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Phase 1</td>
<td>27/197 (12.1)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>32/62 (34.0)</td>
</tr>
<tr>
<td>Dementia</td>
<td>Phase 1</td>
<td>43/181 (19.2)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>7/114 (5.8)</td>
</tr>
</tbody>
</table>

#### 8.2.2 Pesticide exposure

Long-term pesticide exposure in different farming sectors (sheep, cattle, other livestock, crops, and other use) was estimated in Chapter 6 using simple surrogates from the two phases and using models which depended on phase 2 information (Table 8-2 and Table 8-3). Different surrogates and models were used to estimate pesticide exposure in the same sector to find if the results of the association with health outcomes depend on the estimation method. The *a priori* hypothesis was that, if pesticide exposures were associated with ill-health, then exposure estimates based on models are more able to reveal such associations than the continuous surrogates (*i.e.* number of years and days), which in turn are more able to do that than the dichotomous surrogates (*i.e.* ever/never). Pesticide exposures in all sectors were estimated twice, once for all pesticides and once for the OP exposure specifically.

Pesticide exposure from sheep dipping was estimated using models including the NEW model (Section 6.2.4.2). In the NEW model, the REST variables combined all variables in the conceptual model that were not collected in the SHAW study such as the type of concentrate container and duration of the dipping session. REST variables were calculated in two ways either as deterministic or probabilistic variables. In the deterministic method REST variables were calculated based on the most prevalent option in each variable (described in Section 6.2.4.2). In the second method, REST variables were addressed as a probabilistic variable according to the probability of each component (Section 5.2.3). Monte Carlo simulations were used to obtain 20 sets of exposure estimates for Phase 2 farmers.
<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Estimate type</th>
<th>Name</th>
<th>Definition</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>Surrogate</td>
<td></td>
<td>EVSH</td>
<td>Ever having sheep</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVCONSH</td>
<td>Ever handled the concentrate to treat sheep</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVDIP</td>
<td>Ever dipped sheep</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td>General</td>
<td></td>
<td>YRSH</td>
<td>Number of years having sheep</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>YRDIP</td>
<td>Number of dipping years using any pesticides</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DYDIP</td>
<td>Number of dipping days using any pesticides</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>NEW</td>
<td>Cumulative pesticide exposure from sheep dipping according to the NEW model</td>
<td>6.2.4.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PRNEW</td>
<td>Cumulative pesticide exposure from sheep dipping according to the probabilistic NEW model</td>
<td>6.2.4.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SHAPE</td>
<td>Cumulative pesticide exposure from sheep dipping according to the SHAPE model</td>
<td>6.2.4.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TASK</td>
<td>Cumulative pesticide exposure from sheep dipping according to the TASK model</td>
<td>6.2.4.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EXP</td>
<td>Cumulative pesticide exposure from sheep dipping according to the EXPsheep model</td>
<td>6.2.4.5</td>
</tr>
<tr>
<td></td>
<td>Surrogate</td>
<td></td>
<td>OPEVSH</td>
<td>Ever having sheep after 1970</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPYRSH</td>
<td>Number of years having sheep after 1970</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPYRDIP</td>
<td>Number of dipping years using general pesticides after 1970</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPDYDIP</td>
<td>Number of dipping days using general pesticides after 1970</td>
<td>6.2.4.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>OPNEW</td>
<td>Cumulative OP exposure from sheep dipping according to the OPNEW model</td>
<td>6.2.4.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPPRNEW</td>
<td>Cumulative OP exposure from sheep dipping according to the probabilistic OPNEW model</td>
<td>6.2.4.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPSHAPE</td>
<td>Cumulative OP exposure from sheep dipping according to the OPSHAPE model</td>
<td>6.2.4.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPEXPSH</td>
<td>Cumulative OP exposure in sheep sector according to the OPEXPsheep model</td>
<td>6.2.4.5</td>
</tr>
</tbody>
</table>
### Table 8-3: Definitions of pesticide exposure surrogates and models in other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Estimate type</th>
<th>Name</th>
<th>Definition</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cattle</strong></td>
<td>General</td>
<td>Surrogate</td>
<td>EVCAT</td>
<td>Ever having cattle</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVCONCAT</td>
<td>Ever handled the concentrate to treat cattle</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVWAR</td>
<td>Ever applied treatment for warble fly</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>YRCAT</td>
<td>Number of years having cattle</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>EXPCAT</td>
<td>Cumulative pesticide exposure in cattle sector according to the EXP&lt;sub&gt;cat&lt;/sub&gt; model</td>
<td>6.2.5.2</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>Surrogate</td>
<td>OPEVCAT</td>
<td>Ever having cattle after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPYRCAT</td>
<td>Number of years having cattle after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>OPEXPCAT</td>
<td>Cumulative OP exposure in cattle sector according to the OPEXP&lt;sub&gt;cat&lt;/sub&gt; model</td>
<td>6.2.5.2</td>
</tr>
<tr>
<td><strong>Other Livestock</strong></td>
<td>General</td>
<td>Surrogate</td>
<td>EVLIV</td>
<td>Ever having other livestock</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>YRLIV</td>
<td>Number of years having other livestock</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>EXPLIV</td>
<td>Cumulative pesticide exposure in livestock sector according to the EXP&lt;sub&gt;liv&lt;/sub&gt; model</td>
<td>6.2.5.2</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>Surrogate</td>
<td>OPEVLIV</td>
<td>Ever having other livestock after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPYRLIV</td>
<td>Number of years having other livestock after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>OPEXPLIV</td>
<td>Cumulative OP exposure in livestock sector according to the OPEXP&lt;sub&gt;liv&lt;/sub&gt; model</td>
<td>6.2.5.2</td>
</tr>
<tr>
<td><strong>Crops and Grain</strong></td>
<td>General</td>
<td>Surrogate</td>
<td>EVCRP</td>
<td>Ever having crops or grains</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVCONCRP</td>
<td>Ever handled the concentrate to treat crops or grains</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EVAPPCRP</td>
<td>Ever applied insecticides to crops or grains</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>YRCRP</td>
<td>Number of years having crops or grains</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>EXPCRP</td>
<td>Cumulative pesticide exposure in crops sector according to the EXP&lt;sub&gt;crop&lt;/sub&gt; model</td>
<td>6.2.5.3</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>Surrogate</td>
<td>OPEVCRP</td>
<td>Ever having crops or grains after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OPYRCRP</td>
<td>Number of years having crops or grains after 1970</td>
<td>6.2.5.1</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td></td>
<td>OPEXPCRP</td>
<td>Cumulative OP exposure in crops sector according to the OPEXP&lt;sub&gt;crop&lt;/sub&gt; model</td>
<td>6.2.5.3</td>
</tr>
<tr>
<td><strong>Other Use</strong></td>
<td>General</td>
<td>Surrogate</td>
<td>EXPUSE</td>
<td>Pesticide exposure from other pesticide use according to the EXP&lt;sub&gt;other&lt;/sub&gt; model</td>
<td>6.2.5.4</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>Surrogate</td>
<td>OPEXPUSE</td>
<td>OP exposure from other pesticide use according to the OPEXP&lt;sub&gt;other&lt;/sub&gt; model</td>
<td>6.2.5.4</td>
</tr>
</tbody>
</table>
8.2.3 Statistical analysis

Only ten women were interviewed in phase 2 and all of them were controls for all illnesses according to phase 2 definitions, and hence only male farmers were included in the following analysis. All model exposure estimates and number of dipping days (DYDIP and OPDYDIP) were logarithmically transformed (after adding 1 to solve the zero issue) since they were log-normally distributed (see Section 6.3.2), while the distributions of number of years being a farmer in different farming sectors (YRSH, YRDIP, OPYRSH, YRCAT, OPYRCAT, YRLIV, OPYRLIV, YRCRP, and OPYRCRP) were approximately normal.

Farmers were distributed into two groups according to their memory score (low and high score) using the median as a cut-off point. The student's t-test was then used to evaluate associations between memory and ill-health. Multiple logistic regression was then used to determine associations between memory and pesticide exposure estimated by surrogates (dichotomous and continuous) or exposure models when adjusted for age since memory could be affected by age.

Multiple logistic regression was also used to determine associations between ill-health and pesticide exposure. However, Fisher’s exact test was used to study the association between dichotomous surrogates of pesticide exposure and phase 2 ill-health since in few analyses there was no screen-positive farmers in the unexposed group but the results of this test did not show any significant differences so they were not presented. Farmers were then distributed into three groups according to their exposure estimated by models in each farming sector (none, low, and high exposure). The median exposure level was used to define farmers with low or high exposures. Few farmers were unexposed to general pesticides in the sheep sector and few farmers were also unexposed to pesticides (in general or OPs in particular) in the cattle sector, therefore exposure in those sectors was categorised as low, moderate and high. Exposure tertiles were used to define these three categories. Subsequently, multiple logistic regression was applied categorically this time to examine associations between ill-health and pesticide exposure and between memory and pesticide exposure considering the group with lowest exposure as a reference. Since the results of the logistic regressions were comparable with categorisation and without, only the results of the categorised regression were presented in this chapter whereas continuous results are presented in Appendix 19.
Since a model for the total pesticide exposure in all farming sectors is not available, and to take into account pesticide exposures in all farming sectors, total exposure in each farming sector as estimated by EXP model and OPEXP model of that sector (Table 8-2) were included altogether in the multiple logistic regression.

All logistic regression tests were adjusted for age. The number of screen-positive farmers of phase 2 depression and phase 2 dementia was too small (only 7) to adjust for confounders other than age. All regression results were displayed in the form of odds ratio and 95% confidence interval (OR, 95%CI) and p-for-trend (P_t) was also presented.

All analyses were performed using SPSS statistical software (version 16.0) while Stata statistical software (Version 10.1) was used to perform the logistic regression between ill-health and the 20 simulated exposure estimate sets of the NEW model. In this analysis, these 20 sets were treated as multiple-imputed data using the command (mim: logistic) after adding two new variables; “_mi” to order the farmers and “_mj” to order the exposure sets.

8.3 Results

8.3.1 Association between memory and pesticide exposure

Table 8-4 shows the differences in memory scores between screen-positive and screen-negative farmers for each ill-health. No significant differences were found in all illnesses except for phase 1 neuropathy where the memory scores were slightly higher among screen-negatives than among screen-positives (23.0±2.1, 22.1±2.3 respectively, P=0.03).

<table>
<thead>
<tr>
<th>Ill-health</th>
<th>Definition</th>
<th>Mean±SD of memory scores (n)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Screen-positive</td>
<td>Screen-negative</td>
</tr>
<tr>
<td>Depression</td>
<td>Phase 1</td>
<td>23.1 ± 1.8 (31)</td>
<td>22.8 ± 2.2 (189)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>23.1 ± 2.1 (6)</td>
<td>23.1 ± 2.1 (59)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Phase 1</td>
<td>22.4 ± 2.3 (28)</td>
<td>23.0 ± 2.1 (192)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>22.7 ± 2.4 (41)</td>
<td>23.0 ± 2.0 (48)</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Phase 1</td>
<td>22.4 ± 2.7 (27)</td>
<td>23.0 ± 2.0 (193)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>22.3 ± 2.9 (32)</td>
<td>23.2 ± 2.1 (61)</td>
</tr>
<tr>
<td>Dementia</td>
<td>Phase 1</td>
<td>22.6 ± 2.1 (43)</td>
<td>23.0 ± 2.1 (177)</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td>21.8 ± 3.0 (7)</td>
<td>22.9 ± 1.9 (114)</td>
</tr>
</tbody>
</table>
The age of farmers was negatively correlated with the memory scores ($r_s = 0.22$, $P = 0.001$). Farmers who had ever been involved in dipping sheep had lower memory scores than those who had not (OR, 95%CI: 0.33, 0.15-0.72), whilst farmers who had crops anytime in their life or after 1970 had borderline significantly higher memory scores than those who had not (OR, 95%CI: 1.73, 0.98-3.03 and 1.72, 0.99-2.98 respectively). No other differences in memory were found between farmers who had been involved in different farming activities and those who had not (Table 8-5), and no association was found between memory and pesticide exposure estimated by exposure models in different farming sectors (Table 8-6).

Table 8-5: Association between memory and pesticide exposure surrogates in different farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Memory score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n^a</td>
<td>UM^a</td>
</tr>
<tr>
<td>Sheep</td>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVSH</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>EVCONSH</td>
<td>213</td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>EVDIP</td>
<td>215</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>YRSH</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>YRDIP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>DYDIP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVSH</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPYRSH</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPYRDIP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPDYDIP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVCAT</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>EVCONCAT</td>
<td>213</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>EVWAR</td>
<td>218</td>
<td>118</td>
</tr>
<tr>
<td></td>
<td>YRCAT</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVCAT</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPYRCAT</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVLIV</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>YRLIV</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVLIV</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPYRLIV</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVCRP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>EVCONCRP</td>
<td>175</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>EVAPPCRP</td>
<td>217</td>
<td>116</td>
</tr>
<tr>
<td></td>
<td>YRCRPG</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVCRP</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OPYRCRPG</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td>Other use</td>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EXPUSE</td>
<td>220</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEXPUSE</td>
<td>220</td>
<td>119</td>
</tr>
</tbody>
</table>

^a n = number of all farmers and UM = number of farmers with memory scores under median.

^b All results are adjusted for age.
Table 8-6: Association between memory and pesticide exposure estimated by exposure models in different farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Memory scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n*</td>
<td>UM*</td>
</tr>
<tr>
<td>Sheep</td>
<td>General</td>
<td>NEW</td>
<td>Low</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SHAPE</td>
<td>Low</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TASK</td>
<td>Low</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPSH</td>
<td>Low</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>None</td>
<td>Low</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>SHAPE</td>
<td>Low</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>None</td>
<td>Low</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EXPCAT</td>
<td>Low</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>EXPCAT</td>
<td>Low</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>EXPLIV</td>
<td>None</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>EXPLIV</td>
<td>None</td>
<td>199</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td>EXPCRP</td>
<td>None</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td></td>
<td>58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>EXPCRP</td>
<td>None</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td></td>
<td>57</td>
</tr>
</tbody>
</table>

*a n = number of all farmers, UM = number of farmers with memory scores under median, and Pt = p-for-trend.
*b All results are compared to the referent. All results are adjusted for age.
8.3.2 Association between depression and pesticide exposure

8.3.2.1 Phase 1 depression

Phase 1 depression was not associated with pesticide exposure in the sheep farming sector or in any other farming sector either when the exposure was estimated by surrogates (Table 8-7) or when the exposure was estimated by models (Table 8-8 and Table 8-9). No association was also found when the estimation was restricted to OP pesticides specifically.

Table 8-7: Association between depression and pesticide exposure surrogates in different farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n^a</td>
<td>NS^a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sheep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>EVSH</td>
<td>224</td>
<td>32</td>
<td>1.24 (0.39 - 3.87)</td>
</tr>
<tr>
<td></td>
<td>EVCONSH</td>
<td>217</td>
<td>31</td>
<td>2.84 (0.63 - 12.7)</td>
</tr>
<tr>
<td></td>
<td>EVDIP</td>
<td>219</td>
<td>32</td>
<td>1.64 (0.46 - 5.87)</td>
</tr>
<tr>
<td></td>
<td>YRSH</td>
<td>224</td>
<td>32</td>
<td>1.00 (0.98 - 1.02)</td>
</tr>
<tr>
<td></td>
<td>YRDIP</td>
<td>224</td>
<td>32</td>
<td>0.99 (0.97 - 1.01)</td>
</tr>
<tr>
<td></td>
<td>DYDIP</td>
<td>224</td>
<td>32</td>
<td>1.00 (0.62 - 1.61)</td>
</tr>
<tr>
<td>OP</td>
<td>OPEVSHP</td>
<td>224</td>
<td>32</td>
<td>0.90 (0.37 - 2.21)</td>
</tr>
<tr>
<td></td>
<td>OPYRSHP</td>
<td>224</td>
<td>32</td>
<td>0.99 (0.97 - 1.02)</td>
</tr>
<tr>
<td></td>
<td>OPYRDIP</td>
<td>224</td>
<td>32</td>
<td>0.99 (0.96 - 1.02)</td>
</tr>
<tr>
<td></td>
<td>OPDYDIP</td>
<td>224</td>
<td>32</td>
<td>0.88 (0.56 - 1.37)</td>
</tr>
<tr>
<td>Cattle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>EVCAT</td>
<td>224</td>
<td>32</td>
<td>1.58 (0.19 - 13.3)</td>
</tr>
<tr>
<td></td>
<td>EVCONCAT</td>
<td>217</td>
<td>31</td>
<td>3.00 (0.38 - 23.8)</td>
</tr>
<tr>
<td></td>
<td>EWVAR</td>
<td>222</td>
<td>32</td>
<td>0.93 (0.25 - 3.52)</td>
</tr>
<tr>
<td></td>
<td>YRCAT</td>
<td>224</td>
<td>32</td>
<td>1.01 (0.98 - 1.04)</td>
</tr>
<tr>
<td>OP</td>
<td>OPEVCAT</td>
<td>224</td>
<td>32</td>
<td>1.34 (0.37 - 4.83)</td>
</tr>
<tr>
<td></td>
<td>OPYRCAT</td>
<td>224</td>
<td>32</td>
<td>1.01 (0.97 - 1.04)</td>
</tr>
<tr>
<td>Other livestock</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>EVCRP</td>
<td>224</td>
<td>32</td>
<td>1.13 (0.51 - 2.50)</td>
</tr>
<tr>
<td></td>
<td>EVCONCRP</td>
<td>179</td>
<td>24</td>
<td>0.98 (0.39 - 2.48)</td>
</tr>
<tr>
<td></td>
<td>EVAPPICRP</td>
<td>221</td>
<td>32</td>
<td>0.86 (0.37 - 1.98)</td>
</tr>
<tr>
<td></td>
<td>YRCP</td>
<td>224</td>
<td>32</td>
<td>1.00 (0.99 - 1.02)</td>
</tr>
<tr>
<td>OP</td>
<td>OPEVCRP</td>
<td>224</td>
<td>32</td>
<td>1.31 (0.60 - 2.85)</td>
</tr>
<tr>
<td></td>
<td>OPYRCRP</td>
<td>224</td>
<td>32</td>
<td>1.00 (0.98 - 1.03)</td>
</tr>
<tr>
<td>Crops</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>EXPUSE</td>
<td>224</td>
<td>32</td>
<td>0.79 (0.39 - 1.62)</td>
</tr>
<tr>
<td>Other use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>OPEXPOSE</td>
<td>224</td>
<td>32</td>
<td>0.95 (0.44 - 2.06)</td>
</tr>
</tbody>
</table>

^a n = number of all farmers and NS = number of screen-positive farmers, ^b Adjusted for age, ^c All screen-positive farmers were in the exposed group.
8.3.2.2 Phase 2 depression

Phase 2 depression was not associated with exposure to pesticides in general and to OPs in particular in all farming sectors when these exposures were estimated by simple surrogates (Table 8-7) or by the developed models (Table 8-8 and Table 8-9). However, only seven farmers were defined as screen-positive of phase 2 depression and all of those farmers were in the exposed group in the sheep sector according to the dichotomous surrogates (EVSH, EVCONSH, and EVDIP) and in the exposed group in the cattle sector according to (EVCAT, EVCONCAT, EVWAR, and OPEVCAT), while all of them were in the non-exposed group in the other livestock sector according to the OPEXPLIV model.

Table 8-8: Association between depression and pesticide exposure estimated by exposure models in the sheep sector

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n a</td>
<td>NS a</td>
<td>OR (95%CI) b</td>
</tr>
<tr>
<td>General</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRNEW</td>
<td>Without c</td>
<td>222</td>
<td>31</td>
<td>1.01 (0.74 – 1.38)</td>
</tr>
<tr>
<td>NEW</td>
<td>Low</td>
<td>72</td>
<td>9</td>
<td>0.91 (0.34 - 2.45)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>11</td>
<td>11.15 (0.43 - 3.03)</td>
<td></td>
</tr>
<tr>
<td>SHAPE</td>
<td>Low</td>
<td>73</td>
<td>10</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>74</td>
<td>10</td>
<td>0.99 (0.38 - 2.57)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>74</td>
<td>10</td>
<td>1.00 (0.38 - 2.65)</td>
</tr>
<tr>
<td>TASK</td>
<td>Low</td>
<td>74</td>
<td>10</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>74</td>
<td>11</td>
<td>1.05 (0.40 - 2.71)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>11</td>
<td>1.09 (0.42 - 2.84)</td>
</tr>
<tr>
<td>EXPSH</td>
<td>Low</td>
<td>73</td>
<td>10</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>74</td>
<td>11</td>
<td>0.85 (0.33 - 2.24)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>10</td>
<td>0.89 (0.34 - 2.33)</td>
</tr>
<tr>
<td>OP</td>
<td>OPPRNEW</td>
<td>222</td>
<td>31</td>
<td>0.86 (0.65 – 1.15)</td>
</tr>
<tr>
<td>OPNEW</td>
<td>None</td>
<td>79</td>
<td>12</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>71</td>
<td>10</td>
<td>0.69 (0.27 - 1.80)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>72</td>
<td>9</td>
<td>0.67 (0.26 - 1.74)</td>
</tr>
<tr>
<td>OPSHAPE</td>
<td>None</td>
<td>79</td>
<td>12</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>10</td>
<td>0.67 (0.26 - 1.75)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>71</td>
<td>9</td>
<td>0.69 (0.26 - 1.80)</td>
</tr>
<tr>
<td>OPEXPSH</td>
<td>None</td>
<td>76</td>
<td>12</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>9</td>
<td>0.56 (0.21 - 1.50)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>74</td>
<td>10</td>
<td>0.70 (0.28 - 1.80)</td>
</tr>
</tbody>
</table>

a n = number of all farmers, NS = number of screen-positive farmers, and P t = p-for-trend. b All results are compared to the referent. All results are adjusted for age. c PRNEW model cannot be categorised since 20 sets of probabilistic model estimates were used. d No screen-positive farmers were found in this group.
Table 8-9: Association between depression and pesticide exposure estimated by exposure models in other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EXPCAT</td>
<td>Low</td>
<td>72</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>77</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCAT</td>
<td>Low</td>
<td>75</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>72</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>77</td>
<td>14</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>EXPLIV</td>
<td>None</td>
<td>184</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPLIV</td>
<td>None</td>
<td>203</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td>EXPCRP</td>
<td>None</td>
<td>105</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>59</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCRP</td>
<td>None</td>
<td>109</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>57</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>58</td>
<td>10</td>
</tr>
</tbody>
</table>

*a* n = number of all farmers, NS = number of screen-positive farmers, and P<sub>t</sub> = p-for-trend.

*b* All results are compared to the referent. All results are adjusted for age.

*c* No screen-positive farmers were found in this group.
8.3.3 Association between neuropathy and pesticide exposure

8.3.3.1 Phase 1 neuropathy

In the sheep sector, no significant associations were found between phase 1 neuropathy and pesticide exposure surrogates or OP exposure surrogates (Table 8-10). The probabilistic model of sheep dipping (PRNEW) revealed a borderline significant association between phase 1 neuropathy and general pesticide exposure (OR, 95%CI: 1.42, 0.96-2.10) (Table 8-11). Also a borderline significant trend was found in the odds ratios of phase 1 neuropathy when general pesticide exposure increased according to EXPSH model ($P_t=0.08$) but it reached statistical significance in the highest exposure category of EXPSH model (OR, 95%CI: 3.14, 1.07-9.25). No association was found between phase 1 dementia and OP exposure based on the exposure models.

In other farming sectors, phase 1 neuropathy was not associated with general pesticide exposure surrogates or with OP exposure surrogates (Table 8-10). When farmers were categorized into three exposure groups according to the model estimates (Table 8-12), an increased risk of phase 1 neuropathy was found among those farmers in the moderate general pesticide exposure group (but not among the high group) in the cattle sector as compared to the low exposure group (OR, 95%CI: 3.78, 1.18-12.1). An increased risk of phase 1 neuropathy was also found among the low pesticide exposure group (but not among the high group) in other livestock sector compared to the no-exposure group (OR, 95%CI: 3.79, 1.30-11.1). In both cases the trends of odds ratios were not significant ($P_t$ was 0.16 and 0.21 respectively). Phase 1 neuropathy was not associated with OP exposure in other farming sectors based on the exposure models.

8.3.3.2 Phase 2 neuropathy

An increased risk of phase 2 neuropathy was associated with general pesticide exposure in sheep farming according to YRDIP and DYDIP surrogates (OR, 95%CI: 1.02, 1.00-1.05 and 1.96, 1.09-3.51 respectively) and with OP exposure surrogates according to DYDIP (OR, 95%CI: 1.87, 1.11-3.14) (Table 8-10). The probabilistic model of sheep dipping (PRNEW) showed a positive association between phase 2 neuropathy and pesticide exposure. An increased risk of phase 2 neuropathy was also found among all groups with the high general pesticide exposure according to all dipping models and to the model of all treatments (EXPSH); all the trends of the odds ratios were significant.
(Table 8-11). No significant associations were found with OP exposure in sheep farming whatever the model used to assess that exposure.

In other farming sectors, phase 2 neuropathy was not associated with general pesticide exposure surrogates or with OP exposures surrogates whether the exposure was estimated by simple surrogates (Table 8-10) or by developed models (Table 8-12).

### Table 8-10: Association between neuropathy and pesticide exposure surrogates in different farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep General</td>
<td>EVSH</td>
<td>224 28</td>
<td>2.54 (0.57 - 11.3)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>EVCONSH</td>
<td>217 28</td>
<td>2.18 (0.62 - 7.74)</td>
<td>87 41</td>
</tr>
<tr>
<td></td>
<td>EVDIP</td>
<td>219 27</td>
<td>5.44 (0.71 - 41.7)</td>
<td>85 39</td>
</tr>
<tr>
<td></td>
<td>YRSH</td>
<td>224 28</td>
<td>1.00 (0.98 - 1.02)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>YRDIP</td>
<td>224 28</td>
<td>1.01 (0.99 - 1.03)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>DYDIP</td>
<td>224 28</td>
<td>1.53 (0.88 - 2.65)</td>
<td>89 41</td>
</tr>
<tr>
<td>OP General</td>
<td>OPEVSH</td>
<td>224 28</td>
<td>0.74 (0.31 - 1.76)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>OPYRS</td>
<td>224 28</td>
<td>0.98 (0.96 - 1.01)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>OPYRDIP</td>
<td>224 28</td>
<td>0.99 (0.96 - 1.02)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>OPDYDIP</td>
<td>224 28</td>
<td>0.95 (0.60 - 1.51)</td>
<td>89 41</td>
</tr>
<tr>
<td>Cattle General</td>
<td>EVCAT</td>
<td>224 28</td>
<td>1.46 (0.18 - 11.9)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>EVCONCAT</td>
<td>217 27</td>
<td>3.09 (0.40 - 24.1)</td>
<td>86 39</td>
</tr>
<tr>
<td></td>
<td>EWWAR</td>
<td>222 27</td>
<td>2.80 (0.36 - 21.8)</td>
<td>87 40</td>
</tr>
<tr>
<td></td>
<td>YRCAT</td>
<td>224 28</td>
<td>1.01 (0.99 - 1.04)</td>
<td>89 41</td>
</tr>
<tr>
<td>OP General</td>
<td>OPEVCAT</td>
<td>224 28</td>
<td>0.88 (0.28 - 2.75)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>OPYRCAT</td>
<td>224 28</td>
<td>1.01 (0.97 - 1.04)</td>
<td>89 41</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>224 28</td>
<td>2.03 (0.91 - 4.53)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>EVLIV</td>
<td>224 28</td>
<td>2.10 (0.99 - 1.04)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>YRLIV</td>
<td>224 28</td>
<td>1.06 (0.42 - 2.65)</td>
<td>89 41</td>
</tr>
<tr>
<td>Crops General</td>
<td>EVCRP</td>
<td>224 28</td>
<td>0.73 (0.33 - 1.62)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>EVCONCRP</td>
<td>179 19</td>
<td>0.63 (0.24 - 1.64)</td>
<td>71 33</td>
</tr>
<tr>
<td></td>
<td>EVAPPICRP</td>
<td>221 27</td>
<td>0.64 (0.27 - 1.48)</td>
<td>87 40</td>
</tr>
<tr>
<td></td>
<td>YRCRP</td>
<td>224 28</td>
<td>0.99 (0.97 - 1.01)</td>
<td>89 41</td>
</tr>
<tr>
<td>OP General</td>
<td>OPEVCRP</td>
<td>224 28</td>
<td>0.75 (0.34 - 1.67)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>OPYRCRP</td>
<td>224 28</td>
<td>0.98 (0.96 - 1.01)</td>
<td>89 41</td>
</tr>
<tr>
<td>Other use</td>
<td>General</td>
<td>224 28</td>
<td>0.85 (0.40 - 1.81)</td>
<td>89 41</td>
</tr>
<tr>
<td></td>
<td>EXPUSE</td>
<td>224 28</td>
<td>0.77 (0.33 - 1.80)</td>
<td>89 41</td>
</tr>
</tbody>
</table>

* n = number of all farmers and NS = number of screen-positive farmers, ^b Adjusted for age.
Table 8-11: Association between neuropathy and pesticide exposure estimated by exposure models in the sheep sector

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n a</td>
<td>NS a</td>
<td>OR (95%CI) b</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>PRNEW Without c</td>
<td>222</td>
<td>28</td>
<td>1.42 (0.96 - 2.10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NEW</td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.64 (0.87 - 8.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.64 (0.49 - 5.54)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NEW</td>
<td>Low</td>
<td>75</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.61 (0.87 - 7.85)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>74</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.35 (1.09 - 10.3)</td>
</tr>
<tr>
<td></td>
<td>SHAPE</td>
<td>Low</td>
<td>74</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.91 (0.6 - 6.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.14 (1.27 - 13.5)</td>
</tr>
<tr>
<td></td>
<td>TASK</td>
<td>Low</td>
<td>73</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.91 (0.6 - 6.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.14 (1.27 - 13.5)</td>
</tr>
<tr>
<td></td>
<td>EXPSH</td>
<td>Low</td>
<td>74</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.91 (0.6 - 6.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.14 (1.27 - 13.5)</td>
</tr>
<tr>
<td></td>
<td>OP RNEW</td>
<td>Without c</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>OP NEW</td>
<td>Low</td>
<td>79</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.35 (0.12 - 1.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.66 (0.26 - 1.63)</td>
</tr>
<tr>
<td></td>
<td>OP SHAPE</td>
<td>None</td>
<td>79</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.49 (0.18 - 1.32)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50 (0.19 - 1.34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>71</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50 (0.19 - 1.34)</td>
</tr>
<tr>
<td></td>
<td>OP EXPSH</td>
<td>None</td>
<td>76</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.25 (0.08 - 0.82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.72 (0.23 - 2.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>74</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.62 (0.93 - 7.38)</td>
</tr>
</tbody>
</table>

* n = number of all farmers, NS = number of screen-positive farmers, and P t a = p-for-trend. All results are compared to the referent. All results are adjusted for age. c PRNEW model cannot be categorised since 20 sets of probabilistic model estimates were used
### Table 8-12: Association between neuropathy and pesticide exposure estimated by exposure models in other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cattle</strong></td>
<td>General</td>
<td>EXPCAT</td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCAT</td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>77</td>
<td>10</td>
</tr>
<tr>
<td><strong>Other livestock</strong></td>
<td>General</td>
<td>EXPLIV</td>
<td>None</td>
<td>184</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPLIV</td>
<td>None</td>
<td>203</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td><strong>Crops</strong></td>
<td>General</td>
<td>EXPCRP</td>
<td>None</td>
<td>105</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>59</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCRP</td>
<td>None</td>
<td>109</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>57</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>58</td>
<td>6</td>
</tr>
</tbody>
</table>

*a n = number of all farmers, NS = number of screen-positive farmers, and Pt = p-for-trend.

*b All results are compared to the referent. All results are adjusted for age.

*c No screen-positive farmers were found in this group.
8.3.4 Association between Parkinsonism and pesticide exposure

8.3.4.1 Phase 1 Parkinsonism

As Table 8-13 reveals, an increased risk of phase 1 Parkinsonism was associated with two surrogates of general pesticide exposure in the sheep sector; YRDIP and DYDIP (OR, 95%CI: 1.03, 1.00-1.05 and 2.27, 1.18-4.36 respectively) but not with any OP surrogate. Phase 1 Parkinsonism was associated with general pesticide exposure in the sheep sector according to all exposure models whether they were for treatment by dipping only or for all treatments and all OR trends were significant (P, <0.05) (Table 8-14). The Probabilistic model revealed the same association with general pesticides (OR, 95%CI: 1.99, 1.18-3.35) but no association was found with the OP exposure in sheep farming whatever the model used.

Table 8-13: Association between Parkinsonism and pesticide exposure surrogates in different farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n=a  NS=b OR (95%CI)c</td>
<td>n=a  NS=b OR (95%CI)c</td>
</tr>
<tr>
<td>Sheep</td>
<td>General</td>
<td>EVSH</td>
<td>224 27 2.50 (0.56 - 11.2)</td>
<td>94 32 1.72 (0.42 - 6.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVCONSH</td>
<td>217 27 3.86 (0.86 - 17.3)</td>
<td>93 32 1.22 (0.40 - 3.70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVDIP</td>
<td>219 26 5.66 (0.73 - 43.6)</td>
<td>92 31 1.48 (0.36 - 6.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRSR</td>
<td>224 27 1.02 (0.99 - 1.04)</td>
<td>94 32 1.01 (0.99 - 1.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRDIP</td>
<td>224 27 1.03 (1.00 - 1.05)</td>
<td>94 32 1.01 (0.99 - 1.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DYDIP</td>
<td>224 27 2.27 (1.18 - 4.36)</td>
<td>94 32 1.21 (0.68 - 2.14)</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVSH</td>
<td>224 27 1.86 (0.66 - 5.20)</td>
<td>94 32 1.67 (0.57 - 4.90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRSH</td>
<td>224 27 1.02 (0.99 - 1.05)</td>
<td>94 32 1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRDIP</td>
<td>224 27 1.02 (0.99 - 1.05)</td>
<td>94 32 1.01 (0.98 - 1.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPDYDIP</td>
<td>224 27 1.42 (0.86 - 2.34)</td>
<td>94 32 1.19 (0.70 - 2.03)</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EVCAT</td>
<td>224 27 1.46 (0.18 - 12.0)</td>
<td>94 32 0.16 (0.02 - 1.69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVCONCAT</td>
<td>217 26 0.81 (0.10 - 6.48)</td>
<td>91 30 0.94 (0.20 - 4.37)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVWAR</td>
<td>224 26 1.01 (0.98 - 1.03)</td>
<td>93 31 0.71 (0.15 - 3.43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRCAT</td>
<td>224 27 1.01 (0.98 - 1.03)</td>
<td>94 32 1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVCAT</td>
<td>224 27 1.27 (0.36 - 4.55)</td>
<td>94 32 1.26 (0.30 - 5.30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRCAT</td>
<td>224 27 1.00 (0.97 - 1.04)</td>
<td>94 32 1.03 (0.99 - 1.07)</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>EVLIV</td>
<td>224 27 0.90 (0.39 - 2.07)</td>
<td>94 32 0.60 (0.23 - 1.57)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRLIV</td>
<td>224 27 1.01 (0.98 - 1.03)</td>
<td>94 32 0.99 (0.96 - 1.02)</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVLIV</td>
<td>224 27 1.14 (0.45 - 2.88)</td>
<td>94 32 0.79 (0.26 - 2.35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRLIV</td>
<td>224 27 1.01 (0.97 - 1.05)</td>
<td>94 32 0.99 (0.94 - 1.04)</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td>EVCRP</td>
<td>224 27 0.80 (0.36 - 1.81)</td>
<td>94 32 0.62 (0.25 - 1.53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVCONCRP</td>
<td>179 18 0.38 (0.13 - 1.09)</td>
<td>72 23 1.10 (0.40 - 3.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVAPPCRP</td>
<td>221 26 1.11 (0.44 - 2.79)</td>
<td>92 31 0.60 (0.23 - 1.51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>YRCRP</td>
<td>224 27 0.99 (0.97 - 1.01)</td>
<td>94 32 0.99 (0.97 - 1.01)</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEVCRP</td>
<td>224 27 0.70 (0.31 - 1.58)</td>
<td>94 32 0.69 (0.29 - 1.65)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPYRCRP</td>
<td>224 27 0.99 (0.96 - 1.01)</td>
<td>94 32 0.98 (0.95 - 1.01)</td>
</tr>
<tr>
<td>Other use</td>
<td>General</td>
<td>EXPUSE</td>
<td>224 27 0.81 (0.37 - 1.75)</td>
<td>94 32 0.72 (0.30 - 1.75)</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPUSE</td>
<td>224 27 0.88 (0.38 - 2.05)</td>
<td>94 32 0.61 (0.23 - 1.62)</td>
</tr>
</tbody>
</table>

a n = number of all farmers and NS = number of screen-positive farmers, b Adjusted for age, c All screen-positive farmers were in the exposed group.
No associations were found between phase 1 Parkinsonism and pesticide exposure or OP exposure in other farming sectors according to the exposure surrogates (Table 8-13), while according to the exposure models, general pesticide exposure and OP exposure were associated with an increased risk of phase 1 Parkinsonism in the cattle sector (OR = 0.04 for both of them) (Table 8-15). The increased risk was borderline significant among the moderate and the high general pesticide exposure group whereas it was borderline significant among the moderate group and significant among the high OP exposure group compared to the low groups (OR, 95%CI: 3.21, 0.98-10.5, 3.20, 0.96-10.7, 3.15, 0.95-10.5 and 3.57, 1.08-11.8 respectively). No significant associations were found between phase 1 Parkinsonism and OP exposure in other farming sectors.

### 8.3.4.2 Phase 2 Parkinsonism

Phase 2 Parkinsonism was not significantly associated with general or OP pesticide exposure in any farming sector whatever the methodology of exposure assessment was (Table 8-13, Table 8-14 and Table 8-15).

#### Table 8-14: Association between Parkinsonism and pesticide exposure estimated by exposure models in the sheep sector

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>NS⁴</td>
<td>OR (95%CI)¹⁺</td>
</tr>
<tr>
<td>PRNEW</td>
<td>Without ¹⁺</td>
<td>222</td>
<td>27</td>
<td>1.99 (1.18 – 3.35)</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>3</td>
<td>4.70 (1.22 - 18.0)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>11</td>
<td>5.10 (1.38 - 18.9)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>13</td>
<td>Referent</td>
</tr>
<tr>
<td>SHAPE</td>
<td>Low</td>
<td>73</td>
<td>2</td>
<td>5.87 (1.23 - 28.0)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>10</td>
<td>9.24 (2.02 - 42.2)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>74</td>
<td>15</td>
<td>Referent</td>
</tr>
<tr>
<td>TASK</td>
<td>Low</td>
<td>73</td>
<td>8</td>
<td>3.16 (0.80 - 12.6)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>73</td>
<td>8</td>
<td>6.52 (1.80 - 23.6)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>76</td>
<td>16</td>
<td>Referent</td>
</tr>
<tr>
<td>EXPSH</td>
<td>Low</td>
<td>73</td>
<td>2</td>
<td>6.45 (1.34 - 31.0)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>74</td>
<td>10</td>
<td>9.55 (2.08 - 43.8)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>15</td>
<td>Referent</td>
</tr>
<tr>
<td>OPPNEW</td>
<td>None</td>
<td>79</td>
<td>8</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>71</td>
<td>10</td>
<td>1.63 (0.59 - 4.46)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>72</td>
<td>9</td>
<td>1.37 (0.49 - 3.79)</td>
</tr>
<tr>
<td>OPSHAPE</td>
<td>None</td>
<td>79</td>
<td>8</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>10</td>
<td>1.62 (0.59 - 4.46)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>71</td>
<td>9</td>
<td>1.37 (0.50 - 3.80)</td>
</tr>
<tr>
<td>OPEXPSH</td>
<td>None</td>
<td>76</td>
<td>7</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>7</td>
<td>2.26 (0.84 - 6.09)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>73</td>
<td>13</td>
<td>Referent</td>
</tr>
</tbody>
</table>

₄ n = number of all farmers, NS = number of screen-positive farmers, and Pᵣ = p-trend. ⁺⁺ All results are compared to the referent. All results are adjusted for age. ⁺ PRNEW model cannot be categorised since 20 sets of probabilistic model estimates were used.
Table 8-15: Association between Parkinsonism and pesticide exposure estimated by exposure models in other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n^a</td>
<td>NS^a</td>
<td>OR (95%CI)^b</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EXPCAT</td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCAT</td>
<td>Low</td>
<td>72</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>77</td>
<td>11</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>EXPLIV</td>
<td>None</td>
<td>184</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPLIV</td>
<td>None</td>
<td>203</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td>EXPCRP</td>
<td>None</td>
<td>105</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>59</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCRP</td>
<td>None</td>
<td>109</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>57</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>58</td>
<td>5</td>
</tr>
</tbody>
</table>

^a n = number of all farmers, NS = number of screen-positive farmers, and P^t = p-for-trend.
^b All results are compared to the referent. All results are adjusted for age.
8.3.5 Association between dementia and pesticide exposure

8.3.5.1 Phase 1 dementia

In the sheep farming sector, a decreased risk of phase 1 dementia was associated with lifetime sheep dipping years (OR, 95%CI: 0.98, 0.97-1.00) but not with other general pesticide exposure surrogates (Table 8-16). Surrogates of OP exposure from sheep dipping (OPYRDIP and OPDYDIP) were also negatively associated with phase 1 dementia (OR, 95%CI: 0.97, 0.95-1.00, 0.66, 0.45-0.97 respectively).

Similar negative associations were found when pesticide exposure was estimated according to exposure models (Table 8-17). A decreased risk of phase 1 dementia was found in the moderate exposure group according to SHAPE model (OR, 95%CI: 0.40, 0.17-0.97) but not in the high group and the OR trends were not significant (Pt =0.17). The probabilistic model of sheep dipping showed an association between a decreased risk of phase 1 dementia and OP exposure. The same decreased risk was found in the high OP exposure groups according to OPNEW and OPSHAPE, and in the low OP exposure groups according to OPEXPSh; all of them compared to the no-exposure group. All odds ratios trends were significant except for the last model (Pt was 0.03 for the first three and 0.11 for the last).

Phase 1 dementia was not significantly associated with general pesticide exposure and OP exposure in other farming sectors when estimated by surrogates except for other livestock farming where an increased risk of dementia was associated with general pesticide exposure according to EVLIV and YRLIV (OR, 95%CI: 2.25, 1.14-4.45 and 1.03, 1.01-1.05 respectively) (Table 8-16). Similar results were found when farmers were categorised into three groups according to their exposure estimated by exposure models (Table 8-18). In the livestock sector, a borderline significant trend of increased risk of phase 1 dementia was found with general pesticide exposure (Pt =0.06). However, the odds ratios of the increased risk among the moderate and the high groups were not significant (OR, 95%CI: 1.25, 0.39-4.04 and 2.47, 0.92-6.66 respectively). No other significant associations were found in any other farming sectors.

8.3.5.2 Phase 2 dementia

Phase 2 dementia was not associated with exposures to pesticides in general and to OPs in particular in all farming sectors when these exposures were estimated by simple surrogates (Table 8-16) or by the developed models (Table 8-17 and Table 8-18).
However, only seven farmers were defined as screen-positive of phase 2 dementia and all of those farmers were in the exposed group in the sheep sector according to the dichotomous surrogates EVCONSH and EVDIP and in the exposed group in the cattle sector according to EVCAT, EVCONCAT, EVWAR, and OPEVCAT.

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Phase 1 definition n a</th>
<th>NS a</th>
<th>OR (95%CI)b</th>
<th>Phase 2 definition n a</th>
<th>NS a</th>
<th>OR (95%CI)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>EVSH</td>
<td>224 43</td>
<td>0.49 (0.21 - 1.13)</td>
<td>121 7</td>
<td>1.46 (0.17 - 12.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVCONSH</td>
<td>217 39</td>
<td>1.21 (0.46 - 3.17)</td>
<td>116 7</td>
<td>3.08 (0.35 - 26.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVDIP</td>
<td>219 41</td>
<td>0.65 (0.27 - 1.58)</td>
<td>118 7</td>
<td>0.99 (0.94 - 1.05)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>YRSH</td>
<td>224 43</td>
<td>0.99 (0.97 - 1.01)</td>
<td>121 7</td>
<td>1.00 (0.96 - 1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>YRDIP</td>
<td>224 43</td>
<td>0.98 (0.97 - 1.00)</td>
<td>121 7</td>
<td>1.00 (0.96 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DYDIP</td>
<td>224 43</td>
<td>0.71 (0.48 - 1.04)</td>
<td>121 7</td>
<td>1.57 (0.59 - 4.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>224 43</td>
<td>0.66 (0.32 - 1.37)</td>
<td>121 7</td>
<td>0.99 (0.95 - 1.05)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVSH</td>
<td>224 43</td>
<td>0.98 (0.96 - 1.01)</td>
<td>121 7</td>
<td>0.99 (0.95 - 1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPYRSH</td>
<td>224 43</td>
<td>0.97 (0.95 - 1.00)</td>
<td>121 7</td>
<td>0.98 (0.93 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPYRDIP</td>
<td>224 43</td>
<td>0.98 (0.95 - 1.00)</td>
<td>121 7</td>
<td>0.98 (0.93 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPDYDIP</td>
<td>224 43</td>
<td>0.71 (0.48 - 1.04)</td>
<td>121 7</td>
<td>1.57 (0.59 - 4.22)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cattle</td>
<td>EVCAT</td>
<td>224 43</td>
<td>0.38 (0.10 - 1.36)</td>
<td>121 7</td>
<td>1.57 (0.94 - 2.63)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVCONCAT</td>
<td>217 40</td>
<td>0.87 (0.27 - 2.78)</td>
<td>117 7</td>
<td>0.99 (0.94 - 1.05)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVWAR</td>
<td>222 42</td>
<td>0.50 (0.18 - 1.39)</td>
<td>119 7</td>
<td>0.99 (0.95 - 1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>YRCAT</td>
<td>224 43</td>
<td>0.98 (0.97 - 1.01)</td>
<td>121 7</td>
<td>0.98 (0.93 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>224 43</td>
<td>0.45 (0.19 - 1.08)</td>
<td>121 7</td>
<td>0.99 (0.95 - 1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVCAT</td>
<td>224 43</td>
<td>0.98 (0.95 - 1.00)</td>
<td>121 7</td>
<td>0.98 (0.93 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPYRCAT</td>
<td>224 43</td>
<td>0.98 (0.95 - 1.00)</td>
<td>121 7</td>
<td>0.98 (0.93 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other livestock</td>
<td>EVLIV</td>
<td>224 43</td>
<td>2.25 (1.14 - 4.45)</td>
<td>121 7</td>
<td>1.81 (0.39 - 8.48)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>YRLIV</td>
<td>224 43</td>
<td>1.03 (1.01 - 1.05)</td>
<td>121 7</td>
<td>1.01 (0.96 - 1.06)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>224 43</td>
<td>1.68 (0.81 - 3.49)</td>
<td>121 7</td>
<td>1.10 (0.20 - 5.96)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVLIV</td>
<td>224 43</td>
<td>1.03 (0.99 - 1.06)</td>
<td>121 7</td>
<td>1.01 (0.93 - 1.09)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPYRLIV</td>
<td>224 43</td>
<td>1.03 (0.99 - 1.06)</td>
<td>121 7</td>
<td>1.01 (0.93 - 1.09)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crops</td>
<td>EVCRP</td>
<td>224 43</td>
<td>1.14 (0.57 - 2.27)</td>
<td>121 7</td>
<td>0.50 (0.11 - 2.32)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVCONCRP</td>
<td>179 35</td>
<td>1.55 (0.49 - 2.25)</td>
<td>115 7</td>
<td>0.17 (0.02 - 1.62)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVAPPCRP</td>
<td>221 42</td>
<td>1.15 (0.54 - 2.47)</td>
<td>119 7</td>
<td>0.98 (0.18 - 5.35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>YRCRP</td>
<td>224 43</td>
<td>1.00 (0.99 - 1.02)</td>
<td>121 7</td>
<td>0.98 (0.94 - 1.02)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>224 43</td>
<td>1.29 (0.66 - 2.53)</td>
<td>121 7</td>
<td>0.35 (0.07 - 1.90)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OPEVCRP</td>
<td>224 43</td>
<td>1.00 (0.98 - 1.02)</td>
<td>121 7</td>
<td>0.96 (0.90 - 1.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other use</td>
<td>EXPUSE</td>
<td>224 43</td>
<td>0.85 (0.46 - 1.60)</td>
<td>121 7</td>
<td>0.22 (0.05 - 1.04)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>224 43</td>
<td>0.98 (0.50 - 1.93)</td>
<td>121 7</td>
<td>0.33 (0.04 - 2.71)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a = number of all farmers and NS = number of screen-positive farmers, b Adjusted for age, c All screen-positive farmers were in the exposed group.
Table 8-17: Association between dementia and pesticide exposure estimated by exposure models in the sheep sector

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
</tr>
<tr>
<td>General</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRNEW</td>
<td>Without c</td>
<td>222</td>
<td>42</td>
<td>0.81 (0.63 - 1.04)</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>18</td>
<td>0.52 (0.22 - 1.19)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>12</td>
<td>0.56 (0.24 - 1.26)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>12</td>
<td>0.56 (0.24 - 1.26)</td>
</tr>
<tr>
<td></td>
<td>SHAPE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>73</td>
<td>18</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>9</td>
<td>0.40 (0.17 - 0.97)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>74</td>
<td>15</td>
<td>0.78 (0.36 - 1.69)</td>
</tr>
<tr>
<td></td>
<td>TASK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>74</td>
<td>19</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>73</td>
<td>12</td>
<td>0.54 (0.24 - 1.23)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>76</td>
<td>12</td>
<td>0.54 (0.24 - 1.21)</td>
</tr>
<tr>
<td></td>
<td>EXPSH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>73</td>
<td>17</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>74</td>
<td>10</td>
<td>0.37 (0.19 - 1.12)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>75</td>
<td>15</td>
<td>0.80 (0.36 - 1.75)</td>
</tr>
<tr>
<td>OP</td>
<td>OPPRNEW</td>
<td>222</td>
<td>42</td>
<td>0.75 (0.58 - 0.95)</td>
</tr>
<tr>
<td></td>
<td>OPNEW</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>79</td>
<td>21</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>71</td>
<td>12</td>
<td>0.51 (0.23 - 1.15)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>72</td>
<td>9</td>
<td>0.37 (0.15 - 0.88)</td>
</tr>
<tr>
<td></td>
<td>OPSHAPE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>79</td>
<td>21</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>12</td>
<td>0.50 (0.22 - 1.13)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>71</td>
<td>9</td>
<td>0.38 (0.16 - 0.90)</td>
</tr>
<tr>
<td></td>
<td>OPEXPSH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>76</td>
<td>19</td>
<td>Referent</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>72</td>
<td>8</td>
<td>Referent</td>
</tr>
</tbody>
</table>

*a n = number of all farmers, NS = number of screen-positive farmers, and Pr = p-for-trend. b All results are compared to the referent. All results are adjusted for age. c PRNEW model cannot be categorised since 20 sets of probabilistic model estimates were used. d No screen-positive farmers were found in the referent group.*
Table 8-18: Association between dementia and pesticide exposure estimated by exposure models in other farming sectors

<table>
<thead>
<tr>
<th>Farming sector</th>
<th>Pesticide type</th>
<th>Exposure estimates</th>
<th>Rank</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Cattle</td>
<td>General</td>
<td>EXPCAT</td>
<td>Low</td>
<td>72</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>77</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>75</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCAT</td>
<td>Low</td>
<td>72</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moderate</td>
<td>75</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>77</td>
<td>21</td>
</tr>
<tr>
<td>Other livestock</td>
<td>General</td>
<td>EXPLIV</td>
<td>None</td>
<td>184</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPLIV</td>
<td>None</td>
<td>203</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Crops</td>
<td>General</td>
<td>EXPCRP</td>
<td>None</td>
<td>105</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>60</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>59</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>OP</td>
<td>OPEXPCRP</td>
<td>None</td>
<td>109</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low</td>
<td>57</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High</td>
<td>58</td>
<td>15</td>
</tr>
</tbody>
</table>

* n = number of all farmers, NS = number of screen-positive farmers, and P<sub>t</sub> = p-for-trend.

* All results are compared to the referent. All results are adjusted for age.

* No screen-positive farmers were found in this group.
8.4 Discussion

This chapter aimed to use the application of the new developed exposure models to the SHAW study to investigate the effect of using different assessment methodologies for exposure and health outcomes on any potential association between long-term pesticide exposure and neuropsychiatric ill-health. No association was found between pesticide exposure and screen-identified depression. Long-term general pesticide exposure in sheep farming was associated with an increased risk of phase 2 neuropathy and phase 1 Parkinsonism while exposure to pesticides in general and to OPs in specific was also associated with an increased risk of phase 1 Parkinsonism in the cattle sector. In contrast, exposure to OPs from sheep dipping was associated with a decreased risk of phase 1 dementia. These associations were disclosed by using the cumulative exposure estimates, but not by using crude surrogates (i.e. ever/never). However, the associations revealed by using simple cumulative surrogates in sheep dipping (i.e. number of dipping of years and days) or by using more sophisticated models, including the newly developed ones, were comparable with only very small differences.

Increased risk of neuropathy was associated in this study with general pesticide exposure in sheep farming. This result is consistent with previous studies which found that neurological symptoms are prevalent among past users of sheep dips\textsuperscript{9,11,29,186}. These effects were most prominent in farmers who handled OP dip concentrates and was demonstrated by higher sensory and vibration thresholds than the comparison group\textsuperscript{9}. The use of the phase 1 definition of neuropathy revealed only a borderline significant association with pesticide exposure from sheep dipping when the probabilistic model was used, but the use of phase 2 definition revealed significant associations with pesticide exposure in sheep farming in general and from dipping specifically. These associations were not found when crude exposure surrogates were used (i.e. ever/never). These findings support the \textit{a priori} idea that significant associations between pesticide exposure and health effects need more refined estimates of exposures as well as of determining health effects to be detected. Neuropathy was not associated with pesticide exposure in other farming sectors regardless of the methodology of exposure assessment and health identification. Lack of evidence of an association between exposure to OPs in crops and grains farming and peripheral neuropathy or impairment in neuromuscular functions has been reported in previous studies\textsuperscript{218-221}. Vibration sensitivity and motor function (two tests usually used to evaluate peripheral function) were also almost not affected by low-level pesticide exposure\textsuperscript{18,196}.
An increased risk of phase 1 Parkinsonism was associated with exposure to general pesticides (but not with OPs specifically) in sheep farming based on all dipping and general treatment models and based on simple cumulative surrogates in sheep dipping but not on ever/never surrogates. The same association was found with exposure to general and to OP pesticides in the cattle sector based on the model estimates. The association between PD and pesticide exposure has been reported in many studies\(^{27,91,235-239}\). On the other hand, the hospitalisation rate ratios for PD among gardeners was found to be similar to that among the general population\(^{240}\) and PD was not associated with pesticide exposure in a Canadian case-control study\(^{241}\). All associations with Parkinsonism vanished when the more developed phase 2 definition was used instead. This indicates that the sensitivity and/or specificity of phase 1 definition might be poor or that the sample size of SHAW phase 2 was too small to detect such associations. The differences in sample sizes and in methodologies of exposure assessment have been suggested as reasons for the inconsistencies in the results of association studies of PD and pesticide exposure\(^ {24}\).

No evidence was found in this study that depression was associated with pesticide exposure in any farming sector. This is consistent with the results of some previous studies\(^{22,187,199,201}\) but not consistent with other studies which reported psychiatric effects of pesticide exposure mainly among sheep dippers\(^ {8,11,186,198,200}\). However, it should be noted that when depression was mentioned in those studies it was mostly mentioned as a reported symptom not as a clinically diagnosed illness. The results of depression in this study were not affected by the definition used to identify the illness but the number of screen-positive farmers of depression according to phase 2 definition (i.e. the better) was only 7 which might reduce the ability to find any significant associations.

A decreased risk of dementia was associated with OP exposure based on all models and simple cumulative surrogates of sheep dipping when the phase 1 definition was used but the association disappeared when using the phase 2 definition. Again, with only 7 farmers considered to have dementia based on the definition of phase 2, it is difficult to decide whether the association disappeared due to the improvement of identification method or due to the small number of screen-positives. Nonetheless, a lack of an association has been found in previous studies\(^ {22,258-260}\), while other studies reported a higher risk of dementia in general and AD in particular associated with pesticide exposure\(^ {27,244,253,254,256,257}\). The latter studies, however, relied on crude exposure estimates (e.g. environmental exposure and ever/never having specific jobs). The
decreased risk of dementia associated with OP exposure from sheep dipping found in this study is inconsistent with the cognitive dysfunctions detected previously among OP sheep dippers\textsuperscript{8} or among OP exposed farm workers\textsuperscript{252}. However, metrifonate which is an OP cholinesterase inhibitor has been tried as a treatment for the cognitive symptoms of AD since the loss of cholinergic neurons is the basic neurochemical defect in this disease\textsuperscript{262}. This could mean that the OP exposure may play a protective role in dementia.

The results of this study are consistent with the \textit{a priori} hypothesis that the use of more sophisticated exposure assessment methods may reveal associations between pesticide exposure and health effects that could not be demonstrated using crude estimates. The use of crude exposure estimates (\textit{i.e.} ever/never and number of years being a farmer in different sectors) did not reveal any association with any illness. The only exemption was the association found between phase 1 dementia and ever having other livestock and number of years having other livestock. However, this association should be interpreted with a degree of caution due to the lack of literature about this sector specifically. Handling the concentrate in sheep dipping was found to be a major source of exposure in sheep dipping studies\textsuperscript{12,99} and was associated with neuropsychiatric symptoms in a previous study\textsuperscript{9} and with neuropathy in the phase 1 of the SHAW study\textsuperscript{265} but in this study it was not associated with any illness.

On the contrary, the number of dipping years and number of dipping days revealed all the associations revealed by dipping models which is consistent with the high correlations between these two estimates and the model estimates found previously in Chapter 6 and in a previous study\textsuperscript{99}. Similarly, the use of the new sheep dipping model and the use of the two previously used models\textsuperscript{29,99} revealed the same associations which is also in agreement with the high correlations between the estimates of all these models found previously in Chapter 6. These high correlations most likely resulted from the duration component and support the assumption that when estimating lifetime cumulative exposure the degree of misclassification is lower than when estimating exposure intensity in one session\textsuperscript{99}. These findings suggests that chronic neuropsychiatric effects might result from long-term exposure rather than level of exposure or peaks, and as such it seems that the additional gain of estimating cumulative exposure rather than duration is limited. On the other hand, the reason behind such findings might be the random errors added to the cumulative exposure models by any possible mismeasurement embedded in their extensive variables. Such a
reason may suggest that to investigate the health effects of long-term pesticide exposure, the use of surrogates such as number of dipping days might give more preferable estimates for cumulative exposure than the use of more sophisticated models since the former logically tends to less measurement errors than the latter. Further research is required to investigate this.

The association results when the new sheep dipping model was used in a deterministic way or in a probabilistic way were comparable except the borderline significant association with phase 1 neuropathy that was revealed by the probabilistic approach but not the deterministic way. One of the reasons behind this consistency of results might be the attenuation of the variable variations by the length of duration period to which the probability method was applied. This means that because the probability of each uncollected variable in the SHAW study was applied for each year between 1942 and 2005, the collective results of all years were relatively the same between all farmers which made the final result similar to that of using the deterministic approach. Dealing with uncollected variables can be done using a methodology in which the probability of variables is applied to the first year only and all the following years take the same chosen variables. However, this approach ignores the possibility that the same farmer might change some of his/her methods or processes in sheep dipping over time, and therefore this approach was not applied.

In this study, only 20 sets of exposure estimates was generated for each dipper by Monte Carlo simulation and then the association analysis was performed considering these 20 sets similar to multiple-imputed data. However, alternatively using the probabilistic approach it would have been possible to generate much larger sets of simulated results. For example, 10,000 simulations could have been generated to obtain exposure distribution for each farmer using Monte Carlo simulation. Then the median of that distribution could have been used as a surrogate of the exposure of each farmer to perform any standard association analysis (e.g. logistic regression). The 75th percentile or 90th percentiles were recommended by van Hemmen for regulatory risk assessment of long-term effects not for epidemiological analyses; however these two more conservative values might be tried instead of the median for this epidemiological study. This methodology can be used in a future work.

The exposure assessment model for sheep dipping was more developed than the model used in other sectors. This is potentially reason for finding more associations with exposure in sheep farming than in other sectors. However, the same association
identified using the sheep models were also found with the use of dipping years and dipping days indicating that the difference in the associations between the sectors was not due to the improved quality of the dipping models.

Pesticide exposure assessment depended on self-reported exposure history in this study and the validity of the data provided by such technique varied between exposures and between variables\textsuperscript{118,126,132}. Chapter 7 studied the validity of self-reported history among the farmers of SHAW phase 2. The memory scores of phase 1 neuropathy screen-positives were slightly lower than those of screen-negatives. If this difference affected the accuracy of their occupational history, this may explain the absence of the association between neuropathy and exposure in sheep farming based on phase 1 definition although it existed based on phase 2 definition. Although the memory scores of dementia screen-positives were slightly lower than those of screen-negatives, the difference was not significant. This difference might be statistically insignificant due to the small sample size especially in phase 2 (only 7 screen-positives) or might be genuine. The score of memory function in CAMCOG was driven mainly by short-term memory (21 out of 27) which is usually impaired before the long-term memory\textsuperscript{339}. However, the assessment of memory function is only part of defining dementia cases by using CAMCOG instrument (only 27 marks out of 107)\textsuperscript{276} let alone that a previous study found that about a third of AD patients had been diagnosed with no memory dysfunction\textsuperscript{248}.

The differences in the accuracy of self-reported exposure histories between cases and controls have been reported to be not significant\textsuperscript{118,336-338}. Furthermore, associations between exposure estimates and health effects may be subject to error due to the lack of information on the onset of the illness \textit{i.e.} the association analysis might be performed on exposure estimates based on exposure that came after the start of the illness.

This study focused on the association between neuropsychiatric illnesses and exposure to OPs specifically. The assessment of this exposure depended on a new method described in Chapter 6. In summary the probability of the pesticides used in a specific year to contain an OP was included in all exposure models. OP exposure misclassification might result from errors in assessing this probability. Furthermore, farmers are usually exposed to different types of pesticides and these types may contribute synergistically to the OP neurotoxicity\textsuperscript{196} and therefore the exposure to other
pesticides might lead to errors in interpreting any association between exposure to OPs and health outcomes.

More attention has been given recently to the genetic susceptibility to pesticide neurotoxicity, specifically the genetic variation in PON1 related to the neurotoxicity of the OPs\textsuperscript{196}. For example, differences in the frequency of PON1 genotypes were found between sheep dippers who attributed their chronic ill-health to exposure to sheep dips and their referents\textsuperscript{321}. Therefore, such differences in genetic susceptibility may explain differences between individuals and their possible impact should be considered in interpreting the results of association studies.

Further limitations to this study should be recognised. One of them is the insufficient adjustment of potential confounders. Pesticide exposure can be a marker of other exposures associated with pesticide use such as social factors of living in rural area and ingestion of well water let alone chemicals like solvents that are included in many commercial pesticides\textsuperscript{229}. Such factors have been reported to be associated with neuropsychiatric illnesses\textsuperscript{195,203,222,236}. However it is very difficult to adjust such factors but an appropriate matching between comparison groups in the study design might help\textsuperscript{196}. The analyses in this study were adjusted only for age and no women were included. No adjustment for other factors like educational level and smoking was performed mainly because of the low number (only 7) of screen-positive farmers of depression and dementia according to the phase 2 definition.

This study meant to investigate the neuropsychiatric health effects of long-term low-level exposure; however, the inclusion of farmers with a previous short-term high-level exposure is possible especially of those with an unrecognised past pesticide poisoning. Studies which excluded farmers with past short-term high exposure did not found relationship between long-term exposure and neuropsychiatric effects\textsuperscript{22,218,219}. The only information available in the SHAW data about past short-term high exposure was a surrogate taken from a question on “ever sought advice for pesticide poisoning”. No action was taken using this surrogate because, in addition to the reason of the low study sample size mentioned above, this surrogate is likely subject to a recall bias\textsuperscript{265}.

To conclude, the application of the new developed exposure models to the SHAW study suggests neuropsychiatric effects for pesticide exposure, namely peripheral neuropathy and Parkinsonism. A preventive effect of OP exposure on dementia was also mentioned and needs to be explored more. In contrast to the use of crude ever/never surrogates, the
use of simple exposure duration surrogates in sheep dipping revealed the same associations disclosed by more sophisticated models, including the new sheep dipping model. Such a result needs a further investigation on how necessary is the use of sophisticated exposure models that might be subject to more measurement errors compared to the use of simple cumulative estimates that generally tend to less measurement errors.
Chapter 9: General discussion

9.1 A summary of the results and discussion

This PhD project aimed to develop exposure models for estimation of long-term occupational exposure to pesticides among UK farmers, especially among sheep dippers who used OP dips. These models were subsequently applied to the SHAW study to investigate the association between long-term occupational pesticide exposure and neuropsychiatric ill-health. This application was to assess whether improved exposure assessment could address previous inconsistent results in this field, which were attributed primarily to exposure misclassifications resulted from poor assessment of long-term pesticide exposure. The main objectives included developing a comprehensive conceptual exposure model to assess pesticide exposure during sheep dipping, evaluating this new model and developing a probabilistic model from it, estimating occupational pesticide exposure among SHAW farmers using different methodologies, validating self-reported occupational exposure among those farmers, and finally applying the new models to the SHAW study to examine the associations between pesticide exposure and ill-health.

Several previous studies have focused on the neuropsychiatric effects of using sheep dips\textsuperscript{7-11} since sheep dipping is one of the main pesticide applications in the UK\textsuperscript{6} and OPs have been the main ingredients of sheep dips in the UK since 1970s\textsuperscript{12}. Therefore, more attention was given in this study to sheep dipping and a new conceptual model for pesticide exposure through sheep dipping was developed as highlighted in Chapter 3. In summary, five sources of pesticide exposure were included in this model; handling the concentrate, dipping sheep in the bath, handling sheep after dipping, disposal of sheep dip, and any incidental exposure. Exposure routes for all sources were dermal, ingestion and inhalation route and different modifying factors for each route were identified. Total exposure was calculated using an additive model, in which the exposure through each route and from different sources were aggregated, based on expert-assigned relative contributions of routes and sources to total exposure.

Although all five exposure sources in this new model were also included in the SHAPE model\textsuperscript{29} and the main two sources (\textit{i.e.} handling the concentrate and dipping sheep in the diluted dip) were included in the model of Buchanan \textit{et al.}\textsuperscript{99}, the new model included additional modifying factors that were not included in the previous two models. Furthermore, previous sheep dipping models have focused mainly on the
dermal route of exposure$^{29,99}$, and one model included the inhalation route as a constant$^7$, whilst the new exposure model combines exposure through ingestion, inhalation, and dermal routes into one aggregative model. Many modifying factors included in the new model were given a score of one because they were not described in the literature. However, these factors might not affect the use of the model in epidemiological studies since most of them, such as atmospheric conditions and number of sheep handled after treatment, are very variable and therefore are not easy to be recognised or recalled by the dippers.

In this PhD study, the aggregation in the new exposure model was performed by summing up exposures through all routes in each source and then by summing up exposures from all sources. The dermal route is the most important route in occupational diazinon exposure but it was found that only 1% of a dermal dose of diazinon was excreted as DEP and DETP in the urine comparing with 60% of an oral dose$^{13,52}$. Such findings indicate the importance of calibrating the contribution of each exposure route to the total exposure. If the aggregation was made by summing up exposures across routes, comparing model estimates for different routes with urinary metabolites in an evaluation study might help in calibrating the relative importance of each route. This alternative approach can be performed in a future work.

The relative contribution of handling the concentrate to total exposure was estimated much lower in this new model compared to previous models$^{7,29,99}$. The relative contribution of each source to total exposure was based on expert assessment and it is likely that some experts took into consideration the recent use of concentrate sachets which is supposed to reduce significantly the contribution of handling the concentrate. The experts were not asked to take using sachets into account since the effect of using concentrate sachets should be estimated in scoring the modifying factors not in weighing the source of handling the concentrate. Therefore in any further refinements for the new model, the process of assigning scores and weights should be clarified more.

The new sheep dipping model was evaluated in Chapter 4 by comparing its estimates of diazinon exposure among dippers who participated in the HSDS study$^{58}$ with the farmers’ diazinon urinary metabolites after the dipping session. Positive trends in geometric means were found in the total of diazinon metabolites (i.e. DEP and DETP) when compared between three ordinal categories of exposure estimates in the day of sampling. That trend was statistically significant according to exposure estimates of handling the concentrate but not significant according to estimates of exposure from
dipping the sheep in the bath. The poor correlations between exposure estimates and urinary metabolites could be attributed to potential shortcomings in the new model, such as the weight assigned to each source of exposure and the relatively crude assessment of PPE use. However, a more likely explanation is the uncontrolled conditions of the HSDS which was not designed as an evaluation study for this model. For example, the comparison was performed with the metabolite levels measured in a single spot urine sample taken after the dipping session and not in 24h urine sample. The comparison was further done without taking baseline metabolite levels into account since the baseline samples in the HSDS were taken at different times prior to the dipping session. Moreover, two exposure sources and many exposure variables were not available in the HSDS study. Furthermore, exposure estimations depended on self-reported information, but in evaluation studies, correlations between exposure scores and urinary metabolites were higher if exposure was assessed by field observers rather than the farmers themselves. Therefore, a well-controlled study is needed to validate the new exposure model.

To obtain the distribution of exposure estimates from each exposure source and route and the distribution of the total exposure, a probabilistic model for pesticide exposure in sheep dipping was developed in Chapter 5 from the new conceptual model. When the contribution of exposure from handling dipped sheep, disposal of dips, and incidental exposure to total exposure was compared to the contribution of exposure from handling the concentrate, it was found that exposure from the first three sources should not be neglected. Therefore, models that neglected these three sources like that one used by Buchanan et al. might lead to a significant underestimation of the total exposure.

Multiple imputation and other methods have been used by researchers to solve the problem of missing data of both exposures and outcomes in epidemiological studies. This study illustrated examples of how the use of the probabilistic model could help in including unavailable variables of exposure, and therefore the use of this approach might lead to a reduction in exposure misclassification.

Although the use of the results of this probabilistic model as a gold standard is questionable due to the limitations in the input data, this probabilistic model was applied to different scenarios and showed that probabilistic estimates which take into account all conceptual variables may give a more comprehensive description of exposures than deterministic estimates which depend on available variables only. This suggests that even the use of well-derived deterministic estimates might lead to
exposure misclassification. However, there were only small differences in the association results in Chapter 8 when the new sheep dipping model was used in a deterministic or probabilistic way. The only exception was the borderline significant association with phase 1 neuropathy that was revealed by the probabilistic method but not with the deterministic method. Further research is needed to improve the validity of the input data and to include all variables not described in the literature.

In chapter 6 different surrogates and more sophisticated models were developed to estimate pesticide exposure in different farming sectors in the SHAW study. In sheep dipping, the new exposure model along with another two previously used models\textsuperscript{29,99} were used to estimate pesticide exposure from sheep dipping, while a model was developed to estimate exposure from applying pesticides by any method to different types of livestock (sheep, cattle, and other livestock). Another separate model was developed to estimate pesticide exposure in the crops sector. Estimation models in cattle, other livestock and crops sectors were simpler than the model used for sheep dipping since the information collected on pesticide application in those sectors was less.

Exposure to OPs specifically was estimated using the same models as the general pesticides after including the probability of each applied pesticide containing an OP. The correlations between general pesticide exposure estimates and OP exposure estimates were generally high in all farming sectors except in other livestock sector where the correlation was moderate. However, the validity of OP probability might vary between farming sectors and therefore its use in estimating OP exposure might lead to a systematic bias.

Pesticide exposure estimates obtained in chapter 6 were used in Chapter 8 to investigate the association with neuropsychiatric ill-health since the assessment of neurotoxic effects of pesticides has been used as an example to describe the challenges that face studies of health outcomes in farming communities\textsuperscript{24,30}. Long-term exposure to pesticides in sheep farming (but not to OP specifically) was associated with an increased risk of phase 2 neuropathy, which is consistent with previous studies on sheep dippers\textsuperscript{9,11,29,186} but not consistent with studies in crop farmers\textsuperscript{218-221}. An increased risk of phase 1 Parkinsonism was associated with long-term exposure to pesticides in sheep farming and in the cattle sector and was also associated with exposure to OPs specifically in the cattle sector. The association between PD and pesticide exposure has been reported in many studies, mostly ecological \textsuperscript{27,91,235-239}, but not found in other
studies. In contrast, exposure to OPs from sheep dipping in this study was associated with a decreased risk of phase 1 dementia. Although this may have a physiological explanation, this was not reported previously in the literature, and on the contrary cognitive dysfunctions were reported previously among OP sheep dippers and among OP exposed farm workers. No association was found between exposure to pesticides or to OP in specific and depression, which agrees with some previous studies but not with others. The association between pesticide exposures and neuropathy, Parkinsonism and dementia varied according to the methodology used to assess the exposures and to identify the illnesses.

A previous study found that non-differential misclassification of pesticide exposure reduced study power and biased the estimates of relative risks towards the null. The results of the association study in Chapter 8 are consistent with such findings since the use of crude exposure estimates (i.e. ever/never and number of years being a farmer in different sectors) did not show associations with any ill-health whilst the use of more developed exposure estimates revealed some associations. The correlation between model results and number of farming years of each sector varied between farming sectors. However, even in the sheep sector, where the correlation between this surrogate and model exposure estimates was good, the use of this surrogate did not reveal the associations with health effects that were demonstrated by using the more sophisticated models. This indicates that even small differences in estimating the exposure might disclose different associations.

The pesticide exposure estimates of the new sheep dipping model in the SHAW study were well correlated with the estimates of the previous models and all of these estimates demonstrated the same associations with health effects. A good sample-size validation study and also experimental studies may be needed to compare the performance of the utilised sheep dipping models and to study the sensitivity of the various models. However, generally it is expected that the models which include more exposure variables can give more valid estimates, unless the weighting factors of the exposure variables were not assigned correctly in which case more variables would imply increased estimation errors. The validation of the cumulative exposure assessment models is not easy since biological markers are only practical for recent exposures and generalizing it over long-term exposure will lead to errors.

Number of dipping years and number of dipping days were also well correlated with the sheep dipping model estimates and they revealed the same associations revealed by
dipping models. This suggests that exposure estimates that take into account exposure duration seem to perform equally well and hence there was no convincing evidence that the models outperform simple continuous estimates of exposure. This is consistent with the assumption of a previous study that misclassification is less likely in estimating lifetime cumulative exposure than in estimating short-term exposure. However, it remains unclear why exposure duration estimates performed similar to the cumulative exposure models. The reason of this may be that mismeasurement in exposure level was significantly enough that it only added random error to the models. On the other hand, the same performance might be genuine since exposure level might not be that important in chronic neuropsychiatric effects compared to the duration of exposure. Further research will be required to answer this question.

Given that the use of model estimates and exposure duration estimates were well correlated and revealed the same association, it is justifiable to develop a ‘reduced model’ that might reduce the probability of measurement errors and weighing errors without reducing the performance of the model. To consider which variables could be excluded from the estimation algorithm of long-term pesticide exposure from sheep dipping, two criteria can be thought of. The first criterion is the effect on total exposure, i.e. those variables assumed to have small effect on total exposure could be excluded. For example, variables whose categories were scored between 0.6 and 1.9 can be considered as of small effect, and then variables such as bath location and type, number of dippers and atmospheric conditions can be excluded. However, it should be mentioned that the weight of some of these variables could have been underestimated by the experts, and therefore this should ideally be investigated by experimental studies.

The second criterion is practicality, i.e. those variables of which collecting information on them is very difficult in retrospective epidemiological studies could be excluded. These variables include, for example, the size of concentrate container, duration of the dipping sessions, dip rate, and personal hygiene and behaviour. However, these variables may be important and should, if a prospective study could be done, be included.

After the exclusion of these two types of variables, a reduced sheep dipping model may include the following variables: frequency of handling the concentrate and type of the pesticide container in the source of handling the concentrate, number of dipped sheep, dipper’s task and submerging tool in the source of dipping sheep, nature of handling dipped sheep and duration between dipping and handling in the source of handling
dipped sheep, method of the disposal and volume of the sheep dip in the source of the disposal, and number of falls in the bath and frequency of concentrate spillage on the body in the source of incidental exposure, in addition to the use of PPE in all exposure sources. This is however still an extensive list of variables and further reduction of the model may be possible, especially because a good correlation was observed between the full model and the use of exposure duration only. This should be investigated empirically.

Research has shown that the validity of the data provided by self-reported exposure histories varied\textsuperscript{118,126,132}. Therefore, Chapter 7 studied the validity of self-reported exposure history among the farmers of SHAW phase 2 since pesticide exposure assessment depended on this method in the SHAW study. There is lack of studies that examined the validity of self-reported variables like livestock herd size or crop acreages although examining such validity is important since these variables have been used as surrogates of long-term exposures\textsuperscript{8,320}. In this study recall was substantial for having sheep, cattle, and combinable crops but not for vegetables. The recall of sheep and cattle numbers, and barley acreage was also good while the recall of wheat acreage was not valid. Farmer’s recall was generally not affected by farmer’s age and memory or by neuropsychiatric health status.

The results of this study suggest that farmers are better able to recall having a specific type of livestock or crop than the number of livestock or acreage. Similarly, previous studies have shown that farmers can recall the use of a specific pesticide more than recalling specific details of its use\textsuperscript{126,132}. The variation between the recall in different farming sectors might depend on whether the farmer personally was involved in that farm sector. In previous studies subjects’ recall was found better if they were personally involved in the selection of the agents or in the activity required to be recalled\textsuperscript{131} and farmworkers (e.g. harvesters) were less accurate in recalling the utilised pesticides than farmers who personally applied pesticides on crops\textsuperscript{118,331,332}. This study suggests that the accuracy of self-reported exposure is reliable for ranking pesticide exposures in epidemiologic studies in farming activities but not for estimating absolute exposures; however the representation of the recall of the variables investigated in this study of the recall of other pesticide exposure variables is a concern. The reasons for decreased accuracy in obtaining information on specific farming sectors like crops and grains needs further research.
9.2 Strengths and limitations of this PhD project

The work presented in this thesis has several strengths. The main strength is the development of a new sheep dipping model which is more comprehensive than previous models and may lead to improved exposure estimates for sheep dipping practices in UK farmers. The development of a probabilistic model for sheep dipping may form a base to include uncollected exposure variables in the estimation of exposures in epidemiological studies. However, this is a novel approach and as such needs to mature and further be validated. The use of an estimate to assess the probability of pesticides to contain an OP for cases where this information is not known is also a novel approach, which may help to reduce exposure misclassification that is present in an alternative methodology based on yes/no answers about the type of the utilised pesticide\textsuperscript{118,126,132}.

In addition to exploring sheep farming and crop farming sector, this study explored other farming sectors as well \textit{i.e.} cattle and other livestock in which there is a lack of research. This study further investigated the validity of self-reported occupational history in farming activities for variables not examined before although they were used previously as surrogates of exposure \textit{(i.e.} number of animals or acreage of crops\textsuperscript{8,320}).

Finally, this thesis showed the impact of using different techniques on the evaluation of associations between pesticide exposure and health effects. The nature of the SHAW study helped in achieving this since its two phases used quite different methods in exposure and health effects assessment \textit{(i.e.} the use of a self-completed questionnaire with simple questions in phase 1 compared to comprehensive questionnaires completed in an interview by a trained nurse) in the same population.

However, there are also several limitations to the work presented in this thesis; importantly, the aggregation of exposures from different sources and through different routes. Such aggregation should take into account exposure intensity and the rate of uptake in each route. Experts took these two elements into account when they estimated the contribution of each source and each route to the total exposure. However, there were differences between experts’ judgments which have been solved by taking the geometric means of the three middle estimates and discarding the highest and the lowest estimates. Further refinements for the new model might obtain better estimation for the contribution of each source and each route by achieving consensus between the experts through a comprehensive discussion.
This study aimed to estimate long-term low-level exposure to pesticides and assumed a linear association between cumulative exposure and risk. This assumption might be a limitation since the underlying biological mechanism remains unknown, and farmers might instead be exposed to short-term high level exposure that causes health effects. Indeed, previous studies suggested the importance of short-term high-level exposures since they found associations between long-term exposure and neuropsychiatric effects that disappeared after exclusion of farmers with past short-term high-level exposures. In the application of the models to the SHAW study, farmers with a past short-term high-level exposure may have been included especially if the farmers did not recognised that exposure. In the SHAW study there was a question about “ever sought advice for pesticide poisoning” which could have been used to exclude farmers with short-term high-level exposure. However, this was not used to exclude farmers in this thesis because of the small sample size of SHAW phase 2 and because this question is likely subject to a recall bias.

The crops model was simpler than the animal model with very few variables included. The model did not include estimates for exposure through harvesting or other similar activities and did not include any estimates for the use of PPE and the type of protection used in tractor (e.g. enclosed cab and charcoal filter) because this information was not available. Furthermore, studies reported that chronic exposure to herbicides (mainly paraquat), used mainly in crops sector, has been linked with PD and with dementia. Such associations suggest that studies should give more attention to chronic neuropsychiatric effects of pesticides other than OPs.

The limitations of the original SHAW study may have affected the results of the application of exposure models to the SHAW study. The low response rate in the SHAW study might reduce the ability to generalise the results beyond the study population, because voluntary participation of farmers may have depended on their own health status (i.e. participation bias). Furthermore, the low number of farmers interviewed in the second phase might diminish the power of the SHAW study reducing the ability of the study to detect significant associations; only 7 farmers were screen-positive for depression and dementia according to phase 2 definition. Although health outcomes were assessed using better techniques in the phase 2, they were not confirmed clinically, and therefore farmers were classified as screen-positives and screen-negatives not as cases and controls.
A final limitation from the original SHAW study is that the choice to use a comparison group from the farmer population itself might lead to exposure misclassification\textsuperscript{196}. Although farmers may not have been exposed to pesticides in a farming sector they may not be truly unexposed since they might be exposed in other farming sectors. One of the solutions for this problem is to combine exposures from all farming sectors in one aggregative exposure model like the model of Dosemeci \textit{et al.}\textsuperscript{153}. However, this model was designed to assess exposure among mainly pesticide applicators and exposures during animal treatments were only addressed to a very limited extent. The combination of all exposures in one model is very complex due to the difference in exposure determinants and the difference in pesticides used in each farming sector. Exposures from each farming sector could be included as independent variables in one logistic regression analysis. However, this approach is questionable since although the covariates in this logistic regression (\textit{i.e.} the exposure from different sectors) represent different farming sectors, they were in fact representing the same causative agent (\textit{i.e.} pesticides) and the quantities therefore cannot be considered as independent exposures.

\section*{9.3 Conclusion and future work}

This thesis developed a comprehensive model for pesticide exposure from sheep dipping. Other simpler exposure models were also developed for pesticide exposure in other farming sectors. The probability of exposure to OP pesticides specifically was included in the previous models due to the importance of this exposure in sheep dipping and other farming activities. The application of these models and other exposure surrogates to a previously conducted study suggested that long-term exposure to general pesticides may increase the risk of neuropathy and Parkinsonism while such an increase was not suggested following a long-term exposure to OPs specifically. In contrast, OP exposure was associated with a decreased risk of dementia among sheep farmers. These findings were revealed by using the more developed exposure estimates, but not by using crude exposure surrogates. However, the differences between using the duration of sheep dipping exposure and the cumulative exposure models, including the new model, were small indicating that protracted exposure may be more important that the level of exposure. The use of different definitions to determine health effects also revealed different associations.
To substantiate the results of this study, future work is recommended to:

1- Improve the new exposure model of sheep dipping by refining the scores of variables and the weights of exposure sources and routes. This can be done by conducting controlled experimental research to calibrate the scores and weights by measuring the impact of different variables on exposure through different routes. Such research will improve the performance of the new model which will further improve epidemiological research on the chronic health effects of long-term pesticide exposures.

2- Improve the new model by asking the experts to reach a consensus about the effects of all variables, routes and sources instead of taking the average of their assignments. The experts will be asked also to estimate scores for all model variables whose distributions was not found in the literature.

3- Build the sheep dipping algorithm by using an alternative exposure aggregation approach based on aggregation of exposures by routes across all sources and subsequently across all routes.

4- Develop a reduced sheep dipping model that includes only the most important exposure variables whose information is easy to collect in an epidemiological study.

5- Validate the sheep dipping model (the summarised and the more sophisticated one) using a study (either new or previously carried out) in which all variables that are not included in the model and might affect the exposure are well controlled.

6- Improve the probabilistic model by improving the input data especially if the distribution for variables in each year or decade can be obtained and by applying theoretical distributions for unavailable distributions. Subsequently, this model can be used in the association study by using the median or any other chosen representative of the estimated distribution of each dipper.

7- Apply the same method of estimating OP probability to other types of pesticides especially for those linked with neuropsychiatric illnesses in the literature such as herbicide and mainly paraquat.

8- Improve the design of the association studies by specifically investigating different patterns of exposures; for example by including or excluding all subjects who highly likely had short-term high dose pesticide exposure in the past.
Reference List


(2) Hassall KA. The biochemistry and uses of pesticides: structure, metabolism, mode of action, and uses in crop protection. 2nd ed. Basingstoke: Macmillan; 1990.


(45) VMD. Veterinary medicinal products (dips, injectables, pour-ons, sprays and drenches) authorised in the UK for use against ectoparasites in sheep. Veterinary Medicines Directorate; 2011.


(84) VMD. Veterinary medicinal products authorised in the UK for use against warbles and other parasites in cattle. Veterinary Medicines Directorate; 2011.


(100) Photo of sheep scab mite.  

(101) Photo of sheep lice.  

(102) Photo of sheep ked.  

(103) Photo of sheep tick.  


(105) Photo of sheep dipping.  

(106) Photo of sheep pour-on.  

(107) Photo of sheep showering.  

(108) Photo of sheep injection.  

(109) NOAH. Crovec pour-on.  
http://www.noahcompendium.co.uk/Novartis_Animal_Health_UK_Ltd/Crovec_t_1_25_ACU-_w_v_Pour-on_Solution_for_Sheep/-27942.html. Accessed June 2012.

(110) Scottish Agriculture College. Control of sheep scab and other ectoparasites of sheep.  


(120) Photo of backpack sprayer. http://4.bp.blogspot.com/-dkN-Kim8GKg/TkUMLEk-XQI/AAAAAAAAB84/4rTulzTwVP0/s1600/IMG_1461.JPG. Accessed June 2012.


287


(246) Limb M. UK government spends 2m to raise awareness of dementia. BMJ. 2011;343:d7235.


(293) VMD. Veterinary medicinal products (dips, injectables, pour-ons, sprays and drenches) authorised in the UK for use against ectoparasites in sheep. Veterinary Medicines Directorate; 2005.

(294) VMD. Veterinary medicinal products (dips, injectables, pour-ons, sprays and drenches) authorised in the UK for use against ectoparasites in sheep. Veterinary Medicines Directorate; 2006.


(313) Hamey PY. An example to illustrate the potential use of probabilistic modelling to estimate operator exposure to pesticides. Ann Occup Hyg 2001;45(suppl 1):S55-S64.


Appendices

Appendix 1: SHAW Phase 1 Health and Work History Questionnaire

The following pages contain questions about your physical and psychological health, memory and mood, current medication, smoking and drinking habits, and work history and practices. Please answer all the questions, even if some do not seem applicable to you, or the wording seems unusual. These questions have been used in other, similar, studies and to be able to make valid comparisons, we need to use the same questions and phrasing.

Please tick the boxes provided and answer all the questions

Name: ________________________________________________________________

Address: _____________________________________________________________

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________

Postcode: __________________________

Telephone: _______________________

What is your date of birth? .......... day .......... month .......... year

What is your gender?  □ Male   □ Female

What is the current date and time? ................. Date ......................... Time
### A1. During the last 4 weeks, how much have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th></th>
<th>Not bothered</th>
<th>Bothered a little</th>
<th>Bothered a lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Stomach pain</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.2</td>
<td>Back pain</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.3</td>
<td>Pain in your arms, legs, or joints (knees, hips, etc.)</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.4</td>
<td>Menstrual cramps or other problems with your periods</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.5</td>
<td>Pain or problems during sexual intercourse</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.6</td>
<td>Headaches</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.7</td>
<td>Chest pain</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.8</td>
<td>Dizziness</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.9</td>
<td>Fainting spells</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.10</td>
<td>Feeling your heart pound or race</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.11</td>
<td>Shortness of breath</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.12</td>
<td>Constipation, loose bowels, or diarrhoea</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.13</td>
<td>Nausea, gas, or indigestion</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>1.14</td>
<td>Excessive sweating</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### A2. During the last 4 weeks, how much have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th></th>
<th>Not bothered</th>
<th>Bothered a little</th>
<th>Bothered a lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Doing up buttons on your clothes</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.2</td>
<td>Your hands shaking</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.3</td>
<td>Clumsiness</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.4</td>
<td>Slurring your words</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.5</td>
<td>Feeling unsteady when walking</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.6</td>
<td>Problems when using the telephone or cooking a meal</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.7</td>
<td>Moving more slowly or stiffly</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.8</td>
<td>Walking with a stooped posture</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.9</td>
<td>Not swinging your arms when you walk as much as you used to</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.10</td>
<td>Slowing down physically</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.11</td>
<td>Difficulty in turning over in bed at night</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.12</td>
<td>Difficulty in standing up from a chair</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.13</td>
<td>Losing your balance</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.14</td>
<td>Loss of sensation in your hands and feet</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.15</td>
<td>Feeling drunk when you haven’t drunk too much</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td></td>
<td>Not applicable</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.16</td>
<td>Cramps or spasms in your muscles</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.17</td>
<td>Cold hands or feet</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.18</td>
<td>Having a weak feeling in your arms and legs</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>A3.</td>
<td>Over the last 2 weeks, how often have you been bothered by any of the following problems?</td>
<td>Not at all</td>
<td>Half the days or less</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>-----------</td>
<td>----------------------</td>
</tr>
<tr>
<td>3.1</td>
<td>Little interest or pleasure in doing things</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.2</td>
<td>Feeling down, depressed, or hopeless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.3</td>
<td>Trouble with sleep: too little/too much</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4</td>
<td>Feeling tired or having little energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5</td>
<td>Poor appetite or overeating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.6</td>
<td>Feeling bad about yourself - or that you are a failure or have let yourself or your family down</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.7</td>
<td>Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.8</td>
<td>Moving or speaking so slowly that other people could have noticed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.9</td>
<td>Being so fidgety or restless that you have been moving around a lot more than usual</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.10</td>
<td>Thoughts that life is not worth living</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.11</td>
<td>How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A4.</th>
<th>Do you often repeat yourself or ask the same question over and over?</th>
<th>No</th>
<th>Yes</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>Do you often repeat yourself or ask the same question over and over?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2</td>
<td>Are you more forgetful, that is, having trouble with short-term memory?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.3</td>
<td>Do you need reminders to do things like chores, shopping or taking medicine?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.4</td>
<td>Do you forget appointments, family occasions or holidays?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.5</td>
<td>Are you sad, down in the dumps, or cry more often than in the past?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.6</td>
<td>Have you started having trouble doing calculations, managing finances or balancing the chequebook?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.7</td>
<td>Have you lost interest in your usual activities such as hobbies, reading, church or other social activities?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.8</td>
<td>Have you started needing help eating, dressing, bathing, or using the bathroom?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.9</td>
<td>Have you become irritable, agitated or suspicious, or started seeing, hearing or believing things that are not real?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.10</td>
<td>Are you concerned about your driving, for example, getting lost or driving unsafely?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.11</td>
<td>Do you have trouble finding the words you want to say, or naming people or things?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.12</td>
<td>Do you think you're having trouble with your nerves?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### A5 Have you (as an adult) ever had to seek medical advice for any of the following medical problems?

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>No</th>
<th>Yes</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1</td>
<td>Allergy e.g. hay fever, eczema, dermatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.2</td>
<td>Alzheimer’s disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.3</td>
<td>Asthma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.4</td>
<td>Brucellosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.5</td>
<td>Cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.6</td>
<td>Chronic bronchitis or emphysema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.7</td>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.8</td>
<td>Depressive illness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.9</td>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.10</td>
<td>Heart disease including angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.11</td>
<td>High blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.12</td>
<td>Kidney disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.13</td>
<td>Liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.14</td>
<td>ME/chronic fatigue syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.15</td>
<td>Motor neurone disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.16</td>
<td>Multiple sclerosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.17</td>
<td>Parkinson’s Disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.18</td>
<td>Pesticide poisoning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.19</td>
<td>Seizures or epilepsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.20</td>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.21</td>
<td>Tuberculosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### A6. During the last 4 weeks, have you had any tablets or any other treatment for the following?

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>6.2</td>
<td>Asthma</td>
<td></td>
</tr>
<tr>
<td>6.3</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>6.4</td>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>6.5</td>
<td>Heart disease including angina</td>
<td></td>
</tr>
<tr>
<td>6.6</td>
<td>High blood pressure</td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>Parkinson’s disease</td>
<td></td>
</tr>
<tr>
<td>6.8</td>
<td>Stress</td>
<td></td>
</tr>
</tbody>
</table>

### B1. Now we would like to ask some questions about your smoking habits:

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Have you ever smoked cigarettes regularly (i.e. one a day for more than six months)? (If no, please move onto B2)</td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td>If yes, at what age did you start smoking?</td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>Are you still smoking?</td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>If yes, how many per day on average?</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>If no, at what age did you stop smoking?</td>
<td></td>
</tr>
<tr>
<td>1.6</td>
<td>How many cigarettes did you smoke per day, on average?</td>
<td></td>
</tr>
</tbody>
</table>
B2. Which of the following statements best describes your drinking habits? Please tick one
I drink alcohol:
2.1 Six or seven days a week □
2.2 Three to five days a week □
2.3 One or two days a week □
2.4 One to three days a month □
2.5 Less than one day a month □
2.6 Never □

B3. Approximately how many units of alcohol do you drink per week? ......
(One unit = Half a pint of average strength beer, a glass of wine or a standard pub measure of spirits)

C1. Now we would like to ask you some questions regarding your work history:
1.1 At what age did you leave school/full-time education? ........
1.2 At what age did you start working in farming (including any time spent helping out as a child)? ........
1.3 Before you worked/helped out on a farm, did you live on a farm? No □ Yes □

1.4 What is your current employment status?
Working full-time □ Not working because of ill-health/disability □
Working part-time □ Retired □
Unemployed but seeking work □ Other (please specify) ............................................

1.5 If you are no longer working at what age did you stop working? ........

1.6 At your current or last farm (if no longer farming)
Was it your family farm? □ Other □
Were you a tenant farmer? □ (Please specify) ..............................................................
Were you an employee? □

The following pages contain questions about your working history as a farmer since the end of the Second World War. On the first two pages, all you have to do is to put a tick or a line in the relevant boxes, as in the following example:

<table>
<thead>
<tr>
<th>Example</th>
<th>Year</th>
<th>Sheep</th>
<th>Cattle</th>
<th>Other livestock</th>
<th>Combinable Crops</th>
<th>Glasshouse Production</th>
<th>Outdoor Vegetables or Potatoes</th>
<th>Top &amp; Soft Fruit</th>
<th>Other work Please specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>Sheep</td>
<td>Cattle</td>
<td>Other livestock</td>
<td>Please specify</td>
<td>Combinable Crops</td>
<td>Glasshouse Production</td>
<td>Outdoor Vegetables or Potatoes</td>
<td>Top &amp; Soft Fruit</td>
<td>Other work Please specify</td>
</tr>
<tr>
<td>1980</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1982</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1983</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Driver</td>
</tr>
<tr>
<td>1984</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Driver</td>
</tr>
<tr>
<td>1985</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

By ‘Other work’ we mean any work outside the farm either on a casual, part-time or full-time basis.
In this example, this farmer started working in 1980, was a sheep farmer from 1980 to 1984 but also kept cattle in 1980, and was a driver, part-time, between 1983 and 1984. This person retired in 1985.
Please only complete the years that apply to your working life.
If you started working in or before 1975 please complete questions C2.1 and C2.2.
If you started work after 1975 please complete questions C2.2 only.
### C2.1 Work history questionnaires from 1946 to 1975

<table>
<thead>
<tr>
<th>Year</th>
<th>Sheep</th>
<th>Cattle</th>
<th>Other livestock, Please specify</th>
<th>Compost, Crops</th>
<th>Glasshouse Production</th>
<th>Outdoor Vegetables or Potatoes</th>
<th>Top &amp; Soft Fruit</th>
<th>Other work, Please specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>1946</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1947</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1948</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1949</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1951</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1952</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1953</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1954</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1955</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1956</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1957</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1958</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1959</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1961</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1962</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1963</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1964</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1965</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1966</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1967</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1968</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1969</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1970</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1971</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1973</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1975</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### C2.2 Work history questionnaires from 1976 to 2003

<table>
<thead>
<tr>
<th>Year</th>
<th>Sheep</th>
<th>Cattle</th>
<th>Other livestock, Please specify</th>
<th>Compost, Crops</th>
<th>Glasshouse Production</th>
<th>Outdoor Vegetables or Potatoes</th>
<th>Top &amp; Soft Fruit</th>
<th>Other work, Please specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1978</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1979</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1981</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1982</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1983</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1986</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1987</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1993</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### C3. Have you EVER...?

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Applied insecticides to arable, fodder crops, or grassland</td>
<td></td>
</tr>
<tr>
<td>3.2 Treated or fumigated grain or grain storage buildings</td>
<td></td>
</tr>
<tr>
<td>3.3 Applied other agricultural chemicals to crops</td>
<td></td>
</tr>
<tr>
<td>3.4 Carried out any other work with pesticides on farms</td>
<td></td>
</tr>
<tr>
<td>3.5 Used pesticides in any other job (e.g. forestry, road maintenance)</td>
<td></td>
</tr>
<tr>
<td>3.6 Used fertilisers</td>
<td></td>
</tr>
<tr>
<td>3.7 Carried out lambing/calving etc</td>
<td></td>
</tr>
<tr>
<td>3.8 Slaughtered livestock</td>
<td></td>
</tr>
<tr>
<td>3.9 Sheared sheep</td>
<td></td>
</tr>
<tr>
<td>3.10 Dipped sheep</td>
<td></td>
</tr>
<tr>
<td>3.11 Been involved in the worming of cattle or sheep</td>
<td></td>
</tr>
<tr>
<td>3.12 Carried out teat disinfection for cattle</td>
<td></td>
</tr>
<tr>
<td>3.13 Applied treatment for warble fly</td>
<td></td>
</tr>
</tbody>
</table>

### C4. Have you ever handled the concentrate for the treatment of any pests on...?

<table>
<thead>
<tr>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Arable</td>
<td></td>
</tr>
<tr>
<td>4.2 Sheep</td>
<td></td>
</tr>
<tr>
<td>4.3 Cattle</td>
<td></td>
</tr>
<tr>
<td>4.4 Other (Please specify)</td>
<td></td>
</tr>
</tbody>
</table>

### C5. Was your farm affected by BSE?

If No, please move onto question C6. If yes:

- 5.1 What approximate percentage of your livestock was slaughtered? ......................
- 5.2 How did BSE affect your livelihood? Slightly ☐ Moderately ☐ Severely ☐

### C6. Was your farm affected by Foot and Mouth Disease in 2001?

If yes:

- 6.1 What were the restrictions on your livestock?
  - National movement restrictions ☐
  - More severe movement restrictions ☐
- 6.2 What approximate percentage of your livestock was slaughtered? ......................
- 6.3 How did FMD affect your livelihood? Slightly ☐ Moderately ☐ Severely ☐

Thank you for your help. Using the accompanying self addressed envelope, please send the completed form and the top copy of the consent form to: The SHAW Research Team, Centre for Occupational and Environmental Health, 4th Floor Humanities Building, University of Manchester, Oxford Road, Manchester, M13 9PL.
Associated documents:

- CPHN consent form
- Sheep showcards
- Cattle showcards
- Other livestock showcards
- Crops and grains showcards
- Other pesticide use showcards

This questionnaire contains the following sections:

DEMOGRAPHIC INFORMATION
INTERVIEWER CHECKS
PART 1: LIFE EVENTS
PART 2: SHEEP
PART 3: CATTLE
PART 4: OTHER LIVESTOCK
PART 5: CROPS AND GRAINS
PART 6: OTHER PESTICIDE USE
PART 7: GENERAL FARM WORK

Please use these questionnaires to check sections C1 – C6, and complete the photocopy of the grid on pages 6 and 7 of the Health and Work History Questionnaire.

<table>
<thead>
<tr>
<th>ID No:</th>
<th>Start time:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Date: Finish time:

D1. What is your full name? ...........................................

D2. What is your date of birth? .......................................
ID No: ____________________

**DEMOGRAPHIC INFORMATION**

**D3.** Gender  □ Male  □ Female

**D4.** What was the highest qualification you obtained at school or college?  
*(Tick one box)*

□ No certificates  □ A-level / Highers  
□ O-level / standard grade  □ College / University

**D5.** What is your marital status?  

□ Married/Living with partner  
□ Single  
□ Separated/Divorced  
□ Widowed  

Do you live alone?  □ Yes  □ No

**D6.** County Parish Holding Number  __________________________

May we have permission to access information held on your CPHN file?  

□ Yes  →  Ask participant to sign authorisation sheet  
□ No

**D7.** What is the current size of your farm altogether in acres?

**D8.** How much of this do you actively farm yourself? (Acres or %)

**D9.** Has the size of your farm changed at any time?  

□ Yes  →

<table>
<thead>
<tr>
<th>Changes to size *</th>
<th>Year(s)</th>
<th>Postcode of farm if different</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Indicate whether farm was bought (B) or rented (R)

□ No
Please refer to section C of the Health and Work Questionnaire and complete the following table:

<table>
<thead>
<tr>
<th>Section</th>
<th>Notes</th>
<th>Tick when completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Check that record is continuous. Ask about any gaps and write in the activity (e.g. armed forces, student, unemployed, prison, hospital)</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>If answers are not clear, ask for clarification</td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>If answers are not clear, ask for clarification</td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td>If answers are not clear, ask for clarification</td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>If answers are not clear, ask for clarification</td>
<td></td>
</tr>
<tr>
<td>C6</td>
<td>If answers are not clear, ask for clarification</td>
<td></td>
</tr>
</tbody>
</table>
1.1 1.1 External Events and the Life Grid

**Interviewer:**
Please enter the following information to photocopy of the grid on pages 6 and 7 of the Health and Work History Questionnaire.
NB. Some of the following events will have occurred during a year before those on the life grid. In this case, omit.

⇒ The participant’s birth year
⇒ Birth dates of siblings
⇒ Marriages
⇒ Births of children
⇒ Year left school
⇒ Any other significant events the participant can remember, asking for the year / age that these events happened.

**Examples:**
- Any local events (flooding, unusually hot summers/bad winters)
- Any injuries or accidents
- Special birthday / anniversary events, sports, holidays.

Refer to the external events when completing the rest of the grid to verify information and to help recall.
1.2 Occupational/Farming Events

1.2.1 If you purchased a farm, what year was that?

1.2.2 Have you experienced any significant crop or livestock disasters?
   □ Yes  →  Year(s) and Details:
   □ No

1.2.3 Have you had any serious accidents on the farm that prevented you from working?
   □ Yes  →  Year(s) and Details:
   □ No
PART 2: SHEEP

2.1 Have you ever been personally involved in treating your sheep for external parasites?

☐ Yes → Continue
☐ No → Go to Q. 2.10

Interviewer prompt: Sheep dipping was compulsory between 1984 and 1991

2.1.1 What method(s) did you use? Please tick

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Dips</th>
<th>Showers</th>
<th>Injectables</th>
<th>Pour-on’s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.1.2 Complete for **external parasite** treatments only

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>On average, what was: (i) The size of your flock (Ewes/lambs) (ii) The breed(s)</th>
<th>On average, how many days did you treat during the year?</th>
<th>On average, how many sheep/lambs did you treat per day?</th>
<th>What was the greatest number of days in a row that you treated your sheep?</th>
<th>What was the greatest number of sheep/lambs that you treated in one day?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.2 I’m now going to ask you for some details of the **specific products** you have used to treat your sheep, starting with the most recent.

<table>
<thead>
<tr>
<th>Name of sheep dip/pesticide/active ingredient</th>
<th>What was the dip/pesticide used for? †</th>
<th>What method was used to apply it? ††</th>
<th>Amount of conc. used (pints, litres, gallons)</th>
<th>Years used (Please indicate if only a sample was used)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† 1 = infection  2 = endoparasites  3 = ectoparasites  4 = other (specify)
†† 1 = injection  2 = topical (e.g. pour-on)  3 = oral  4 = eartag  5 = spray  6 = Dip  7 = other (specify)
2.3 Did you ever **handle concentrates**?
- Yes → Go to Q. 2.4
- No → Go to Q. 2.6

2.4 Did you ever **spill any concentrate** on any part of your body?
- Yes → Go to Q. 2.5
- No → Go to Q. 2.6

2.5 When did you wash the concentrate off? *(Please tick)*

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Name of concentrate/chemical</th>
<th>Never usually washed when applying treatment</th>
<th>Immediately after contact</th>
<th>At the end of the treatment session</th>
<th>Other interval (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Please tick one box only*
Questions 2.6 – 2.8 are only for participants who have treated their sheep using dips or showers. Please go to question 2.9 if these methods have never been used.

2.6 The next questions are about where you carry out parasite treatment. Can you have a look at this card and answer the questions for each decade/year you have dipped or showered your sheep?

<table>
<thead>
<tr>
<th>Ask for dips and showers</th>
<th>Only ask for dips</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which type(s) of dipping bath did you use?</td>
<td>Where was the dipping bath/shower located?</td>
<td>How did the sheep enter the dip?</td>
</tr>
<tr>
<td>1=straight swim 2=circular 3=other (specify) 4=used a shower</td>
<td>1=outside 2=in a building 3=in a mobile trailer 4=covered area 5=other (specify)</td>
<td>1=walked in (angled ramp/slope) 2=dropped in (tilt/slide mechanism) 3=manually thrown in (by hand)</td>
</tr>
</tbody>
</table>
2.7 These questions are about working with the treatment wash, by which I mean the sheep dip after it has been diluted by water in the **dipping bath or shower**. Can you have a look at this card and answer the questions for the years you have dipped?

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Did you ever perform the following tasks?</th>
<th>If you were a plunger/dipper/paddler, what did you use to submerge the sheep?</th>
<th>How many people were normally involved in sheep dipping?</th>
<th>Did you ever get soaked to the skin with dip wash on any part of your body?</th>
<th>Did you regularly enter the dipping bath, either accidentally or purposely e.g. to rescue a sheep?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1=Put sheep in shower</td>
<td>1=implement/tool</td>
<td>1=one</td>
<td>Y/N/DK</td>
<td>Y/N/DK</td>
</tr>
<tr>
<td></td>
<td>2=Plunger/dipper/paddler</td>
<td>2=hands</td>
<td>2=two</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3=Chucker</td>
<td>3=feet</td>
<td>3=three</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4=Helper</td>
<td>4=other (specify)</td>
<td>4=four</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5=Other (specify)</td>
<td>5 = NA</td>
<td>5=&gt; four</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.8 Now could you answer the following questions for each year that you have dipped or showered sheep?

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Were you ever involved in the disposal of the sheep dip?</th>
<th>Did you ever come into contact with the used dip wash?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y/N/DK</td>
<td>Y/N/DK</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.9 Did you ever use **personal protective equipment** when **handling or mixing concentrated products, or applying pesticides**?

- Yes → Complete table below
- No → Go to Q. 2.10

<table>
<thead>
<tr>
<th>Which type of protective equipment did you use?</th>
<th>Year(s) and Activity e.g. dipping, pour-on, shower, injectables</th>
<th>Gloves *</th>
<th>Rubber boots</th>
<th>Apron/Overall</th>
<th>Leggings</th>
<th>Face shield</th>
<th>Respirator</th>
<th>Other (specify)</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>When handling concentrated products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When applying pesticide products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Specify

Material: rubber (R), other synthetic (S), cotton (C), leather (L), other (O)
Length: wrist length (W), 12-inch/mid-forearm (F), above elbow (E)
2.10 Were you ever in contact with your sheep within 24 hours of pesticides being applied to them (applied by self or someone else)?
- Yes
- No

2.11 Have you ever used any other type of product on sheep that we have not yet discussed?

<table>
<thead>
<tr>
<th>Product</th>
<th>Reason for use</th>
<th>Year(s)</th>
<th>Comments on usage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Yes

- No

End of Section 2
3.1 Have you ever used any *veterinary products, including pesticides*, to treat cattle?
- Yes  ➔ Complete table below
- No ➔ Go to Q. 3.7

**Interviewer prompt: Compulsory warble fly treatment was introduced in 1978**

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>On average, what was the size of your herd?</th>
<th>On average, how many cattle did you treat with veterinary products in one day (or specify other time-scale)?</th>
<th>What was the maximum number of cattle treated in one day?</th>
<th>On average, how many days did you apply veterinary products to cattle in one year?</th>
<th>In one year, what was the greatest number of days that you applied veterinary products to cattle for?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
I’m now going to ask you about the **specific veterinary products** you have used on cattle

<table>
<thead>
<tr>
<th>Name of veterinary product</th>
<th>What was the product used for? †</th>
<th>How was the product applied? ††</th>
<th>Amount of conc. used (pints, litres, gallons)</th>
<th>Years used</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHOW CARD 1</td>
<td>SHOW CARD 2</td>
<td>SHOW CARD 3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|                           | † 1 = infection  
2 = endoparasites 
3 = ectoparasites 
4 = other (specify)  
†† 1 = injection 
2 = topical 
3 = oral 
4 = eartag 
5 = spray 
6 = other (specify) |
3.3 Did you ever **handle concentrates** when treating cattle?
- Yes → Go to Q. 3.4
- No → Go to Q. 3.6

3.4 Did you ever spill any **concentrate** on any part of your body?
- Yes → Go to Q. 3.5
- No → Go to Q. 3.6

3.5 When did you wash the concentrate off? *(Please tick)*

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Name of concentrate/chemical</th>
<th>Never usually washed when applying treatment</th>
<th>Immediately after contact</th>
<th>At the end of the treatment session</th>
<th>Other interval (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Please tick one box only*
3.6 Did you ever use **personal protective equipment** when **handling or mixing concentrated products, or applying pesticides**?

- ☐ Yes → Complete table below
- ☐ No → Go to Q. 3.7

**Which type of protective equipment did you use:**

<table>
<thead>
<tr>
<th></th>
<th>Year(s) and Activity</th>
<th>Gloves</th>
<th>Rubber boots</th>
<th>Apron/Coverall</th>
<th>Leggings</th>
<th>Face shield</th>
<th>Respirator</th>
<th>Other (specify)</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>When handling</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>concentrated products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>When applying</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pesticide products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Specify  

Material: rubber (R), other synthetic (S), cotton (C), leather (L), other (O) 

Length: wrist length (W), 12-inch/mid-forearm (F), above elbow (E)
3.7 Were you ever in contact with your cattle within 24 hours of pesticides being applied to them (applied by self or someone else)?
- Yes
- No

3.8 Have you ever used any other type of product on cattle that we have not yet discussed?

<table>
<thead>
<tr>
<th>Product</th>
<th>Reason for use</th>
<th>Year(s)</th>
<th>Comments on usage</th>
</tr>
</thead>
</table>

- Yes

- No

End of Section 3
4.1 Have you ever used **any veterinary medicines, including those that contain pesticides** on **any other livestock**?

- Yes: Complete table below
- No/Don’t know: Go to Q. 4.7

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Livestock</th>
<th>On average, what was the size of your herd etc.?</th>
<th>On average, how many other livestock did you treat with veterinary products in one day (or specify other time-scale)?</th>
<th>What was the maximum number of other livestock treated in one day?</th>
<th>On average, how many days did you apply veterinary products to other livestock in one year?</th>
<th>In one year, what was the greatest number of days that you applied veterinary products to other livestock for?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.2 I’m now going to ask you about the **specific veterinary products** you have used on other livestock

<table>
<thead>
<tr>
<th>Name of pesticide/veterinary product used on other livestock</th>
<th>Type of livestock</th>
<th>What was the product used for? †</th>
<th>How was the product applied? ††</th>
<th>Amount of concentrate per treatment (pints, litres, gallons)</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If unknown, refer to SHOW CARD 1a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If still unknown, refer to SHOW CARD 1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† 1 = infection 2 = endoparasites 3 = ectoparasites 4 = other (specify)

†† 1 = injection 2 = topical 3 = oral 4 = eartag 5 = spray 6 = dip 7 = other (specify)
4.3 Did you ever **handle concentrates** when treating other livestock?
- Yes → Go to Q. 4.4
- No → Go to Q. 4.7

4.4 Did you ever spill any **concentrate** on any part of your body?
- Yes → Go to Q. 4.5
- No → Go to Q. 4.7

4.5 When did you wash the concentrate off? *(Please tick)*

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Name of concentrate/chemical</th>
<th>Never usually washed when applying treatment</th>
<th>Immediately after contact</th>
<th>At the end of the treatment session</th>
<th>Other interval (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Show card 4
4.6 Did you ever use personal protective equipment when handling or mixing concentrated products, or applying pesticides?

☐ Yes → Complete table below
☐ No → Go to Q. 4.7

<table>
<thead>
<tr>
<th>Which type of protective equipment did you use:</th>
<th>Year(s) and Activity</th>
<th>Gloves[*]</th>
<th>Rubber boots</th>
<th>Apron/Overall</th>
<th>Leggings</th>
<th>Face shield</th>
<th>Respirator</th>
<th>Other (specify)</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>When handling concentrated products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When applying pesticide products?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Specify Material: rubber (R), other synthetic (S), cotton (C), leather (L), other (O)
Length: wrist length (W), 12-inch/mid-forearm (F), above elbow (E)
4.7 Were you ever in contact with your livestock within 24 hours of pesticides being applied to them (applied by self or someone else)?

☐ Yes
☐ No

4.8 Have you ever used any other type of product on other livestock that we have not yet discussed?

<table>
<thead>
<tr>
<th>Product</th>
<th>Reason for use</th>
<th>Year(s)</th>
<th>Comments on usage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

☐ Yes

☐ No

End of Section 4
### PART 5: CROPS AND GRAINS

#### 5.1 Have you ever used **pesticides** to treat **crops or grains**?

- **Yes**  ➔ Complete table below
- **No/Don’t know**  ➔ End of Section 5

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Type of crop †</th>
<th>Hectares/ acres* of crop</th>
<th>Type of pesticide used ††</th>
<th>Did it contain OPs Y/N/DK</th>
<th>Average no. hours/day that you used a pesticide</th>
<th>Average no. days/year that you used pesticides</th>
<th>How were pesticides applied †††</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† 1=wheat  2=barley  3=sugar beet  4=outdoor veg/potatoes  5=top & soft fruit  6=glasshouse production  7=other (specify)

†† 1=herbicide  2=fungicide  3=insecticide  4=other (specify)

††† 1 = Tractor mounted/trailed boom sprayer: hydraulic nozzles  2 = Tractor mounted/trailed boom sprayer: rotary atomisers  
3 = Tractor mounted/trail broadcast air-assisted sprayer  4 = Hand-held sprayer  5 = Aerial application  6 = Other (specify)
5.2 Have you ever handled **pesticide concentrate** when treating crops or grains?

☐ Yes        ➔ Complete table below

☐ No         ➔ End of Section 5

<table>
<thead>
<tr>
<th>Name of Pesticide</th>
<th>Type of crop †</th>
<th>How often did you handle concentrate ††</th>
<th>Did you mix the concentrate yourself? Y/N/DK</th>
<th>How/where did you do this ††† (include all that apply) SHOW CARD 7</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHOW CARD 4</td>
<td>SHOW CARD 5</td>
<td>SHOW CARD 6</td>
<td></td>
<td>SHOW CARD 7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†  1=wheat  2=barley  3=sugar beet  4=outdoor veg/potatoes  5=top & soft fruit  6=glasshouse production  7=other (specify)

††  1 = daily  2 = several times a week  3 = once a week  4 = more than once a month  5 = don’t know

†††  1 = directly in the pesticide adaptor  2 = in a bucket in the field  3 = indoors  4 = outdoors  5 = other (specify)  6 = don’t know
### PART 6: OTHER PESTICIDE USE

**6.1** Have you ever used any of the following products *in or around any buildings on the farm*?

- ☐ Yes → Complete table below
- ☐ No → Go to Q. 6.4

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Product</th>
<th>Reason for use</th>
<th>How was product applied †</th>
<th>Was personal protective equipment worn? Y/N/DK</th>
<th>Specify PPE worn ††</th>
<th>Did you handle the concentrate? Y/N/DK</th>
<th>Did you regularly get wet from concentrated or diluted pesticide/ medicine †††</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† 1 = Tractor mounted/trailed boom sprayer: hydraulic nozzles  
2 = Tractor mounted/trailed boom sprayer: rotary atomisers  
3 = Tractor mounted/trail broadcast air-assisted sprayer  
4 = Hand-held sprayer  
5 = Aerial application  
6 = Other (specify)

†† 1 = gloves (applies only to rubber or other synthetic materials. Specify the length of the gloves)  
2 = rubber boots  
3 = coverall/apron  
4 = leggings  
5 = face shield  
6 = respirator  
7 = other (specify)

††† 1 = yes-concentrated  
2 = yes-diluted  
3 = no

**6.2** Did the farm have a grain bin or any other grain storage building?  
☐ Yes  
☐ No

**6.3** Did you apply any pesticides to the grain storage building or the grain itself?  
☐ Yes  
☐ No
6.4 **For any farming job that you have held** have you ever used any of the following?

- [ ] Yes — Complete table below
- [ ] No — End of Section 6

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Product</th>
<th>Reason for use</th>
<th>How was product applied †</th>
<th>Was personal protective equipment worn? Y/N/DK SHOW CARD 5</th>
<th>Specify PPE worn ††</th>
<th>Did you handle the concentrate? Y/N/DK SHOW CARD 6</th>
<th>Did you regularly get wet from concentrated or diluted pesticide/medicine †††</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†  1 = Tractor mounted/trailed boom sprayer: hydraulic nozzles  2 = Tractor mounted/trailed boom sprayer: rotary atomisers  3 = Tractor mounted/trail broadcast air-assisted sprayer  4 = Hand-held sprayer  5 = Aerial application  6 = Other (specify)

†† 1 = gloves – specify:
   Material: rubber (R), other synthetic (S), cotton (C), leather (L), other (O)
   Length: wrist length (W), 12-inch/mid-forearm (F), above elbow (E)

2 = rubber boots  3 = coverall/apron  4 = leggings  5 = face shield  6 = respirator  7 = other (specify)

††† 1 = yes-concentrated  2 = yes-diluted  3 = no
### PART 7: GENERAL FARM WORK

#### 7.1 Do you use, or have you ever used the following equipment?

<table>
<thead>
<tr>
<th>Name of Equipment</th>
<th>Regularly</th>
<th>Sometimes</th>
<th>Never</th>
<th>No. hours used per week</th>
<th>Specify years used equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chainsaws/wood work machines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power hammers/ percussion drills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grinding and rotary tools</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riveting tools</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fork lift driving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tractor/quad bike driving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 3: A letter to the farmers asking for their permission to observe a sheep dipping session

Dear Mr

Re: Study of Health in Agricultural Work

Thank you very much for taking part in the Study of Health in Agricultural Work and for being so helpful when we rang you recently to request further information. Two students in our Department are doing research on pesticide exposure in sheep farmers but they have never seen sheep dipping or similar treatments. As you have helped us in the past we wondered whether you might be willing to have these students come and see the dipping/treatment process on your farm. The students would not be intrusive but just wish to observe sheep dipping/treatment. The idea is to help the students understand the nature of this process.

If you are able to help by allowing 1-2 students to observe sheep dipping would you be kind enough to return the form below and the student will contact you to arrange a mutually convenient time. Or you can e-mail or ring us, our details are below.

Once again thank you very much for your previous help with this study.

Yours sincerely

Jill Stocks
Jill.stocks@manchester.ac.uk
0161 2751631

Andy Povey
Andy.povey@manchester.ac.uk
0161 2755232
I would be willing to allow 1-2 students from Manchester University observe sheep dipping or similar treatments on my farm.

Name:

Tel:

Type of sheep treatments:

Approximate dates treating sheep:

Please return to:

Haytham Alhamwi
COEH, 4th Floor Ellen Wilkinson Building
University of Manchester
Oxford Rd
Manchester
M13 9PL
Appendix 4: Exposure scores for all variables of sheep dipping exposure algorithm assigned by experts

Table.App. 4-1: Exposure scores for variables of handling the concentrate assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td>Dermal</td>
<td></td>
<td>COVOL$_{der}$</td>
<td>1$^{st}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2$^{nd}$ tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3$^{rd}$ tertile</td>
<td>3</td>
</tr>
<tr>
<td>Ingestion</td>
<td></td>
<td>COVOL$_{ing}$</td>
<td>1$^{st}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2$^{nd}$ tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3$^{rd}$ tertile</td>
<td>3</td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td>COVOL$_{inh}$</td>
<td>1$^{st}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2$^{nd}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3$^{rd}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td>Type of container</td>
<td>Dermal</td>
<td>TYP$_{der}$</td>
<td>With a pouring mechanism</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>TYP$_{ing}$</td>
<td>With a pouring mechanism</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>TYP$_{inh}$</td>
<td>With a pouring mechanism</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without a pouring mechanism</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sachets</td>
<td>1</td>
</tr>
<tr>
<td>Size of container</td>
<td>Dermal &amp; Ingestion</td>
<td>SIZ</td>
<td>5 litres</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 litres</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20 litres</td>
<td>1.2</td>
</tr>
<tr>
<td>Duration of the session</td>
<td>Dermal</td>
<td>DUR$_{con,der}$</td>
<td>1$^{st}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2$^{nd}$ tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3$^{rd}$ tertile</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>DUR$_{con,ing}$</td>
<td>1$^{st}$ tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2$^{nd}$ tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3$^{rd}$ tertile</td>
<td>3</td>
</tr>
</tbody>
</table>
Table.App. 4-1: Exposure scores for variables of handling the concentrate assigned by experts (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td>How mixed with bath</td>
<td>Dermal</td>
<td>MIX&lt;sub&gt;der&lt;/sub&gt;</td>
<td>Pouring directly in bath or sachets</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using a jug</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using automatic unit</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>MIX&lt;sub&gt;ing&lt;/sub&gt;</td>
<td>Pouring directly in bath or sachets</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using a jug</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using automatic unit</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>MIX&lt;sub&gt;inh&lt;/sub&gt;</td>
<td>Pouring directly in bath or sachets</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using a jug</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Using automatic unit</td>
<td>0.8</td>
</tr>
<tr>
<td>Atmospheric conditions</td>
<td>Dermal</td>
<td>ATM&lt;sub&gt;con.der&lt;/sub&gt;</td>
<td>Still</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>ATM&lt;sub&gt;con.ing&lt;/sub&gt;</td>
<td>Still</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>ATM&lt;sub&gt;con.inh&lt;/sub&gt;</td>
<td>Still</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>0.1</td>
</tr>
<tr>
<td>Bath location</td>
<td>All</td>
<td>LOC</td>
<td>Outside and exposed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Outside and sheltered</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trailer</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inside</td>
<td>1.5</td>
</tr>
</tbody>
</table>
### Table.App. 4-2: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td>Number of dippers</td>
<td>Dermal</td>
<td>NUM\textsubscript{der}</td>
<td>1-3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>0.3</td>
</tr>
<tr>
<td>Ingestion</td>
<td>NUM\textsubscript{ing}</td>
<td>1-3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>0.3</td>
</tr>
<tr>
<td>Inhalation</td>
<td>NUM\textsubscript{inh}</td>
<td>1-3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>0.3</td>
</tr>
<tr>
<td>Duration of the session</td>
<td>Dermal</td>
<td>DUR\textsubscript{dip,der}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
<tr>
<td>Ingestion</td>
<td>DUR\textsubscript{dip,ing}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
<tr>
<td>Inhalation</td>
<td>DUR\textsubscript{dip,inh}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
<tr>
<td>Dip rate</td>
<td>Dermal</td>
<td>RATE\textsubscript{der}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
<tr>
<td>Ingestion</td>
<td>RATE\textsubscript{ing}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
<tr>
<td>Inhalation</td>
<td>RATE\textsubscript{inh}</td>
<td>1\textsuperscript{st} tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2\textsuperscript{nd} tertile</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3\textsuperscript{rd} tertile</td>
<td>3</td>
</tr>
</tbody>
</table>
Table.App. 4-2: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td><strong>Bath type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>BATH&lt;sub&gt;dip.der&lt;/sub&gt;</td>
<td>Linear</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Circular</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mobile</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Ingestion</td>
<td>BATH&lt;sub&gt;dip.ing&lt;/sub&gt;</td>
<td>Linear</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Circular</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mobile</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Inhalation</td>
<td>BATH&lt;sub&gt;dip.inh&lt;/sub&gt;</td>
<td>Linear</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Circular</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>Bath location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>LOC&lt;sub&gt;dip.der&lt;/sub&gt;</td>
<td>Outside</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Ingestion</td>
<td>LOC&lt;sub&gt;dip.ing&lt;/sub&gt;</td>
<td>Outside</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Inhalation</td>
<td>LOC&lt;sub&gt;dip.inh&lt;/sub&gt;</td>
<td>Outside</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trailer</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Splash guard</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>GUARD&lt;sub&gt;dip.der&lt;/sub&gt;</td>
<td>No</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Ingestion</td>
<td>GUARD&lt;sub&gt;dip.ing&lt;/sub&gt;</td>
<td>No</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Sheep entry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>ENTRY&lt;sub&gt;dip.der&lt;/sub&gt;</td>
<td>Walk in method (slope or ramp)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slipway (tilt)</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Ingestion</td>
<td>ENTRY&lt;sub&gt;dip.ing&lt;/sub&gt;</td>
<td>Walk in method (slope or ramp)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slipway (tilt)</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Inhalation</td>
<td>ENTRY&lt;sub&gt;dip.inh&lt;/sub&gt;</td>
<td>Walk in method (slope or ramp)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slipway (tilt)</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>
Table.App. 4-2: Exposure scores for variables of dipping sheep in diluted pesticides assigned by experts (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td>Dermal</td>
<td>Submerge tool</td>
<td>TOOL&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td>Metal tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>TOOL&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>Metal tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>TOOL&lt;sub&gt;dip,inh&lt;/sub&gt;</td>
<td>Metal tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wooden tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hands</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Feet and tool</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Personal hygiene and behaviour (washing off sheep dip)</td>
<td></td>
<td>Occasionally or at end Regularly</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dermal</td>
<td>PHB&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td>Occasionally or at end Regularly</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>PHB&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>Occasionally or at end Regularly</td>
<td>0.3</td>
</tr>
<tr>
<td>Atmospheric conditions (wind)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal &amp; Ingestion</td>
<td>ATM&lt;sub&gt;dip,der&lt;/sub&gt;</td>
<td></td>
<td>Still</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ATM&lt;sub&gt;dip,ing&lt;/sub&gt;</td>
<td>Breezy</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>ATM&lt;sub&gt;dip,inh&lt;/sub&gt;</td>
<td>Still</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezy</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gusting</td>
<td>0.1</td>
</tr>
</tbody>
</table>

342
### Table.App. 4-3: Exposure scores for variables of the disposal of sheep dip and incidental exposure assigned by experts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exposure route</th>
<th>Variable abbreviation</th>
<th>Variable categories</th>
<th>Scores assigned by experts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td><strong>Method of the disposal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>METHODdis.der</td>
<td>Drain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Ingestion</td>
<td>METHODdis.ing</td>
<td>Drain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Inhalation</td>
<td>METHODdis.inh</td>
<td>Drain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mechanical</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Manual</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Volume of sheep dip</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>VOLdis.der</td>
<td>1st tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2nd tertile</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3rd tertile</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Ingestion&amp;Inhalation</td>
<td>VOLdis.ing</td>
<td>1st tertile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>VOLdis.inh</td>
<td>2nd tertile</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3rd tertile</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Bath location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>LOCdis.der</td>
<td>Outside</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ingestion</td>
<td>LOCdis.ing</td>
<td>Outside</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inside</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Inhalation</td>
<td>LOCdis.inh</td>
<td>Outside</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Personal hygiene and behaviour (washing out concentrate spills)</td>
<td></td>
<td>At the end of the session</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before meal break</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediately</td>
<td>0.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Dermal</td>
<td>PHBspil.der</td>
<td>At the end of the session</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before meal break</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediately</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Ingestion</td>
<td>PHBspil.ing</td>
<td>At the end of the session</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Before meal break</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediately</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Table.App. 4-5: Contribution of exposure through each route to the total exposure from each exposure source in sheep dipping

<table>
<thead>
<tr>
<th>Exposure source</th>
<th>Route</th>
<th>Contribution of exposure through each route (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expert 1</td>
<td>Expert 2</td>
</tr>
<tr>
<td>Handling the concentrate</td>
<td>Dermal</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>5</td>
</tr>
<tr>
<td>Dipping sheep in the bath</td>
<td>Dermal</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>5</td>
</tr>
<tr>
<td>Handling dipped sheep</td>
<td>Dermal</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>5</td>
</tr>
<tr>
<td>Disposal of sheep dip</td>
<td>Dermal</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>5</td>
</tr>
<tr>
<td>Incidental exposure</td>
<td>Dermal</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>Ingestion</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>1</td>
</tr>
</tbody>
</table>

Table.App. 4-6: Contribution of exposure from each source to the total exposure in sheep dipping

<table>
<thead>
<tr>
<th>Exposure source</th>
<th>Contribution of exposure from each source (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expert 1</td>
</tr>
<tr>
<td>Handling the concentrate</td>
<td>10</td>
</tr>
<tr>
<td>Dipping sheep in the bath</td>
<td>40</td>
</tr>
<tr>
<td>Handling dipped sheep</td>
<td>40</td>
</tr>
<tr>
<td>Disposal of sheep dip</td>
<td>10</td>
</tr>
<tr>
<td>Incidental exposure</td>
<td>99.9 a</td>
</tr>
</tbody>
</table>

a Expert 1 said: 99.9 if yes and 0 if no
Appendix 5: Assumptions for the missing information in the HSDS used for the validation study

<table>
<thead>
<tr>
<th>Num.</th>
<th>Assumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In wash concentrate spills: one farmer said (other interval) and was assumed before meal.</td>
</tr>
<tr>
<td>2</td>
<td>In mixing concentrate method: pouring on assumed with jug.</td>
</tr>
<tr>
<td>3</td>
<td>One missing mixing concentrate method was assumed pouring on.</td>
</tr>
<tr>
<td>4</td>
<td>Missing tool was assumed metal implement.</td>
</tr>
<tr>
<td>5</td>
<td>Missing number of dippers was assumed 3 since all 1-4 have the same score.</td>
</tr>
<tr>
<td>6</td>
<td>Type of container was set according to mixing concentrate method, either sachets or a container with pouring mechanism.</td>
</tr>
</tbody>
</table>
| 7    | Model constants: scores were set according to the most frequent category:  
RATE: 1st tertile = 1  
BATH: Linear = 1  
LOC: Outside = 1  
ENTRY: Manual = 3  
ATM: Breezy = 2  
GUARD: No = 0  
PHWH: Occasionally = 1  
COVOL: 1st tertile = 1  
SIZ: 5 litres = 1 |
Appendix 6: Abstracts of studies used to obtain the distributions of variables used in the probabilistic model

Eight studies were used to obtain the distributions of the conceptual algorithm’s variables. The HSDS and SHAW studies were presented in details in Chapter 2. The abstracts of the remaining six are adapted from the original reports or papers.

Appendix 6-1: Abstract of occupational hygiene assessment of sheep dipping practices and processes


A collaborative Health and Safety Executive (HSE); Institute of Occupational Medicine (IOM) study of sheep dipping practices was conducted in 1992 using occupational hygiene evaluations of the five most common sheep dipping practices to rank the potential for and extent of operator exposure, the uptake of OP insecticide, and the working practices contributing to this exposure.

Pilot work was undertaken to evaluate and refine a customised visual assessment proforma developed to record working practices as well as the extent and duration of workers' skin and clothing contact with sheep dip. Airborne concentrations of the OP insecticide diazinon measured during these studies were all less than the analytical detection limit of the method (<0.01 mg m⁻³). The OES is 0.1 mg m⁻³.

In the main study sheep dipping with proprietary formulations containing only diazinon were evaluated. Fourteen different sheep dipping operations were studied which involved 38 individuals. The human metabolism and excretion of the active OP ingredient of sheep dip under the conditions observed were assessed. Samples of blood obtained from participating workers were analysed for red cell and plasma cholinesterase activity. Corresponding urine samples were analysed for the metabolites of the OP diazinon; diethyl phosphate (DEP) and diethylthiophosphate (DETP). Photographic records and video recordings were obtained for all visits and were used to assist descriptions of working methods encountered and interpretation of the results.

Splashing was caused by a variety of factors mainly related to working practices such as the speed of dipping, the method for sheep entering the bath, the interaction between dipping team members and general operator fatigue during long sessions. The use of appropriate protective clothing was generally poor with personal hygiene and standards of housekeeping variable. Hazard perception was also generally inadequate. Some
workers were visibly soaked, particularly paddlers and chuckers, while some helpers were hardly splashed. A number of useful control measures such as splash-guards and remote operation of gates were in use on a number of farms. It was not possible to assess directly exposure caused by contact with contaminated surfaces or concentrated dip although those individuals who handled concentrate had significantly higher concentrations of urinary metabolites.

The levels of diazinon metabolites in urine were low, indicating some but relatively little absorption of OP insecticide during the sheep dipping processes. Metabolites of diazinon (DEP + DETP) were detected in the pre-dipping urine samples of 15 out of 36 workers on farms where diazinon was used. This may have resulted from earlier sheep VI dipping with diazinon. There was little change in the amount of diazinon metabolites detected from pre- to post dipping samples. Sixteen individuals showed no increase; in the remainder increases ranged from 1 to 56 nmol/mmol creatinine. Thirty out of 36 exhibited an increase in metabolites from pre-dipping to next morning; this ranged from 1 to 146 nmol/mmol creatinine. The amount of metabolite present in next morning samples, adjusted for the initial pre-dipping levels, ranged from 0 to 151 nmol/mmol creatinine, the mean being 22.6 and the median 16 nmol/mmol creatinine. When urinary metabolite results were compared with visual occupational hygiene information no association was found between increases in metabolites and particular occupations or dipping bath type. Individual working practice was the overwhelming explanatory factor for increased exposure.

The largest decrease observed in plasma cholinesterase activity for any worker was 14%, which was accompanied by a decrease in red cell cholinesterase activity of 2%. This decrease is within the variation which could occur in a normal, unexposed individual. For red cell cholinesterase activity the largest decrease was 10% (experienced by 1 individual) which is the upper limit of intra-individual variation. No worker experienced what would be considered a clinically significant change in either plasma or red cell cholinesterase activity, that is a decrease of more than 30%.

Field trials of the HSE’s fluorescent imaging technique for assessing skin contamination were performed at six of the participating farms. Contamination was observed but the quantitative estimates may be a little low because of technical problems with the method. The highest observed skin contamination, however, was found on an individual who was observed to be heavily splashed and to have a relatively high urinary metabolite concentration. The study suggests that the most important cause of exposure was from handling concentrated dip with direct splashes from the working strength dip less significant.
Appendix 6-2: Abstract of occupational hygiene assessment of exposure to insecticides and the effectiveness of protective clothing during sheep dipping operations


A study of sheep dipping was conducted in 1992 and 1993 to assess the adequacy of guidelines for protective clothing and working methods to protect sheep dipping operators against skin exposure to sheep dips containing OPs. Occupational hygiene evaluations, biological monitoring and biological effect monitoring were used to establish the effectiveness of recommended protective clothing and the body uptake of OP when sheep dips were used according to manufacturers' guidelines.

The main study was undertaken at twelve farms during two phases. In the first phase surveys lasted two days on each farm. Contamination and penetration of protective clothing with OP (propetamphos or diazinon) was assessed using garment samplers. These absorbent suits were worn outside protective clothing on one day and inside on another. Absorbent gauze patches were attached to the outer layer of clothing on both days to obtain an estimate of differences in external contamination between the two days. At the end of each dipping session garment samples were sectioned into 6 pieces, and stabilised where necessary before removal to the laboratory, with the patch samples, for analysis.

Penetration of insecticide through the protective clothing was generally minimal with protection factors ranging between approximately 4 and > 1000. The maximum amount on an entire internal sampling suit was approximately 6 mg, although 90% were less than 1 mg of insecticide compared with up to approximately 100 mg when the sampling suit was worn outside the protective clothing. Most of this penetration was detected on the lower arms and legs. A positive association was observed between total patch insecticide masses and the amount found on the corresponding sampling suits. The relationship was less clear when individual suit areas were compared with their associated patches. To assist with evaluation of contamination and comparison of the survey days factual information, such as number and rate of sheep dipped, length of dipping session, amount of concentrated dip used, the method of replenishing the dip bath and the size and composition of the dipping team was recorded.

A semi-quantitative assessment of observed splashes on each member of the team was also made using a simple scoring system during every dipping session. At almost every farm, on both days, individuals who plunged the sheep under the dipping liquid
(paddlers) had the highest splashing score and, where present, helpers had the lowest score (those gathering sheep). These findings were similar to those obtained from the external garment samplers.

During the second phase of the study 32 individuals provided two samples of blood (pre- and post-dipping) and three urine specimens (pre-, post-dipping and next morning) for cholinesterase activity determination and urinary metabolite analysis respectively. Half the farms studied used dips based on the OP diazinon while the remaining six farms used chlorfenvinphos-based dips.

Concentrations of metabolites of diazinon (diethyl phosphate (DEP) and diethyl thiophosphate (DETP)) ranged from less than the detection limit (approximately 1 n mole/m mole creatinine) up to 227 nmol/mmol creatinine. Increases in urinary concentrations of over 20 nmol/mmol creatinine were observed in only four individuals. Urinary concentrations only increased by up to 20 nmol/mmol creatinine for all other workers and the urinary metabolite concentrations actually dropped for two individuals. Concentrations of dimethyl derivatives (which are not metabolites of diazinon) were found in at least one urine sample from all participants and in some increased during the sampling period. The reasons for this are not clear.

The pattern for urinary concentrations of dichlorobenzoic acid, a product of the metabolites of chlorfenvinphos, was similar to that of diazinon. No urinary metabolites of chlorfenvinphos were detected in the urine of 10 of the 15 workers studied, even after dipping. The highest observed concentration was 47 n moles/m mole creatinine, with other concentrations ranging from 20 to 35 n moles/m mole creatinine.

No subject experienced a clinically significant fall in plasma (> 15%) or erythrocyte (> 10%) cholinesterase activity. The highest recorded fall in plasma cholinesterase activity was 9% which was not accompanied by change in erythrocyte cholinesterase activity.

A weak positive association was found between splashing score and the increase in urinary metabolite concentration. This relationship was, however, overwhelmed by events at, at least, one farm. The study concludes that supervised use of protective clothing ensembles recommended by NOAH in 1992 resulted in minimal contamination underneath the garments. The guidelines, if followed correctly, effectively reduced the potential exposure and can be regarded, however, as adequate.

Concentrations of urinary metabolites in urine were low indicating some but relatively little absorption of OP insecticide during the sheep dipping process. The range of results was similar to that found in another study where no special protective clothing was worn.
Appendix 6-3: Abstract of epidemiological study of the relationships between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers, Phase 2, development and validation of an organophosphate uptake model for sheep dippers.


The abstract is adapted from:


OBJECTIVES: To derive a method for retrospectively estimating cumulative exposure to OP pesticides among a cross section of United Kingdom sheep dippers, as part of a wider epidemiological study of neurological abnormality within this group of workers.

METHODS: A hygiene study of dipping sessions at 20 farms using diazinon based dips was carried out by two experienced occupational hygienists. Observations on the exposure of people to concentrate and dilute dip were recorded throughout each dipping session, together with the other relevant factors including the use and condition of protective clothing. Concentrations of urinary metabolites of diazinon were used to measure actual exposure to OPs. To estimate exposure in the subsequent epidemiological study, an occupational exposure history questionnaire was developed using results from the hygiene study and an empirical exposure model. RESULTS: In the hygiene study, increased urinary metabolites were associated with the handling of concentrate dip and exposure to dilute dip wash through splashing. Very few dippers wore the recommended protective clothing. The handling of concentrate dip was the principal source of exposure to OPs. Dipping task was used as a surrogate for splashing of dilute dip in retrospective exposure estimation. In the epidemiological study, cumulative exposure to OP sheep dips was highly correlated with the total number of dipping days, but not with age. CONCLUSIONS: Sheep dip concentrate is the most important source of OP exposure among sheep dippers and estimates of exposure to OPs during routine dipping should take due account of exposure to concentrate dip as well as to the dilute dip wash. The observed use of recommended protective clothing by most subjects was insufficient to allow a proper empirical assessment of its effectiveness.
Appendix 6-4: Abstract of An investigation into the possible chronic neuropsychological and neurological effects of occupational exposure to organophosphates in sheep farmers


The abstract is adapted from:


OP-based pesticides are widely used throughout the world. The acute effects of over-exposure to such compounds are well known. Concern has also been expressed that long-term exposure may result in damage to the nervous system. In a cross-sectional study, we compared neuropsychological performance in 146 sheep farmers who were exposed to OPs in the course of sheep dipping with 143 non-exposed quarry workers (controls). The farmers performed significantly worse than controls in tests to assess sustained attention and speed of information processing. These effects remained after adjustment for covariates. The farmers also showed greater vulnerability to psychiatric disorder than did the controls as measured by the General Health Questionnaire. There were no observed effects on short-term memory and learning. Repeated exposure to OP-based pesticides appears to be associated with subtle changes in the nervous system. Measures should be taken to reduce exposure to OPs as far as possible during agricultural operations.
Appendix 6-5: Abstract of exposure to sheep dip and the incidence of acute symptoms in a group of Welsh sheep farmers


OBJECTIVES: To measure the exposure of a group of farmers to OP pesticide in sheep dip, and to record the incidence of symptoms after exposure. DESIGN: A prospective study of the autumn 1992 dipping period. Working methods were assessed by questionnaire. Absorption of OP pesticide was estimated before, immediately after, and six weeks after dipping by measuring plasma cholinesterase, erythrocyte cholinesterase, and dialkylphosphate urinary metabolites of OPs. Symptoms were recorded by questionnaire at the same time as biological monitoring. Possible confounding factors were identified by medical examination of the subjects. SETTING: Three community council electoral wards in Powys, typical of hill sheep farming areas in Wales. SUBJECTS: All (38) men engaged in sheep dipping living in the three community council electoral wards. RESULTS: 23 sheep farmers and one dipping contractor completed the study--a response rate of 63%. A sample of seven men who refused to enter the full study had similar working practices to the 24 subjects. Subjects reported inadequate handling precautions, and significant skin contamination with dip. Two men reported under diluting dip concentrate for use. Both had significant depression of erythrocyte cholinesterase after dipping. This indicated some absorption of OP pesticide--but this did not reach levels usually associated with toxicity. It was not clear whether the symptoms of these two men were caused by OP exposure. Measurement of dialkylphosphate urinary metabolites in a single specimen of urine voided shortly after the end of dipping could not be correlated with individual exposure. CONCLUSIONS: Sheep dipping is strenuous and dirty work and sheep farmers find it difficult to wear personal protective equipment and avoid skin contamination with dip. In this limited study, farmers did not seem to have significant OP toxicity, despite using inadequate handling precautions.
Appendix 6-6: Abstract of SHAPE: Survey of Health and Pesticide Exposure, The Telephone Survey


A number of organisations in the UK have been providing support to sheep farmers and others who have experienced ill-health, attributed by them in many cases to exposure to OP formulations. Four of these organisations agreed to cooperate in the present study, which aimed to describe the health and exposure of support group members. The study consisted of a structured assessment of the health and exposure of those who took part; the information was gathered principally by means of telephone interviews. A sub sample was examined clinically with a range of neurological tests; methods and results from the clinical study will be reported in a further report.

The support groups were able to contact 907 of the total of 1844 individuals for whom they had sufficient and current contact details. Following screening out of those without potential OP exposure, 524 eligible participants were invited for telephone interview, of whom 471 were interviewed. Analyses focused on 367 individuals after excluding those with reported diagnoses (such as diabetes) or use of medications with potential neurological side-effects.

A quantitative cumulative OP exposure score was calculated, by linking estimates of OP concentrations in various occupations and tasks obtained by modelling and expert judgement, with individuals’ corresponding frequency and/or duration of exposure, using information obtained from the telephone surveys. The 367 individuals showed a wide range of estimated cumulative OP exposures. For sheep dippers and handlers the estimated cumulative exposure was broadly comparable to that found in an earlier cross sectional survey of active sheep farmers; i.e. on average, the sheep dippers and handlers studied from the four support groups had not experienced unusually high lifetime exposures to OPs in the course of their work.

The study participants had been self-selected as people with chronic illness which they attributed to OP exposures. Results from the telephone survey confirmed that the health of those studied was generally poor, with 75% reporting their overall health as only fair or poor. A wide range of symptoms was reported, including 81% of participants reporting concentration/memory difficulties, and 74% fatigue. For only a small proportion (18%) could we identify other reported medical history or medication which
might prompt these or other symptoms of neurological damage. After excluding this 18%, symptoms consistent with neurological damage remained especially prevalent.

Four out of five of those interviewed reported having had an acute OP exposure episode; on average these had on poorer health than the others. This is consistent with the view that people who experience an acute response to OP exposures may also suffer long-term neurological health effects.

From our survey it appears that most of the reported illness is therefore among those with at one time or another rather high OP exposures, though their lifetime cumulative exposures were not unusually high compared with other exposed workers. It is plausible that the ill-health of many of these is related to, or made worse by, their OP exposure history. However, methods of self-selection into the support groups and therefore into the study could generate similar findings even if exposure to OPs had not caused the neurological damage found. We have no way of distinguishing reliably, from within this study, whether or to what extent OPs caused or contributed to the symptoms of neurological damage reported by the study participants.

A significant minority, about one in five, had reported that they had not experienced an acute response but nevertheless included many with neuropathy signs and symptoms. We are cautious in drawing conclusions from these patterns but it may be that some of these are a long term effect of OPs on health, and we conclude that these results support the need for further research addressing this specific question.
Appendix 7: Distributions of the conceptual algorithm variables used in the probabilistic model

Table.App. 7-1: Abbreviations of studies used in this appendix to decide the distributions of the conceptual algorithm variables

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOM93</td>
<td>Occupational Hygiene Assessment of Sheep Dipping Practices and Processes</td>
</tr>
<tr>
<td>IOM96</td>
<td>Occupational hygiene assessment of exposure to insecticides and the effectiveness of protective clothing during sheep dipping operations</td>
</tr>
<tr>
<td>IOM99</td>
<td>Epidemiological study of the relationships between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers, Phase1, Development and Validation of an Organophosphate Uptake Model for Sheep Dippers</td>
</tr>
<tr>
<td>HSE95</td>
<td>An investigation into the possible chronic neuropsychological and neurological effects of occupational exposure to organophosphates in sheep farmers</td>
</tr>
<tr>
<td>REES</td>
<td>Exposure to sheep dip and the incidence of acute symptoms in a group of Welsh sheep farmers</td>
</tr>
<tr>
<td>SHAPE</td>
<td>Survey of Health and Pesticide Exposure: The Telephone Survey</td>
</tr>
<tr>
<td>HSDS</td>
<td>Health and Sheep Dipping Survey</td>
</tr>
<tr>
<td>SHAW</td>
<td>The Study of Health in Agricultural Work</td>
</tr>
</tbody>
</table>

Probability of handling the concentrate

The IOM93 study reported that 14 out of 38 farmers (37%) handled the concentrate in one session while in the SHAW study, 176 out of 193 dippers (91%) had handled the concentrate at some point in their life. Generally, one person is responsible for handling the concentrate in one session. However, the probability of handling the concentrate also depends to a great extent on dipper’s task. Therefore, for the probabilistic model the probability of handling the concentrate was related to the task depending on data from the IOM99 study (Table.App. 7-2).

Table.App. 7-2: Probability of handling the concentrate according to the dipper’s task

<table>
<thead>
<tr>
<th>Dipper’s task</th>
<th>Probability of handling the concentrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plunger</td>
<td>70%</td>
</tr>
<tr>
<td>Chucker</td>
<td>30%</td>
</tr>
<tr>
<td>Helper</td>
<td>5%</td>
</tr>
<tr>
<td>Plunger/chucker</td>
<td>95%</td>
</tr>
<tr>
<td>Chucker/helper</td>
<td>10%</td>
</tr>
<tr>
<td>All tasks</td>
<td>100%</td>
</tr>
</tbody>
</table>
Probability of handling dipped sheep

In SHAW, 28.7% of dippers (54/188) had handled treated sheep at some point in their life, while 22% of dippers (32/146) in HSE95 handled dipped sheep within two days of dipping in the previous ten years. 28.9% of dippers (11/38) in IOM93 handled dipped sheep within 24 hours of the dipping session. Since IOM93 reported the handling of dipped sheep in one session and not over a long period of time, it was used to assume that the probability of handling dipped sheep is 28.9%.

Probability of getting involved in the disposal of sheep dip

77.1% of dippers (145/188) in SHAW had been involved in the disposal of the sheep dip in their life, while in 70% of jobs in SHAPE (199 jobs) the dippers had cleaned out the bath after the session was completed. 5% of 146 dippers in HSE95 were not involved in the disposal of sheep dip in the previous ten years. All of these three studies gave the farmer’s involvement in dip disposal over a long period of time rather than for an individual session, hence the probability was assumed to be dependent on the number of dippers in one session. Therefore it was theoretically assumed that the probability of getting involved in dip disposal is 50%.

Probability of a farmer falling in the bath

In the SHAW study, 10% of farmers reported entering the bath regularly either intentionally or accidently throughout their life while no one mentioned getting wet through entering the bath in the HSDS. Falling into the bath was not mentioned in other studies. This study assumed that the probability of falling in the dipping bath is related to the dipper’s task according to Table.App. 7-3.

<table>
<thead>
<tr>
<th>Dipper’s task</th>
<th>Probability of falling in the bath</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plunger</td>
<td>1%</td>
</tr>
<tr>
<td>Chucker</td>
<td>0.05%</td>
</tr>
<tr>
<td>Helper</td>
<td>0%</td>
</tr>
<tr>
<td>Plunger/chucker</td>
<td>1.5%</td>
</tr>
<tr>
<td>Chucker/helper</td>
<td>0.05%</td>
</tr>
<tr>
<td>All tasks</td>
<td>1.5%</td>
</tr>
</tbody>
</table>
Probability of spilling concentrate on a part of the body

The number of dippers who spilt the concentrate on their body during one session has been reported in two studies; namely HSDS and REES. In the HSDS 4 out of 38 (10.5%) dippers split the concentrate on their skin, while in REES 5 out of 24 (20.8%) split a few drops of concentrate on their body. On the other hand, in SHAPE more than half of the dippers (150/283) reported that they had never spilt any concentrate on any part of their body in their life, 20% spilt the concentrate once a year, 15% 2-3 times a year, and 7% more than 3 times a year. In SHAW about 40% of farmers said that they had spilt the concentrate on some part of their bodies during their lifetime.

Taking into account that these percentages is for all dippers including those who handled the concentrate and those who did not, and that the probability of handling the concentrate in general is 33%, the probability of the spillage of concentrate on a part of the body among dippers who handled the concentrate was assumed 47% depending on HSDS and REES.

Frequency of handling the concentrate

IOM99 reported that 81% of the events of handling the concentrate were to refill the bath, while 10% of the handling events happened during the preparation of the bath. The rest of the events happened during moving the containers to the storage and during washing the empty ones. The average number of handling events in a session was 8. The same study indicated that the average actual replenishments occurred in their study after every 100 sheep but they reported that manufacturers’ recommendation was that the dip should be replenished after every 50 or 60 sheep. The average number of sheep dipped before replenishment was assumed to be 60 according to this recommendation.

Using this average and the distribution of the number of sheep dipped in one session and by adding one compulsory handling event at the beginning of each session, the number of handling concentrate events ranged from 1 to 34 with a mean and standard deviation of 9±6 and a median of 7. The frequency of handling the concentrate was lognormally distributed (Figure.App. 7-1) and hence a lognormal distribution was used for the probabilistic model.
Volume of the concentrate used

This variable was found in three studies as shown in Table.App. 7-4. By using the raw data of three studies the volume of concentrate ranged from 450 to 31600 ml with a mean and standard deviation of 4690±4266. The median was 3825 and the tertiles were 2500 and 5000 ml. Figure.App. 7-2 presents the distribution of this variable.

Table.App. 7-4: Volume of concentrate used in a sheep dipping session

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Volume (ml)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Range</td>
<td></td>
</tr>
<tr>
<td>IOM93</td>
<td>14</td>
<td>2757 ± 1452</td>
<td>2375</td>
<td>450 – 5000</td>
<td></td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>5382 ± 5375</td>
<td>3900</td>
<td>1200 – 31600</td>
<td></td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>4797 ± 2784</td>
<td>4125</td>
<td>1640 – 9700</td>
<td></td>
</tr>
<tr>
<td>All studies a</td>
<td>70</td>
<td>4690 ± 4266</td>
<td>3825</td>
<td>450 – 31600</td>
<td></td>
</tr>
</tbody>
</table>

a Using the raw data of all studies

Figure.App. 7-2: Distribution of volume of concentrate used in the probabilistic model
Type of container

In HSDS 80% of dippers (36/45) used containers of concentrated pesticide and 20% (9/45) used concentrate sachets. Only IOM99 mentioned the shape of the container and out of 20 containers 6 were cylindrical (30%) and 14 were rectangular (70%) whilst no dip sachets was used. Four types of opening and pouring mechanism were found in this study. 14.3% of the containers had a ring pull cap with a pull up plastic spout and a fixed metal carrying handle, 47.6% had a ring pull cap with a pull up plastic spout and a plastic handle, 19% had a metal screw cap with a secondary metal seal, a wide neck, no pouring mechanism and a fixed metal handle, and 19% had a metal screw cap with a secondary metal seal, a plastic pouring trough and a fixed metal handle.

From HSDS and IOM99, the probability of using concentrate sachets was assumed to be 10% and using containers of pesticide concentrate 90%. From IOM99 the probability of the container to have a pouring mechanism was assumed to be 81% and 19% without a pouring mechanism.

Size of container

Only IOM99 mentioned the size of the container. The capacity of all 14 rectangular containers was 5 litres. Three of the cylindrical containers had a capacity of 20 litres, two 5 litres and one 10 litres. Therefore, the probability of the container to be 5 litres was assumed 80%, 10 litres 5%, and 20 litres 15%.

How the concentrate was mixed with bath

Two studies mentioned the way the concentrate was added to the bath. In IOM93, eight farmers out of 14 (57%) used a jug, 3 (21.5%) poured the concentrate directly in the bath, and 3 (21.5%) used an automatic unit. In HSDS 71% of dippers (32/45) poured the concentrate directly in the dipping bath, 20% (9/45) of them used concentrate sachets, and 9% (4/45) used an automatic unit.

The usage of the sachets was not included in the estimation of the probabilities of this variable (MIX) since it was included in the variable of type of container (TYP). Guided by the IOM93 and HSDS studies and assuming that the farmers in the HSDS study who said that they poured the concentrate directly in the bath included those who used a jug, the probabilities of using different ways of mixing was estimated as follows: pouring the concentrate directly in the bath is 28%, using a jug is 55%, and using an automatic unit is 17%.
Duration of the session

The duration of one dipping session ranged from 30 minutes to 750 minutes in different studies (Table.App. 7-5).

Table.App. 7-5: Duration of sheep dipping sessions in UK studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Duration of sheep dipping sessions (minutes)</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOM93</td>
<td>14</td>
<td>225 ± 115</td>
<td>193</td>
<td></td>
<td>75 – 465</td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>145 ±75</td>
<td>123</td>
<td></td>
<td>45 – 372</td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>294 ±105</td>
<td>292</td>
<td></td>
<td>155 – 491</td>
</tr>
<tr>
<td>HSDS</td>
<td>59</td>
<td>282 ±170</td>
<td>270</td>
<td></td>
<td>30 – 750</td>
</tr>
<tr>
<td>All studies a</td>
<td>93</td>
<td>276 ± 151</td>
<td>270</td>
<td></td>
<td>30 – 750</td>
</tr>
</tbody>
</table>

*a Using the raw data of all studies except IOM96

The duration of IOM96 sessions tended to be short due to the nature of that study (i.e. studying the effectivity of PPE) and therefore it was not included in the calculation of all studies. By using the raw data of three studies, the mean and standard deviation of session duration was 276±151 minutes with a median of 270 and tertiles of 180 and 330 minutes. The results are different to what was stated in the SHAPE study which reported that about a half of the sessions lasted between 360 to 480 minutes. However the SHAPE study has depended on the recall of the farmers which is not always accurate. The raw data of the SHAPE study was not available so it was not included in obtaining the distribution of the session durations (Figure.App. 7-3).

Figure.App. 7-3: Distribution of duration of sheep dipping sessions used in the probabilistic model
Number of dipped sheep

The number of sheep dipped in one session is shown in Table.App. 7-6. From these studies, the number of sheep dipped in one session ranged from 1 to 2000 with a mean±SD of 476±385, a median of 369, and of tertiles 250 and 500. Figure.App. 7-4 shows that number of dipped sheep is resembled a normal distribution after square root transformation.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Number of sheep dipped in one session</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOM93</td>
<td>14</td>
<td>659 ± 410</td>
<td>578</td>
<td>200 – 1406</td>
<td></td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>561 ± 436</td>
<td>390</td>
<td>100 – 1670</td>
<td></td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>815 ± 440</td>
<td>650</td>
<td>250 – 1700</td>
<td></td>
</tr>
<tr>
<td>HSDS a</td>
<td>121</td>
<td>532 ± 431</td>
<td>400</td>
<td>1 – 2000</td>
<td></td>
</tr>
<tr>
<td>SHAW b</td>
<td>177</td>
<td>368 ± 284</td>
<td>300</td>
<td>10 – 1717</td>
<td></td>
</tr>
<tr>
<td>All studies c</td>
<td>368</td>
<td>476 ± 385</td>
<td>369</td>
<td>1 – 2000</td>
<td></td>
</tr>
</tbody>
</table>

* A claim of dipping 5600 sheep was ignored, *b* Average of dipping sessions in all years was used for each farmer, *c* Using the raw data of all studies

Dip rate

IOM93 and IOM96 gave the actual dip rates (sheep/hour) in the dipping sessions, whilst it can be calculated from the data given in IOM99. Table.App. 7-7 presents the dip rate in these three studies while Figure.App. 7-5 presents the distribution of this variable when the data of the three studies was combined. Overall the dip rate ranged from 49 to 457 sheep per hour with a mean±SD of 205±99 and a median of 185 with the tertiles (153, 216).
Table.App. 7-7: Dip rate in UK studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Dip rate (sheep/hour)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>IOM93</td>
<td>14</td>
<td>183 ± 98</td>
<td>175</td>
<td>56 – 440</td>
<td></td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>233 ± 106</td>
<td>200</td>
<td>84 – 457</td>
<td></td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>169 ± 72</td>
<td>157</td>
<td>49 – 348</td>
<td></td>
</tr>
<tr>
<td>All studies *</td>
<td>70</td>
<td>205 ± 99</td>
<td>185</td>
<td>49 – 457</td>
<td></td>
</tr>
</tbody>
</table>

* Using the raw data of all studies

![Distribution of dip rate in sheep dipping sessions](image.png)

**Figure.App. 7-5: Distribution of dip rate in sheep dipping sessions used in the probabilistic model**

**Number of dippers**

As shown in Table.App. 7-8, the number of dippers in all studies has ranged from one to five. About 45% of the dipping sessions was performed in the presence of three workers and a third of them was performed by two workers.

Table.App. 7-8: Number of dippers in one dipping session in UK studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Farms with specific number of dippers, number (%)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>One (7)</td>
<td>Two (36)</td>
<td>Three (36)</td>
<td>Four (21)</td>
<td>Five (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOM93</td>
<td>14</td>
<td>1 (7)</td>
<td>5 (36)</td>
<td>5 (36)</td>
<td>3 (21)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOM96</td>
<td>24</td>
<td>0 (0)</td>
<td>11 (46)</td>
<td>11 (46)</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>16 (80)</td>
<td>2 (10)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSDD</td>
<td>49 *</td>
<td>5 (10)</td>
<td>21 (43)</td>
<td>15 (31)</td>
<td>5 (10)</td>
<td>3 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHAW</td>
<td>189 *</td>
<td>7 (4)</td>
<td>64 (34)</td>
<td>85 (45)</td>
<td>28 (15)</td>
<td>5 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All studies b</td>
<td>296</td>
<td>13 (4.4)</td>
<td>103 (34.8)</td>
<td>132 (44.6)</td>
<td>40 (13.5)</td>
<td>8 (2.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Number of farmers, b Using the raw data of all studies

**Farmer’s task**

Usually there are three different tasks in any dipping session; paddler (plunger), chucker and helper. However, sometimes the farmer may do two tasks in the same session, for
example being a plunger and chucker or a chucker and helper at the same time, and sometimes a contractor may do the whole dipping session by himself. Therefore there are seven combinations of tasks; plunger, chucker, helper, plunger and chucker, plunger and helper, chucker and helper, and all the tasks. However it is not reasonable for the plunger to work also as a helper if he was not the only dipper (i.e. there was a chucker) because it is easier to the chucker to bring the sheep while the plunger usually stays close to the bath. Therefore working as a plunger and helper in the same time was not mentioned in previous studies (Table.App. 7-9).

In HSE95 (n = 146), 36% of farmers performed more than one task over the previous ten years, 36% worked as a plunger, 25% worked as a chucker, and only 3% worked as a helper. In SHAW (n = 188), 37.7% of the farmers worked only as a plunger in all their dipping sessions, 13.3% only as a chucker, 4.3% only as a helper, and 13.8% carried out different tasks but in different sessions. The rest worked in more than one task in the same session; 22.9% worked as plunger and chucker, 1.1% worked as chucker and helper, and 6.9% carried out all tasks.

Table.App. 7-9 presents the number of farmers carrying out each task or combinations of tasks in those studies which gave information on tasks in one dipping session. By combining the studies together, the assumed probability of the farmer to be a plunger is 35%, a chucker 22%, a plunger and chucker 12.5%, a helper 24.5%, a chucker and helper 5%, and the probability of doing all the tasks is 0.5% (all figures were rounded to the closest 0.5).

**Table.App. 7-9: Dippers’ tasks in UK studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farmers</th>
<th>Dippers’ task, number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Plunger</td>
</tr>
<tr>
<td>IOM93</td>
<td>38</td>
<td>11 (28.9)</td>
</tr>
<tr>
<td>IOM96</td>
<td>63</td>
<td>24 (38.1)</td>
</tr>
<tr>
<td>IOM99</td>
<td>60</td>
<td>18 (30)</td>
</tr>
<tr>
<td>HSDS*</td>
<td>123</td>
<td>47 (38.2)</td>
</tr>
<tr>
<td>All Studies *</td>
<td>284</td>
<td>100 (35.2)</td>
</tr>
</tbody>
</table>

* Using the raw data of all studies

**Submerging tool**

Table.App. 7-10 presents the tools used to submerge sheep in the dip as used in different studies. Guided by the data in the table and taking into account the nature of the studies, it was assumed that the probability of using wooden tool is 45%, using metal tool is 35%, using feet is 8%, using hands is 8%, and using feet and tool is 4%.
Table.App. 7-10: Submerging tool used by plungers in UK studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of plungers</th>
<th>Wooden (%)</th>
<th>Metal (%)</th>
<th>Feet (%)</th>
<th>Hands (%)</th>
<th>Feet/Hands (%)</th>
<th>Feet/Tool (%)</th>
<th>Other (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOM93</td>
<td>14</td>
<td>11(78.6)</td>
<td>1 (7.1)</td>
<td>1 (7.1)</td>
<td>0 (0)</td>
<td>1 (7.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>IOM96</td>
<td>12</td>
<td>5(41.7)</td>
<td>6 (50)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (8.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>9(45)</td>
<td>8 (40)</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>HSDD</td>
<td>48</td>
<td>38(79.2)</td>
<td>7 (14.6)</td>
<td>1 (2.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (4.2)</td>
<td></td>
</tr>
<tr>
<td>HSE95 a</td>
<td>Unknown</td>
<td>(51) b</td>
<td>(30) b</td>
<td>(11) b</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>(8) b</td>
</tr>
<tr>
<td>SHAPE c</td>
<td>149</td>
<td>96(64.4)</td>
<td>2(1.3)</td>
<td>26(17.4)</td>
<td>1(0.7)</td>
<td>1(0.7)</td>
<td>23(15.4)</td>
<td></td>
</tr>
<tr>
<td>SHAPE d</td>
<td>224</td>
<td>121(54)</td>
<td>64(29)</td>
<td>11(5)</td>
<td>20(9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>8(4)</td>
</tr>
</tbody>
</table>

* a Over the previous ten years, b Number of plungers is unknown, c Throughout the working life

Bath location

In SHAW 86% of the farmers used an outdoor bath throughout their working life, 2.5% of them used a bath in a covered area, and 2.5% of them used a bath inside buildings, while one dipper 0.5% used the bath only in a trailer. The rest (8.5%) used baths in different locations at different periods of times. 58% of the dippers in IOM99 used baths outside buildings in an exposed area, 21% of the dippers used them in a sheltered area, and 21% used them within a trailer (i.e. those who used a mobile bath). Guided by these two studies, it was assumed that the probability of using an outside bath in an exposed area was 70%, in a sheltered area 10%, in a building 10%, and in a trailer 10%.

Bath type

Three studies mentioned bath type used throughout the working life of the farmer and four studies mentioned use for one session only. The percentages of the utilised bath type in each study are shown in Table.App. 7-11. Guided by the data of all these studies, it was assumed that the probability to use straight bath was 75%, circular bath 20%, and mobile bath 5%.

Table.App. 7-11: Bath type used for sheep dipping in UK studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Straight (%)</th>
<th>Circular (%)</th>
<th>Mobile (%)</th>
<th>Mixed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Short swim</td>
<td>Long swim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOM93</td>
<td>14</td>
<td>3(21)</td>
<td>3(21)</td>
<td>5(36)</td>
<td>3(21)</td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>9(25)</td>
<td>9(25)</td>
<td>18(50)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>4(20)</td>
<td>6(30)</td>
<td>5(25)</td>
<td>5(25)</td>
</tr>
<tr>
<td>REES</td>
<td>24 a</td>
<td>24(100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>HSE95 b</td>
<td>Unknown</td>
<td>(63) c</td>
<td>(17) c</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>SHAW d</td>
<td>188 a</td>
<td>139(74)</td>
<td>10(5)</td>
<td>0 (0)</td>
<td>39(21)</td>
</tr>
<tr>
<td>SHAPE d</td>
<td>284 a</td>
<td>229(81)</td>
<td>27(10)</td>
<td>17(6)</td>
<td>11(4)</td>
</tr>
</tbody>
</table>

* a Number of farmers, b Over the previous ten years, c Number of baths is unknown, d Throughout the working life
Sheep entry

Four studies mentioned the method of the sheep entry into the bath. In IOM93, sheep entered the bath from their front in three farms out of 12 (25%), backwards in three farms (25%), from their side in 5 (41.7%), and at one farm (8.3%) the sheep were thrown into the bath. In IOM96, sheep entered from the front in one farm out of 12 (8.3%), backwards in four farms (33.3%), from the side in two farms (16.7%), and five farms used mixed methods (41.7%).

In IOM99, a manual method was used in 8 farms out of 20 (40%), a slipway in 10 (50%), a slope in one (5%), and a walk in method in one farm (5%). In the SHAW study 52.7% of the farmers had used a manual method to enter their sheep in the bath throughout their life, 27.4% used a slipway, 2.2% used a walk in method, and the rest used mixed methods. Guided by all these studies it was assumed that the probability of using manual method is 50%, slipway method (tilt) 40%, and walk in method (slope or ramp) 10%.

Splash guard

The presence of a splash guard alongside the bath varied between the studies. 15% of the baths in IOM99 had splash guards which was similar to that reported in IOM93, while 75% of the baths in IOM96 had splash guards. In SHAW, 15.7% of farmers always worked with baths which had a splash guard, while 8% of the farmers worked sometimes with a bath with a splash guard. Guided by these studies it was assumed that 20% of the baths have splash guards.

Method of the disposal of the sheep dip

Three studies mentioned this variable. 5% of the farmers (7/146) in HSE95 were not involved in the disposal of sheep dip in the previous ten years, whereas 32% of them removed it manually (bucket), 2% used a manual pump, 23% used a mechanical pump, 24% used a drain, 1% used other methods, and 12% used more than one method. In IOM93, nine out of 13 dippers (69.2%) pumped the wash into a tank, one used a tanker (7.7%), one used a drain to soak-away (7.7%), and 2 removed the dip manually (15.4%). In SHAPE, 50% of dippers removed the dip manually, whereas 20% used a slurry tanker and the rest used other methods. Guided by these studies and taking into account that the nature of “other methods” in SHAPE is unknown, the probability of
using manual method was assumed to be 35%, mechanical pump or a tanker 50%, and using a drain 15%.

**Volume of sheep dip**

This variable has been described in three studies and was summarised in Table.App. 7-12. The volume of sheep dip in these studies ranged from 755 to 4500 litres with a mean±SD of 1934.2±807 and a median of 1820 with the tertiles (1630, 2000). Figure.App. 7-6 presents the distribution of this variable when the data of the three studies combined together.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of farms</th>
<th>Litres</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>IOM93</td>
<td>14</td>
<td>2150 ± 1086</td>
<td>1900</td>
<td>900 – 4500</td>
<td></td>
</tr>
<tr>
<td>IOM96</td>
<td>36</td>
<td>1932 ± 658</td>
<td>1820</td>
<td>755 – 3640</td>
<td></td>
</tr>
<tr>
<td>IOM99</td>
<td>20</td>
<td>1787 ± 838</td>
<td>1700</td>
<td>800 – 4000</td>
<td></td>
</tr>
<tr>
<td>All studies *</td>
<td>70</td>
<td>1934 ± 807</td>
<td>1820</td>
<td>755 – 4500</td>
<td></td>
</tr>
</tbody>
</table>

* Using the raw data of all studies

**Atmospheric conditions**

Information about atmospheric conditions was only found in IOM99. The weather was still in 2 farms out of 20 (10%), breezy in 17 (85%) and gusting in 1 farm (5%). The temperature ranged from 10.5 to 22 °C while the relative humidity ranged from 48 to 85%. Only the distribution of the wind was used in the probabilistic model since it was assumed that it is the most important atmospheric exposure determinants.
PPE used during dipping activities

All studies except REES mentioned the frequency of using PPE during dipping sessions. IOM96 was excluded because it was performed to study the efficacy of PPE in the dipping process. Three studies (SHAW, SHAPE, and HSE93) gave the frequency of the usage over a long period of time while the other three gave it for only one dipping session. Three studies (SHAW, SHAPE, and IOM99) differentiated between using PPE in handling the concentrate and in dipping sheep in the diluted dip, while other studies did not consider this difference. The way of combining different types of PPE varied from one study to another and therefore relatively similar types of PPE were combined into one category to get the final distribution. For example leggings and waterproof trousers were combined in one category while boiler suit and an overall were also combined together. Table.App. 7-13 presents the frequency of using PPE in sheep dipping process in different studies.

Table.App. 7-13: PPE use during sheep dipping activities in UK studies

<table>
<thead>
<tr>
<th>PPE</th>
<th>IOM99 CON (n=32)</th>
<th>DIP (n=60)</th>
<th>SHAPE a CON (n=206)</th>
<th>DIP (n=330)</th>
<th>SHAW b CON (n=176)</th>
<th>DIP (n=188)</th>
<th>IOM93 All activities (n=38)</th>
<th>HSE93 All activities (n=144)</th>
<th>HSDS All activities (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves</td>
<td>44</td>
<td>18</td>
<td>49</td>
<td>27</td>
<td>36</td>
<td>28</td>
<td>8</td>
<td>23</td>
<td>40</td>
</tr>
<tr>
<td>Boots</td>
<td>88</td>
<td>80</td>
<td>NR</td>
<td>63</td>
<td>92</td>
<td>94</td>
<td>95</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>Trousers/legging</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>58</td>
<td>60</td>
<td>72</td>
<td>74</td>
<td>88</td>
<td>72</td>
</tr>
<tr>
<td>Apron/overall</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>21</td>
<td>44</td>
<td>54</td>
<td>13</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Coat</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>33</td>
<td>NR</td>
<td>NR</td>
<td>37</td>
<td>41</td>
<td>33</td>
</tr>
<tr>
<td>Face protection</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>2.6</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Head protection</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>15</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Respirator</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0.6</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

a Over the last ten years, b Throughout working life, c This is the percentage of farmers who used glove always during handling the concentrate, d NR: not reported, e When handling the concentrate at the start of dipping

Using judgment guided by the frequencies in these studies and taking into account the nature of each study, the final probabilities of using PPE during handling the concentrate and during dipping sheep were assumed as shown in Table.App. 7-14.

Since only the prevalence of using PPE in handling the concentrate and in dipping sheep in the diluted pesticide is available, it has been assumed that the use of PPE during
handling dipped sheep and during the disposal of sheep dip is the same as that during sheep dipping.

### Table.App. 7-14: Probability of using PPE during sheep dipping activities

<table>
<thead>
<tr>
<th>PPE</th>
<th>Probability of using PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>During handling the concentrate</td>
</tr>
<tr>
<td>Gloves</td>
<td>40%</td>
</tr>
<tr>
<td>Waterproof boots</td>
<td>90%</td>
</tr>
</tbody>
</table>
| Waterproof trousers/legging | 60%  
  (67% if apron was not worn) | 75%  
  (83% if apron was not worn) |
| Waterproof apron/overall  | 10%                                      | 10%                        |
| Waterproof coat           | 41%                                      | 41%                        |
| Face protection (visor)   | 7%                                      | 7%                        |
| Head protection (hat)     | 6%                                      | 6%                        |
| Respirator                | 0.5%                                     | 0.5%                      |

### Personal hygiene and behaviour

Three studies reported farmers’ behaviour related to their personal hygiene after any concentrate spillage. In SHAW 57 dippers out of 111 (51.3%) said that they generally washed the concentrate off immediately after spillage, 53 (47.7%) did that at the end of the session, and only one person (1%) never washed off the spillage. REES mentioned that 2 dippers out of 5 washed the concentrate off immediately while the remaining 3 did so later in the day. In HSDS study, 12 out of 39 dippers (30.8%) washed off the sheep dip immediately, 10 (25.6%) before meal breaks, 11 (28.2%) at the end of the day, and 6 (15.4%) at other intervals. However, this duration is for both concentrate and diluted dip and only two dippers spilt the concentrate on a part of their body. Guided by these three studies it was assumed that 50% of dippers would wash the spillage off immediately, 25% before meal breaks, and 25% at the end of the session.

Three studies also recorded farmers’ behaviour related to washing any contamination from the diluted sheep dip; the HSDS which is just mentioned, the IOM93 and the IOM96. In IOM93 only one farm team out of 14 (7%) washed off the contamination regularly, 6 (43%) occasionally did so and 7 (50%) never did. In IOM96 farmers rarely washed after splashing and only six farmers in all farms did that occasionally after a major splash to the face. In the same study, all dippers at 10 farms out of 12 (83.3%) washed at the end of the session, whereas in one farm (8.3%) only some farmers did and in another farm (8.3%) nobody washed. Guided by these studies it was assumed that the
The probability of washing the sheep dip off regularly is 15%, occasionally or at the end of day is 85%.

All dippers who smoked in IOM93 and IOM96 did not wash their hands before smoking. However, since the prevalence of smoking among dippers is not available, smoking was not included in the probabilistic model.

**Other variables**

No information was available about the following variables that were described as exposure determinants: the area of bath surface, the nature of handling dipped sheep, the duration between dipping and handling dipped sheep, the number of dipped sheep handled, the length of fleece, the place for gathering sheep after dipping, the duration of the dip disposal, how old was the sheep dip when it was disposed, atmospheric conditions during handling the dipped sheep and during the disposal of sheep dip, number of falls in the bath in one session, level of immersion when fall in the bath, frequency of spilling the concentrate on the body, and the personal hygiene and behaviour during and after handling the dipped sheep, during and after the disposal of sheep dip, and after any fall in the bath.
Appendix 8: Telephone Questionnaire: Using pesticides in cattle farming

Farmer IN:

1. Warble fly treatment
   - No:
   - Yes:
     - From: To: pre 1982: Derris
     - Frequency:
     - OP Frequency:
     - post 1982: pour-on
     - Frequency:
     - injection Frequency:

2. Flies treatment
   - No:
   - Yes:
     - non OP:
     - OP: Usage: Years:
     - Frequency:

3. Lice treatment
   - No:
   - Yes:
     - non OP:
     - OP: Usage: Years:
     - Frequency:

4. Other OP cattle treatment:

   - If dose not know the type, write DK in the OP section and then the frequency.
   - Frequency means number of cattle and how many times per year.
Appendix 9: Rules used for data handling of occupational pesticide exposure

Table.App. 9-1: General rules for phase 2 data entry in all farming sectors

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Consider year 1942 as the start year for the cumulative exposure</td>
</tr>
<tr>
<td>2</td>
<td>Age of 10 was considered as the first year of work included in the cumulative exposure</td>
</tr>
<tr>
<td>3</td>
<td>Remove the overlap between periods by deleting a year from the second period</td>
</tr>
<tr>
<td>4</td>
<td>If the farmer used a contractor or was not involved personally in the treatment in specific years, those years were not included in the exposure</td>
</tr>
<tr>
<td>5</td>
<td>All antibiotics, iodine, hormones, formalin, formaldehyde, and vaccines were ignored</td>
</tr>
<tr>
<td>6</td>
<td>(Do not know) was considered as (NO) in handling the concentrate, concentrate spillage, using PPE and contacting treated livestock</td>
</tr>
<tr>
<td>7</td>
<td>If the farmer mentioned PPE for a specific method of applying (e.g. dipping) but not about using PPE in other application methods, consider it as none for those methods</td>
</tr>
</tbody>
</table>

Table.App. 9-2: Rules for phase 2 sheep farming data entry

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If the farmer treated his sheep x times during a period of time, choose x years from that period and put one treatment per year</td>
<td>General</td>
</tr>
<tr>
<td>2</td>
<td>If the flock size was with (X/1½), consider X as ewes and (X×1.5) as lamb</td>
<td>2.1.2</td>
</tr>
<tr>
<td>3</td>
<td>If the farmer gave (times per year) instead of (days per year), (days per year) will be (flock size/average treated per day × times per year)</td>
<td>2.1.2</td>
</tr>
<tr>
<td>4</td>
<td>Farmers who have multiple treatment methods in the same year, the average number of treating days per year was divided by the number of methods in that year</td>
<td>2.1.2</td>
</tr>
<tr>
<td>5</td>
<td>If the file mentioned (all) or (half) in the average number of treated sheep per day and max num of sheep and the number after the word (all) or (half) is not consistent with the real number which we have, ignore that figure and write the right number (which written in flock size)</td>
<td>2.1.2</td>
</tr>
<tr>
<td>6</td>
<td>Delete (what pesticide used for) and (amount of concentrate)</td>
<td>2.2</td>
</tr>
<tr>
<td>7</td>
<td>If the task is showering then entering bath will be not applicable (N/A)</td>
<td>2.7</td>
</tr>
<tr>
<td>8</td>
<td>(Do not know) was considered as (NO)</td>
<td>2.7&amp;2.8</td>
</tr>
<tr>
<td>9</td>
<td>If the farmer mentioned using PPE in handling concentrate in period smaller than the original period, consider the years before the period of using PPE as (none PPE) and the years after as stop handling concentrate, i.e. N/A</td>
<td>2.9</td>
</tr>
</tbody>
</table>
Table.App. 9-3: Rules for phase 2 cattle farming data entry

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All farmers who had cattle but said that they did not treat them at all with pesticides were given zero exposure from cattle treatment. One farmer had mentioned treating cattle in the TQ, although he did not mentioned that in the OEQ; this treatment was ignored.</td>
<td>General</td>
</tr>
<tr>
<td>2</td>
<td>Five farmers have not contacted by phone and the answers were taken from the original OEQ since they were clear.</td>
<td>General</td>
</tr>
<tr>
<td>3</td>
<td>When there is a disagreement between herd size in the TQ and in the OEQ, the number found in the OEQ was used.</td>
<td>General</td>
</tr>
<tr>
<td>4</td>
<td>When no years were mentioned it is assumed that it was used in all years, while for warble fly treatment treating years were assumed to be only the compulsory years.</td>
<td>General</td>
</tr>
<tr>
<td>5</td>
<td>Injections were ignored because it is taken into account in a different part in the model.</td>
<td>TQ a</td>
</tr>
<tr>
<td>6</td>
<td>If the farmer said that he used the same treatment for two reasons, in order not to be counted twice the treatment was used for only one reason as follows: warble and lice (one farmer) keep it to warble, flies and lice (two farmers) keep it to lice.</td>
<td>TQ</td>
</tr>
<tr>
<td>7</td>
<td>In the frequency of treatment, if number of treating years or number of treated cattle was given in range, the average was used.</td>
<td>TQ</td>
</tr>
<tr>
<td>8</td>
<td>Many farmers said that they used warble treatment for x years between zzzz and yyyy, although the mentioned years were more than x, so we deleted years which are farthest from the compulsory years of warble fly treatment (1978-1985).</td>
<td>TQ.1</td>
</tr>
<tr>
<td>9</td>
<td>Missing DPY was assumed 1 day per year and missing ATA was assumed all cattle.</td>
<td>TQ.1</td>
</tr>
<tr>
<td>10</td>
<td>For DPY, (Summer) and (Everyday) was considered as 90 days per year, while (occasionally) was considered as 1 day per year.</td>
<td>TQ.2</td>
</tr>
<tr>
<td>11</td>
<td>For ATA, (Milking) or (Dairy) was considered as (herd size/50) rounded up to the nearest one, because it was mostly spray in the air not on each cattle. (50) is arbitrary and means that for each 50 cattle there will be one an additional unit for ATA.</td>
<td>TQ.2</td>
</tr>
<tr>
<td>12</td>
<td>Missing ATA was assumed (Dairy) while missing DPY was assumed (Summer).</td>
<td>TQ.2</td>
</tr>
<tr>
<td>13</td>
<td>For DPY, (not every year) was assumed as every other year, while for ATA, (a few) was assumed 10% of the herd. And if the farmer said just (Occasionally) or (a few), DPY was assumed (every other year) and ATA was assumed 10% of the herd.</td>
<td>TQ.3</td>
</tr>
<tr>
<td>14</td>
<td>Missing DPY was assumed 1 and missing ATA was assumed all cattle.</td>
<td>TQ.3</td>
</tr>
</tbody>
</table>

a TQ: Telephone Questionnaire  
b OEQ: Occupational and Exposure Questionnaire  
c ATA: average treated animals  
d DPY: average treating days per year

Table.App. 9-4: Rules for phase 2 other livestock farming data entry

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All poultry, laying hens and chickens were considered as poultry.</td>
<td>4.1</td>
</tr>
<tr>
<td>2</td>
<td>One farmer used (other method), this method was supposed (pour-on).</td>
<td>4.2</td>
</tr>
<tr>
<td>3</td>
<td>One farmer did not remember start date of treatment and it was considered to be from the first year of having that livestock.</td>
<td>4.2</td>
</tr>
<tr>
<td>4</td>
<td>One farmer used a pump to apply fly repellent on Pigs once per week therefore ATA was assumed 1.</td>
<td>4.2</td>
</tr>
<tr>
<td>5</td>
<td>ATA was set as number of thousands in poultry since it was used like that in the exposure assessment model.</td>
<td>4.2</td>
</tr>
<tr>
<td>6</td>
<td>Missing ATA in pigs was assumed all the herd, while in poultry (2 cases) was assumed less than 1000 (which means score 1 in the model).</td>
<td>4.2</td>
</tr>
<tr>
<td>7</td>
<td>Missing DPY was assumed 1.</td>
<td>4.2</td>
</tr>
</tbody>
</table>

a ATA: average treated animals  
b DPY: average treating days per year
### Table.App. 9-5: Rules for phase 2 crops and grains data entry

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>One farmer did not apply pesticides, he only mixed chemicals therefore he is included only in concentrate part of the model</td>
</tr>
<tr>
<td>2</td>
<td>One farmer used pesticides pre-seeding and he was ignored</td>
</tr>
<tr>
<td>3</td>
<td>If farmer gave a range in any question, the average will be used</td>
</tr>
<tr>
<td>4</td>
<td>A full working day was assumed 8 hours</td>
</tr>
<tr>
<td>5</td>
<td>If the answer for average number of hours per day was ½ it was considered as half a day</td>
</tr>
<tr>
<td>6</td>
<td>Average number of days/year was rounded up (e.g. 0.5 will be 1)</td>
</tr>
<tr>
<td>7</td>
<td>All grass lands, thistles, and weed were ignored because it has been assumed that all farmers who had sheep or cattle would have grasslands but not all of them would mention it in this section</td>
</tr>
<tr>
<td>8</td>
<td>Application on grain were ignored (2 farmers) since it is included in different part</td>
</tr>
<tr>
<td>9</td>
<td>Two farmers has said that they used aerial application, they were assumed using airblast since their farm area is too small for aerial application</td>
</tr>
<tr>
<td>10</td>
<td>One farmer did not know the application method on kale and it was assumed similar to those farmers who worked with turnips</td>
</tr>
<tr>
<td>11</td>
<td>Two farmers gave the area of treated crops including the grass land, grass land was assumed half of the area</td>
</tr>
<tr>
<td>12</td>
<td>One farmer gave total area for all crops so we estimated that half of it was for (wheat and barley) a quarter for (oil seed and potatoes) and a quarter for (sugar beet)</td>
</tr>
<tr>
<td>13</td>
<td>Missing area was found in two cases and we don’t have their info in JSAH, the area was taken from question D9 and the grass land was assumed half of the farm land.</td>
</tr>
<tr>
<td>14</td>
<td>When farmer gave days/year for all crops together it was divided for each crop including grass according to the area as all of them were applied by same method</td>
</tr>
<tr>
<td>15</td>
<td>For days/year: 3 cases were unknown and 1 case was missing. They were assumed by looking for similar farmers according to crop, area and application method</td>
</tr>
<tr>
<td>16</td>
<td>For hours/day: “varied” was assumed as 6 hours</td>
</tr>
<tr>
<td>17</td>
<td>For hours/day: 5 cases were unknown and 4 cases were missing. They were assumed by looking for similar farmers according to crop, area and application method</td>
</tr>
</tbody>
</table>

### Table.App. 9-6: Rules for phase 2 other pesticide use data entry

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If there was no date and no name, the line was ignored</td>
</tr>
<tr>
<td>2</td>
<td>Product names without dates and reasons were ignored</td>
</tr>
<tr>
<td>3</td>
<td>When the product was unknown it was assumed a pesticide if it was used as spot treatments around the farm or was used to kill insects, molluscs or rodents</td>
</tr>
<tr>
<td>4</td>
<td>One farmer did not answer a question about having a grain storage or application on it, and the answer was assumed (No)</td>
</tr>
</tbody>
</table>
Appendix 10: Deterministic values of REST variables in the SHAW algorithm

<table>
<thead>
<tr>
<th>Variable</th>
<th>Equation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>REST\textsubscript{con.der}</td>
<td>COVOL(2)\times TYP(1)\times MIX(1.9)\times SIZ(1)\times DUR(1.8)\times PHWH(1)\times ATM(1.1)</td>
<td>7.524</td>
</tr>
<tr>
<td>REST\textsubscript{con.ing}</td>
<td>COVOL(2)\times TYP(1)\times MIX(2.4)\times SIZ(1)\times DUR(1.6)\times PHWH(1)\times ATM(1.1)</td>
<td>8.448</td>
</tr>
<tr>
<td>REST\textsubscript{con.inh}</td>
<td>COVOL(2)\times TYP(1)\times MIX(1.7)\times ATM(0.7)</td>
<td>2.38</td>
</tr>
<tr>
<td>REST\textsubscript{dip.der}</td>
<td>DUR(2)\times RATE(2)\times PHWH(1)\times ATM(1.1)</td>
<td>4.4</td>
</tr>
<tr>
<td>REST\textsubscript{dip.ing}</td>
<td>DUR(2)\times RATE(2)\times PHWH(1)\times ATM(1.1)</td>
<td>4.4</td>
</tr>
<tr>
<td>REST\textsubscript{dip.inh}</td>
<td>DUR(2)\times RATE(2)\times SUR(1)\times ATM(0.9)</td>
<td>3.6</td>
</tr>
<tr>
<td>REST\textsubscript{aft.der}</td>
<td>NAT(1)\times FLOAFT(1)\times DUR(1)\times LENGTH(1)\times GATHER(1)\times PHWH(1)\times ATM(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{aft.ing}</td>
<td>NAT(1)\times FLOAFT(1)\times DUR(1)\times LENGTH(1)\times GATHER(1)\times PHWH(1)\times ATM(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{aft.inh}</td>
<td>NAT(1)\times FLOAFT(1)\times DUR(1)\times LENGTH(1)\times GATHER(1)\times ATM(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{dis.der}</td>
<td>METHOD(1.2)\times VOL(2)\times DURDIS\times OLD(1)\times PHWH(1)\times ATM(1)</td>
<td>2.4</td>
</tr>
<tr>
<td>REST\textsubscript{dis.ing}</td>
<td>METHOD(1.1)\times VOL(2)\times DURDIS\times OLD(1)\times PHWH(1)\times ATM(1)</td>
<td>2.2</td>
</tr>
<tr>
<td>REST\textsubscript{dis.inh}</td>
<td>METHOD(1)\times VOL(2)\times DURDIS\times OLD(1)\times ATM(1)</td>
<td>2</td>
</tr>
<tr>
<td>REST\textsubscript{inc.der1}</td>
<td>FALL(1)\times LEVEL(1)\times PHWH(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{inc.der2}</td>
<td>SPI(1)\times AMOUNT(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{inc.ing1}</td>
<td>FALL(1)\times PHWH(1)</td>
<td>1</td>
</tr>
<tr>
<td>REST\textsubscript{inc.inh}</td>
<td>SPI(1)\times AMOUNT(1)</td>
<td>1</td>
</tr>
</tbody>
</table>
Appendix 11: Details of exposure assessment model in the SHAPE study

The following tables in this appendix are taken from Appendix D in the SHAPE study

Table.App. 11-1: Variables used in the exposure assessment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Constant or Formula</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{sk,dip}$</td>
<td>1</td>
<td>Dimensionless concentration measure</td>
</tr>
<tr>
<td>$C_{sk,conc}$</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>$C_{sk,residue}$</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>$S_{sk}$</td>
<td>1.35 m²</td>
<td>Days dipping.</td>
</tr>
<tr>
<td>$S_{sk, hands}$</td>
<td>0.1 m²</td>
<td></td>
</tr>
<tr>
<td>$S_{sk, total}$</td>
<td>1.9 m²</td>
<td></td>
</tr>
<tr>
<td>$d$</td>
<td>-</td>
<td>Years in this job.</td>
</tr>
<tr>
<td>$y$</td>
<td>-</td>
<td>Hours per day dipping.</td>
</tr>
<tr>
<td>$N_{falls}$</td>
<td>-</td>
<td>Number of instances of falling into dip bath.</td>
</tr>
<tr>
<td>$N_{clean}$</td>
<td>-</td>
<td>Number of instances of cleaning dip bath.</td>
</tr>
<tr>
<td>$t_{beforewash}$</td>
<td>0.1</td>
<td>Days</td>
</tr>
<tr>
<td>$t_{clean}$</td>
<td>0.2</td>
<td>Time in days from starting cleaning until washing or showering</td>
</tr>
<tr>
<td>$t_{dip}$</td>
<td>$d.y.(h+1)\Delta_{dip} ÷ 8$</td>
<td>One hour added to allow for the time from finishing work until the time the person washed.</td>
</tr>
<tr>
<td>$\Delta_{dip}$</td>
<td>-</td>
<td>Chucker and paddler combined. Always = 1; Mostly = 0.75; Some = 0.25; None = 0</td>
</tr>
<tr>
<td>$t_{conc}$</td>
<td>$d.y.(1+1)\Delta_{dip} ÷ 8$</td>
<td>Assumes maximum of one hour spent diluting concentrate each dipping day plus one hour from time finished until time washed.</td>
</tr>
<tr>
<td>$\Delta_{conc}$</td>
<td>-</td>
<td>Always = 1; Mostly = 0.75; Some = 0.25; None = 0</td>
</tr>
<tr>
<td>$t_{splash}$</td>
<td>$y \cdot SR$</td>
<td></td>
</tr>
<tr>
<td>$SR$</td>
<td>-</td>
<td>Never = 0; 1 per yr = 1; 2-3 per yr = 2.5; 3+ per yr = 5</td>
</tr>
<tr>
<td>$t_{wethand}$</td>
<td>$d.y.(h+1)\Delta_{wethand} ÷ 8$</td>
<td>As above</td>
</tr>
<tr>
<td>$\Delta_{wethand}$</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>$t_{dryhand}$</td>
<td>$d.y.(h+1)\Delta_{dryhand} ÷ 8$</td>
<td>As above</td>
</tr>
<tr>
<td>$\Delta_{dryhand}$</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>$P_{clo,n}$, $P_{gloves}$</td>
<td>-</td>
<td>Always = 1; Mostly = 0.75; Some = 0.25; None = 0</td>
</tr>
</tbody>
</table>

Table.App. 11-2: Model Factors for Clothing and Gloves during Dipping

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk}$</th>
<th>$S_{sk}$</th>
<th>$A_{clo}$</th>
<th>$\eta_{clo,dip}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Legs and lower torso</td>
<td>Trousers (overalls)</td>
<td>0.8</td>
<td>0.83</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>Feet</td>
<td>Footwear</td>
<td>1</td>
<td>0.13</td>
<td>1</td>
<td>0.9 b</td>
</tr>
<tr>
<td>3</td>
<td>Arms and upper torso</td>
<td>Jacket (overalls and bib)</td>
<td>0.6</td>
<td>0.71</td>
<td>1</td>
<td>0.9 e</td>
</tr>
<tr>
<td>4</td>
<td>Head</td>
<td>Hat and Visor</td>
<td>0.2</td>
<td>0.13</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>Hands</td>
<td>Gloves</td>
<td>1</td>
<td>0.10</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

* It is not always possible to add the clothing parts together since some will cover all or part of the body of another item. For example, an overall will cover the same area as trousers and a jacket. Some pre-processing of the data will be needed to remove items of clothing that duplicate the protection, e.g. wearing a jacket over overalls. More detail is given below in Table 3. This approach should also be used for other situations where clothing combinations may be used, e.g. Table 5 and 6.

b Except when the respondent says they used their feet to submerge the sheep when zero should be used.

e Except when the respondent says they used hands to submerge the sheep when zero should be substituted.
Table.App. 11-3: Details of clothing combinations for dipping

<table>
<thead>
<tr>
<th>Clothing combination</th>
<th>Final assignment of clothing</th>
</tr>
</thead>
<tbody>
<tr>
<td>If overall worn in any combination with jacket and/or trousers</td>
<td>Trousers and jacket</td>
</tr>
<tr>
<td>If bib worn without jacket or trousers</td>
<td>$A_{clo,1} = 0.5$ and $A_{clo,1} = 0.25$</td>
</tr>
<tr>
<td>If bib worn with trousers</td>
<td>$A_{clo,1} = 0.5$ and $A_{clo,1} = 1$</td>
</tr>
<tr>
<td>If bib worn with jacket</td>
<td>$A_{clo,1} = 1$ and $A_{clo,1} = 0.25$</td>
</tr>
<tr>
<td>If only hat worn on head</td>
<td>$A_{clo,4} = 0.4$</td>
</tr>
<tr>
<td>If only visor worn</td>
<td>$A_{clo,4} = 0.3$</td>
</tr>
</tbody>
</table>

The following tables give corresponding details for handling concentrate and the other exposure activities.

Table.App. 11-4: Model Factors for Gloves during handling concentrate

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk,conc}$</th>
<th>$S_{sk,hns}$</th>
<th>$A_{glv}$</th>
<th>$\eta_{glv}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Hands</td>
<td>Gloves</td>
<td>0.05</td>
<td>0.10</td>
<td>1</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Table.App. 11-5: Model Factors for Clothing and Gloves for concentrate splash

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk}$</th>
<th>$S_{sk}$</th>
<th>$A_{clo}$</th>
<th>$\eta_{clo,dip}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Legs and lower torso</td>
<td>Trousers (overalls)</td>
<td>0.0005</td>
<td>0.83</td>
<td>1</td>
<td>0.99</td>
</tr>
<tr>
<td>2</td>
<td>Feet</td>
<td>Footwear</td>
<td>0.0001</td>
<td>0.13</td>
<td>1</td>
<td>0.99</td>
</tr>
<tr>
<td>3</td>
<td>Arms and upper torso</td>
<td>Jacket (overalls and bib)</td>
<td>0.0005</td>
<td>0.71</td>
<td>1</td>
<td>0.99</td>
</tr>
<tr>
<td>4</td>
<td>Head</td>
<td>Hat and/or Visor</td>
<td>0.0001</td>
<td>0.13</td>
<td>0.7</td>
<td>0.99</td>
</tr>
<tr>
<td>5</td>
<td>Hands</td>
<td>Gloves</td>
<td>0.0005</td>
<td>0.1</td>
<td>1</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Table.App. 11-6: Model Factors for Clothing and Gloves for handling sheep

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk}$</th>
<th>$S_{sk}$</th>
<th>$A_{clo}$</th>
<th>$\eta_{clo,dip}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Legs and lower torso</td>
<td>Trousers (overalls)</td>
<td>0.1</td>
<td>0.83</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>Feet</td>
<td>Footwear</td>
<td>0</td>
<td>0.13</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>Arms and upper torso</td>
<td>Jacket (overalls and bib)</td>
<td>0.1</td>
<td>0.71</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>4</td>
<td>Head</td>
<td>Hat and/or Visor</td>
<td>0</td>
<td>0.13</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>Hands</td>
<td>Gloves</td>
<td>1</td>
<td>0.1</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table.App. 11-7: Model Factors for Clothing and Gloves for falling into the dip

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk}$</th>
<th>$S_{sk}$</th>
<th>$A_{clo}$</th>
<th>$\eta_{clo,dip}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whole Body</td>
<td>Not relevant</td>
<td>n/a</td>
<td>1.9</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Table.App. 11-8: Model Factors for Clothing and Gloves for cleaning dip bath

<table>
<thead>
<tr>
<th>n</th>
<th>Body area</th>
<th>Clothing</th>
<th>$\delta_{sk}$</th>
<th>$S_{sk}$</th>
<th>$A_{clo}$</th>
<th>$\eta_{clo,dip}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whole Body</td>
<td>Jacket, trousers etc.</td>
<td>n/a</td>
<td>1.9</td>
<td>0.7</td>
<td>0.6</td>
</tr>
</tbody>
</table>
### Appendix 12: Rules for applying SHAPE models for the SHAW study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>d (dipping days)</td>
<td>Average dipping days per year</td>
</tr>
<tr>
<td>y (dipping year)</td>
<td>In each equation these years were scored 1, others 0:</td>
</tr>
<tr>
<td></td>
<td>Eq.3.9.1: years which have the task of plunger or chucker</td>
</tr>
<tr>
<td></td>
<td>Eq.3.9.2: years of handling the concentrate</td>
</tr>
<tr>
<td></td>
<td>Eq.3.9.3: years of handling the concentrate and at the same time</td>
</tr>
<tr>
<td></td>
<td>working as a plunger or as a chucker</td>
</tr>
<tr>
<td></td>
<td>Eq.3.9.4: years which have the task of helper</td>
</tr>
<tr>
<td>h (dipping hours/day)</td>
<td>This variable is not available so it was assumed depending on a</td>
</tr>
<tr>
<td></td>
<td>regression model derived from the HSDS study using the average</td>
</tr>
<tr>
<td></td>
<td>number of sheep treated per day as an independent factor. This model</td>
</tr>
<tr>
<td></td>
<td>was: ( h = 0.003 \times \text{number of sheep treated per day} + 3.6 )</td>
</tr>
<tr>
<td>SR (splash concentrate/year)</td>
<td>This variable is not available so it was assumed depending on the</td>
</tr>
<tr>
<td></td>
<td>task. If the task did not included helping, the SR assumed 2-3 times</td>
</tr>
<tr>
<td></td>
<td>a year, if it did SR was assumed once a year</td>
</tr>
<tr>
<td>( \Delta_{\text{dip}} )</td>
<td>This variable is not available but we have what the task was each</td>
</tr>
<tr>
<td>(proportion of the</td>
<td>year, and only few of the farmers worked as helpers with other tasks</td>
</tr>
<tr>
<td>time spent in chucking</td>
<td>in the same year, so it was assumed:</td>
</tr>
<tr>
<td>and plunging)</td>
<td>Always: in the years of (plunger, chucker or both)</td>
</tr>
<tr>
<td></td>
<td>Mostly: in the years of (helper and other tasks)</td>
</tr>
<tr>
<td></td>
<td>Some: in the years of (helper and another one task)</td>
</tr>
<tr>
<td></td>
<td>None: in the year of (helper)</td>
</tr>
<tr>
<td>( \Delta_{\text{conc}} )</td>
<td>This variable is not available, so as the plunger is most likely who add</td>
</tr>
<tr>
<td>(frequency of adding the</td>
<td>the concentrate it was assumed:</td>
</tr>
<tr>
<td>concentrate to the bath)</td>
<td>Always: in the years of (plunger, or plunger and chucker)</td>
</tr>
<tr>
<td></td>
<td>Mostly: in the years of (chucker or all tasks)</td>
</tr>
<tr>
<td></td>
<td>Some: in the years of (helper and helper and chucker)</td>
</tr>
<tr>
<td>( \Delta_{\text{dryhand}} )</td>
<td>This variable is not available, but we know if the farmer worked as a</td>
</tr>
<tr>
<td>(proportion of time</td>
<td>helper in each year, and if he ever contacted the dipped sheep within</td>
</tr>
<tr>
<td>spent as a dry helper)</td>
<td>24 hours. So it was assumed:</td>
</tr>
<tr>
<td></td>
<td>Always: in the years of (helper).</td>
</tr>
<tr>
<td></td>
<td>Mostly: in the years of (helper and another one task)</td>
</tr>
<tr>
<td></td>
<td>Some: in the years of (all tasks).</td>
</tr>
<tr>
<td></td>
<td>None: in the year of no helping task</td>
</tr>
<tr>
<td>( \Delta_{\text{wethand}} )</td>
<td>Same as ( \Delta_{\text{dryhand}} ) unless there was no contact with sheep after dipping</td>
</tr>
<tr>
<td>(proportion of time</td>
<td>then ( \Delta_{\text{dryhand}} ) is none (0). Contacting dipped sheep was ignored if the</td>
</tr>
<tr>
<td>spent as a wet helper)</td>
<td>farmer did not mention working as a helper</td>
</tr>
<tr>
<td>N(_{\text{falls}}) (the</td>
<td>Assumed that the farmers fell only once into the bath in the year</td>
</tr>
<tr>
<td>total number of falls</td>
<td>that they indicated in their questionnaire response</td>
</tr>
<tr>
<td>into the dip bath)</td>
<td>It was assumed that each year equals one occasion</td>
</tr>
<tr>
<td>N(_{\text{clean}}) (the</td>
<td>( P ) will be (1/0) according to the usage in SHAW. The usage of PPE</td>
</tr>
<tr>
<td>total number of occasions</td>
<td>during handling the concentrate will be used for Eq.3.9.2 and Eq.3.9.3</td>
</tr>
<tr>
<td>the person cleaned the</td>
<td>while the usage during the application will be used for Eq.3.9.1 and</td>
</tr>
<tr>
<td>dip bath)</td>
<td>Eq.3.9.4</td>
</tr>
<tr>
<td>PPE</td>
<td>Tables 1, 3 and 5 in Appendix 11 were matched with the usage of PPE</td>
</tr>
<tr>
<td></td>
<td>in the SHAW study as follows:</td>
</tr>
<tr>
<td></td>
<td>Legs and lower torso: leggings</td>
</tr>
<tr>
<td></td>
<td>Feet: rubber boots</td>
</tr>
<tr>
<td></td>
<td>Arms and upper torso: apron/coverall</td>
</tr>
<tr>
<td></td>
<td>Head: face shield</td>
</tr>
<tr>
<td></td>
<td>Hands: gloves</td>
</tr>
</tbody>
</table>
Appendix 13: Rules for applying TASK models for the SHAW study

<table>
<thead>
<tr>
<th>Num.</th>
<th>Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>When the farmer did only one task through all years the percentage will be 100% for this task.</td>
</tr>
<tr>
<td>2</td>
<td>When the farmer did more than one task in the same years through all years, the percentage of each task will be 100/number of tasks.</td>
</tr>
<tr>
<td>3</td>
<td>When the farmer did a task in some years and another task in other years, the percentage of the task will depend on the number of treating days in every year.</td>
</tr>
<tr>
<td>4</td>
<td>The percentages will be rounded up in favour of plunger then chucker</td>
</tr>
<tr>
<td>5</td>
<td>If the farmer did not mention handling concentrate then the score of CONC will be zero</td>
</tr>
<tr>
<td>6</td>
<td>If the farmer did not mention working as a plunger and told that he handled the concentrate then the percentage of being a chucker will be used to calculate CONC instead of using the percentage of being a plunger</td>
</tr>
</tbody>
</table>

**Example for rule 3:** a farmer worked as a chucker for 20 years in which he dipped 2 days/year and worked as a plunger for 10 years in which he dipped 3 days/year, the percentages will be calculated as follows:

- Number of dipping days = 20 × 2 + 10 × 3 = 70
- Number of dipping days as a chucker = 20 × 2 = 40
- Number of dipping days as a plunger = 10 × 3 = 30
- Plunger percentage = 30/70 = 43%
- Chucker percentage = 40/70 = 57%
**Appendix 14: Assumptions to determine OP probability in livestock sectors**

**Table.App. 14-1: Assumptions for OP probability in sheep sector**

<table>
<thead>
<tr>
<th>Num.</th>
<th>Assumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All products before 1972 are non OPs</td>
</tr>
<tr>
<td>2</td>
<td>All missing dates before 1972 will be ignored as they will not affect the scores</td>
</tr>
<tr>
<td>3</td>
<td>Organochlorines are banned after 1984 so this year will be used as an end year of using all products contained organochlorines if their specific withdrawal years of from the market are unknown</td>
</tr>
<tr>
<td>4</td>
<td>If the farmer mentioned a specific trade name, which is unknown, the general trade name will be used instead of the specific name</td>
</tr>
<tr>
<td>5</td>
<td>If the farmer mentioned using the pesticide during a specific decade, the whole decade will be included, and if he said (early 19XX’s), the first half of the decade will be included</td>
</tr>
<tr>
<td>6</td>
<td>When the farmer said that he used a product after it had been withdrawn from the market, the withdrawal year will be used as an end year, unless there were no other pesticides mentioned after that date assuming that the farmer kept using it.</td>
</tr>
<tr>
<td>7</td>
<td>Unknown products will be excluded, and known products in a wrong period of time (i.e. when the product was not on the market) will be also excluded</td>
</tr>
<tr>
<td>8</td>
<td>When the farmer said that he used general trade name (e.g. Youngs) the probability of being that name OP will be used. This probability is obtained by dividing the number of OP products from that general name in a specific year by the number of all products of the general name in that year</td>
</tr>
<tr>
<td>9</td>
<td>In the model, the highest probability to be OP among the pesticides used in a specific year is taken</td>
</tr>
<tr>
<td>10</td>
<td>Some of the missing dates of OPs were ignored as there is another pesticide known in the same period and its probability to be OP is more than 90%</td>
</tr>
<tr>
<td>11</td>
<td>When the farmer said that he used a certain name of general trade name, the period in which that name was existed in the market will be used and the general trade name will be used for the other years. E.g. the farmer said that he used (Youngs Winter Dip) between 1954-1995, and this specific name was existed in the market between 1972-1993, so the last period will be used for that specific name and the general name (Youngs) will be used for before and after this period</td>
</tr>
<tr>
<td>12</td>
<td>Pesticides used less than 5 times were ignored if there are other pesticides in the same period</td>
</tr>
<tr>
<td>13</td>
<td>If there was no mention of a specific treatment method in Table 2.1 in the questionnaire and this method was in Table 2.2 used once or the product was absolutely not OP, this method will be ignored.</td>
</tr>
<tr>
<td>14</td>
<td>If ectoforce named before 2001 and it makes difference in the estimation, ectoforce will be treated as ectomort (OP: 1980-2000).</td>
</tr>
<tr>
<td>15</td>
<td>All injections and oral treatments were assumed to be non OP as most of injections are avermectins, and most of oral treatments are wormers (e.g. avermectins, benzimidazol)</td>
</tr>
<tr>
<td>16</td>
<td>Cydectin is considered as only injection not a dip</td>
</tr>
</tbody>
</table>
Table App. 14-2: Assumptions for OP probability in other livestock and cattle farming sectors

<table>
<thead>
<tr>
<th>Num.</th>
<th>Assumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All products before 1960 are non OPs</td>
</tr>
<tr>
<td>2</td>
<td>All injections and oral treatments were assumed to be non OP as most of injections are avermectins, and most of oral treatments are wormers (e.g. avermectins, benzimidazol)</td>
</tr>
<tr>
<td>3</td>
<td>In other livestock sector: when farmers used one of these products: Flit, Louse powder or spray, Red mites mix, or Spot-on, OPPROB was assumed (0.2). This figure was arbitrary set because it has been found through the internet search that most of these products are not OP.</td>
</tr>
<tr>
<td>4</td>
<td>In cattle sector: In warble fly treatment ‘powder’ was coded ‘probably not OP’ because it is mostly “Derris” and ‘pour-on’ was coded ‘DK’.</td>
</tr>
<tr>
<td>5</td>
<td>In cattle sector: In lice treatment ‘louse powder’ was coded ‘DK’ and in flies treatment ‘Flit’ and ‘spot-on’ were coded also as ‘DK’.</td>
</tr>
</tbody>
</table>
| 6    | In cattle sector: Arbitrary scores were assigned to OPPROB after thorough internet search:  
In warble fly treatment: DK = 0.5, probably not OP = 0.1, and probably OP = 0.9  
In lice and flies treatment: DK = 0.2, probably not OP = 0.05, and probably OP = 0.9 |
Appendix 15: OPPROB for different types of crops

Table.App. 15-1: OPPROB of different types of crops from 1965 to 1984

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Field crops (other arable)</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All arable (all above)</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.30</td>
<td>0.30</td>
<td>0.30</td>
<td>0.30</td>
<td>0.30</td>
<td>0.29</td>
<td>0.29</td>
<td>0.29</td>
<td>0.29</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fodder crops</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orchards</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft fruit</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.13</td>
<td>0.13</td>
<td>0.13</td>
<td>0.13</td>
<td>0.13</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasshouse crops (protected)</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.14</td>
<td>0.14</td>
<td>0.14</td>
<td>0.14</td>
<td>0.14</td>
<td>0.14</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hardy nursery stock</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td>0.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All crops</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.09</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a 0.00 means less than < 0.01, the accurate figure was used in the model.
Table.App. 15-2: OPPROB of different types of crops from 1985 to 2005
Crop
Cereals
Maize & sweet corn
Oilseeds
Peas & beans
Potatoes
Beet crops
Other arable crops
All arable (all above)
Vegetable brassicas
Lettuce & other leafy salads
Onions & leeks
Carrots & parsnips
Other root vegetables
Other outdoor vegetables
Mushrooms
Other fodder crops
Top fruit & hops
Strawberries
Other soft fruit
Protected edible crops
Outdoor ornamental crops
Protected ornamental crops
All crops
a

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.04
0.03
0.09
0.06
0.03
0.00
0.03
0.35
0.32
0.02
0.42
0.33
0.18
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.03
0.05
0.03
0.06
0.06
0.02
0.00
0.03
0.36
0.22
0.01
0.37
0.37
0.19
0.20
0.06
0.06
0.09
0.11
0.08
0.00
0.16
0.04

0.02
0.05
0.01
0.04
0.05
0.05
0.00
0.02
0.36
0.22
0.01
0.37
0.37
0.19
0.20
0.06
0.09
0.09
0.11
0.08
0.00
0.16
0.03

0.02
0.02
0.01
0.04
0.05
0.05
0.00
0.02
0.36
0.22
0.01
0.37
0.37
0.19
0.20
0.03
0.09
0.09
0.11
0.08
0.09
0.16
0.03

0.00 means less than < 0.01, the accurate figure was used in the model.

382

0.04
0.02
0.01
0.04
0.04
0.04
0.00
0.03
0.36
0.22
0.01
0.37
0.37
0.19
0.20
0.03
0.09
0.05
0.06
0.08
0.09
0.16
0.04

0.04
0.03
0.01
0.04
0.04
0.04
0.00
0.03
0.31
0.14
0.02
0.20
0.36
0.14
0.08
0.03
0.09
0.05
0.06
0.07
0.09
0.17
0.04

0.01
0.03
0.00
0.03
0.04
0.01
0.00
0.01
0.31
0.14
0.02
0.20
0.36
0.14
0.08
0.03
0.09
0.05
0.06
0.07
0.09
0.17
0.02

0.01
0.02
0.00
0.03
0.04
0.01
0.00
0.01
0.31
0.14
0.02
0.20
0.36
0.14
0.08
0.02
0.09
0.05
0.06
0.07
0.06
0.17
0.02

0.01
0.02
0.00
0.03
0.01
0.01
0.00
0.01
0.31
0.14
0.02
0.20
0.36
0.14
0.08
0.02
0.09
0.05
0.06
0.07
0.06
0.17
0.02

0.01
0.02
0.00
0.03
0.01
0.01
0.00
0.01
0.21
0.08
0.02
0.04
0.36
0.03
0.01
0.02
0.09
0.05
0.06
0.10
0.06
0.07
0.01

0.01
0.02
0.00
0.01
0.00
0.00
0.00
0.01
0.21
0.08
0.02
0.04
0.36
0.03
0.01
0.02
0.06
0.05
0.06
0.10
0.06
0.07
0.01

0.01
0.02
0.00
0.01
0.00
0.00
0.00
0.01
0.21
0.08
0.02
0.04
0.36
0.03
0.01
0.02
0.06
0.05
0.04
0.10
0.06
0.07
0.01

0.00 a
0.01
0.00
0.01
0.00
0.00
0.00
0.00
0.21
0.08
0.02
0.04
0.36
0.03
0.01
0.01
0.05
0.05
0.04
0.10
0.06
0.07
0.01

0.00
0.01
0.00
0.00
0.00
0.00
0.00
0.00
0.02
0.00
0.01
0.00
0.12
0.03
0.01
0.01
0.05
0.05
0.04
0.02
0.06
0.03
0.00

0.01
0.01
0.00
0.00
0.00
0.00
0.00
0.00
0.02
0.00
0.01
0.00
0.12
0.03
0.01
0.01
0.04
0.05
0.04
0.02
0.06
0.03
0.01

0.01
0.01
0.00
0.00
0.00
0.00
0.00
0.00
0.02
0.00
0.01
0.00
0.12
0.03
0.01
0.01
0.04
0.05
0.04
0.02
0.04
0.03
0.01


Appendix 16: Consent form for CPH number

Appendix 17
CPHN consent form

ID No. □

CPHN Consent Form

Study of Health in Agricultural Work (SHAW Study)

Thank you for taking part in the SHAW study. As part of this study we would like to examine Agricultural and Horticultural (June) census data held by Defra. To obtain this information we need your written permission. Hence if you agree to this can you please confirm that:

Please initial box

- I agree to give permission for SHAW to access information held on my County Parish Holding file

Name of participant

Date

Name in BLOCK capitals
Appendix 17: Comparisons of age and memory between farmers who had the same answers in SHAW and JSAH and those who had different answers

Table.App. 17-1: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>108</td>
<td>65.7±5.7</td>
<td>12</td>
</tr>
<tr>
<td>Cattle</td>
<td>107</td>
<td>65.3 ± 5.7</td>
<td>13</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>103</td>
<td>65.8 ± 5.5</td>
<td>17</td>
</tr>
<tr>
<td>Vegetables</td>
<td>95</td>
<td>65.6 ± 5.7</td>
<td>25</td>
</tr>
</tbody>
</table>

Table.App. 17-2: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>103</td>
<td>65.8±5.8</td>
<td>13</td>
</tr>
<tr>
<td>Cattle</td>
<td>104</td>
<td>65.2 ± 5.7</td>
<td>12</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>100</td>
<td>65.7 ± 5.5</td>
<td>16</td>
</tr>
<tr>
<td>Vegetables</td>
<td>101</td>
<td>65.5 ± 5.9</td>
<td>15</td>
</tr>
</tbody>
</table>

Table.App. 17-3: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>83</td>
<td>65.8 ± 5.7</td>
<td>15</td>
</tr>
<tr>
<td>Cattle</td>
<td>85</td>
<td>65.1 ± 5.6</td>
<td>13</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>87</td>
<td>65.7 ± 5.5</td>
<td>11</td>
</tr>
<tr>
<td>Vegetables</td>
<td>92</td>
<td>65.4 ± 5.7</td>
<td>6</td>
</tr>
</tbody>
</table>

Table.App. 17-4: Age of farmers who had the same answers in SHAW and JSAH and those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>80</td>
<td>65.9 ± 5.7</td>
<td>15</td>
</tr>
<tr>
<td>Cattle</td>
<td>87</td>
<td>65.0 ± 5.6</td>
<td>8</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>83</td>
<td>65.6 ± 5.5</td>
<td>12</td>
</tr>
<tr>
<td>Vegetables</td>
<td>90</td>
<td>65.5 ± 5.7</td>
<td>5</td>
</tr>
</tbody>
</table>
Table.App. 17-5: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>107</td>
<td>23.35 ± 1.79</td>
<td>12</td>
</tr>
<tr>
<td>Cattle</td>
<td>106</td>
<td>23.35 ± 1.71</td>
<td>13</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>103</td>
<td>23.26 ± 1.73</td>
<td>16</td>
</tr>
<tr>
<td>Vegetables</td>
<td>94</td>
<td>23.22 ± 1.64</td>
<td>25</td>
</tr>
</tbody>
</table>

Table.App. 17-6: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>102</td>
<td>23.33 ± 1.78</td>
<td>13</td>
</tr>
<tr>
<td>Cattle</td>
<td>103</td>
<td>23.4 ± 1.75</td>
<td>12</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>99</td>
<td>23.31 ± 1.67</td>
<td>16</td>
</tr>
<tr>
<td>Vegetables</td>
<td>100</td>
<td>23.26 ± 1.67</td>
<td>15</td>
</tr>
</tbody>
</table>

Table.App. 17-7: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>83</td>
<td>23.27 ± 1.77</td>
<td>14</td>
</tr>
<tr>
<td>Cattle</td>
<td>84</td>
<td>23.29 ± 1.75</td>
<td>13</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>86</td>
<td>23.26 ± 1.66</td>
<td>11</td>
</tr>
<tr>
<td>Vegetables</td>
<td>91</td>
<td>23.21 ± 1.81</td>
<td>6</td>
</tr>
</tbody>
</table>

Table.App. 17-8: Memory scores of farmers who had the same answers in SHAW and JSAH and those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Same answers</th>
<th>Different answers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Mean ± SD</td>
<td>Number</td>
</tr>
<tr>
<td>Sheep</td>
<td>80</td>
<td>23.18 ± 1.68</td>
<td>14</td>
</tr>
<tr>
<td>Cattle</td>
<td>86</td>
<td>23.24 ± 1.75</td>
<td>8</td>
</tr>
<tr>
<td>Combinable Crops</td>
<td>82</td>
<td>23.21 ± 1.66</td>
<td>12</td>
</tr>
<tr>
<td>Vegetables</td>
<td>89</td>
<td>23.18 ± 1.77</td>
<td>5</td>
</tr>
</tbody>
</table>
Appendix 18: Distributions of screen-identified neuropsychiatric illnesses among farmers whose answers in SHAW study were same as the JSAH and among farmers whose answers were different

Table.App. 18-1: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>15/108 (13.9%)</td>
<td>1/12 (8.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>16/107 (15%)</td>
<td>0/13 (0%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>12/103 (11.7%)</td>
<td>4/17 (23.5%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Vegetables</td>
<td>13/95 (13.7%)</td>
<td>3/25 (12%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table.App. 18-2: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>14/103 (13.6%)</td>
<td>1/13 (7.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>15/104 (14.4%)</td>
<td>0/12 (0%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>12/100 (12%)</td>
<td>3/16 (18.8%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Vegetables</td>
<td>14/101 (13.9%)</td>
<td>1/15 (6.7%)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Table.App. 18-3: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>10/83 (12%)</td>
<td>2/15 (13.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>11/85 (12.9%)</td>
<td>1/13 (7.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>9/87 (10.3%)</td>
<td>3/11 (27.3%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Vegetables</td>
<td>11/92 (12%)</td>
<td>1/6 (16.7%)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Table.App. 18-4: Depression among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>8/80 (10%)</td>
<td>4/15 (26.7%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Cattle</td>
<td>11/87 (12.6%)</td>
<td>1/8 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>9/83 (10.8%)</td>
<td>3/12 (25%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Vegetables</td>
<td>11/90 (12.2%)</td>
<td>1/5 (20%)</td>
<td>0.50</td>
</tr>
</tbody>
</table>
### Table App. 18-5: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>13/108 (12%)</td>
<td>2/12 (16.7%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Cattle</td>
<td>14/107 (13.1%)</td>
<td>1/13 (7.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>14/103 (13.6%)</td>
<td>1/17 (5.9%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Vegetables</td>
<td>12/95 (12.6%)</td>
<td>3/25 (12%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Table App. 18-6: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>12/103 (11.7%)</td>
<td>3/13 (23.1%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Cattle</td>
<td>13/104 (12.5%)</td>
<td>2/12 (16.7%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>12/100 (12%)</td>
<td>3/16 (18.8%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Vegetables</td>
<td>14/101 (13.9%)</td>
<td>1/15 (6.7%)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

### Table App. 18-7: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>9/83 (10.8%)</td>
<td>2/15 (13.3%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Cattle</td>
<td>11/85 (12.9%)</td>
<td>0/13 (0%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>9/87 (10.3%)</td>
<td>2/11 (18.2%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Vegetables</td>
<td>10/92 (10.9%)</td>
<td>1/6 (16.7%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

### Table App. 18-8: Neuropathy among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>9/80 (11.2%)</td>
<td>2/15 (13.3%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Cattle</td>
<td>10/87 (11.5%)</td>
<td>1/8 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>9/83 (10.8%)</td>
<td>2/12 (16.7%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Vegetables</td>
<td>10/90 (11.1%)</td>
<td>1/5 (20%)</td>
<td>0.47</td>
</tr>
</tbody>
</table>
Table.App. 18-9: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>14/108 (13%)</td>
<td>1/12 (8.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>12/107 (11.2%)</td>
<td>3/13 (23.1%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>13/103 (12.6%)</td>
<td>2/17 (11.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables</td>
<td>12/95 (12.6%)</td>
<td>3/25 (12%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table.App. 18-10: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>12/103 (11.7%)</td>
<td>2/13 (15.4%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Cattle</td>
<td>11/104 (10.6%)</td>
<td>3/12 (25%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>12/100 (12%)</td>
<td>2/16 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables</td>
<td>13/101 (12.9%)</td>
<td>1/15 (6.7%)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Table.App. 18-11: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>10/83 (12%)</td>
<td>1/15 (6.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>11/85 (12.9%)</td>
<td>0/13 (0%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>10/87 (11.5%)</td>
<td>1/11 (9.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables</td>
<td>10/92 (10.9%)</td>
<td>1/6 (16.7%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Table.App. 18-12: Parkinsonism among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>9/80 (11.2%)</td>
<td>1/15 (6.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>9/87 (10.3%)</td>
<td>1/8 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>8/83 (9.6%)</td>
<td>2/12 (16.7%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Vegetables</td>
<td>9/90 (10%)</td>
<td>1/5 (20%)</td>
<td>0.43</td>
</tr>
</tbody>
</table>
Table App. 18-13: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1988

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>18/108 (16.7%)</td>
<td>3/12 (25%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Cattle</td>
<td>20/107 (18.7%)</td>
<td>1/13 (7.7%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>19/103 (18.4%)</td>
<td>2/17 (11.8%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Vegetables</td>
<td>16/95 (16.8%)</td>
<td>5/25 (20%)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Table App. 18-14: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1993

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>16/103 (15.5%)</td>
<td>4/13 (30.8%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Cattle</td>
<td>18/104 (17.3%)</td>
<td>2/12 (16.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>15/100 (15%)</td>
<td>5/16 (31.2%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Vegetables</td>
<td>18/101 (17.8%)</td>
<td>2/15 (13.3%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table App. 18-15: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 1998

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>15/83 (18.1%)</td>
<td>3/15 (20%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cattle</td>
<td>16/85 (18.8%)</td>
<td>2/13 (15.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>14/87 (16.1%)</td>
<td>4/11 (36.4%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Vegetables</td>
<td>18/92 (19.6%)</td>
<td>0/6 (0%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table App. 18-16: Dementia among farmers who had the same answers in SHAW and JSAH and among those who had different answers in 2000

<table>
<thead>
<tr>
<th>Type of farm</th>
<th>Screen-positives among farmers with same answers (%)</th>
<th>Screen-positives among farmers with different answers (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td>13/80 (16.2%)</td>
<td>5/15 (33.3%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Cattle</td>
<td>17/87 (19.5%)</td>
<td>1/8 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Combinable crops</td>
<td>14/83 (16.9%)</td>
<td>4/12 (33.3%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Vegetables</td>
<td>17/90 (18.9%)</td>
<td>1/5 (20%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
# Appendix 19: Association between neuropsychiatric illnesses and pesticide exposure in different farming sectors

Table. App. 19-1: Association between memory and pesticide exposure in different farming sectors

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Farming sector</th>
<th>Exposure estimates</th>
<th>Memory score</th>
<th>n a</th>
<th>UM a</th>
<th>OR (95%CI) b</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Pesticides</strong></td>
<td>Sheep</td>
<td>NEW 218 118</td>
<td>0.86 (0.70 - 1.07)</td>
<td>218</td>
<td>118</td>
<td>0.86 (0.70 - 1.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SHAPE 218 118</td>
<td>0.87 (0.64 - 1.19)</td>
<td>218</td>
<td>118</td>
<td>0.87 (0.64 - 1.19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TASK 219 119</td>
<td>0.90 (0.74 - 1.09)</td>
<td>219</td>
<td>119</td>
<td>0.90 (0.74 - 1.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPSH 218 118</td>
<td>0.88 (0.76 - 1.02)</td>
<td>218</td>
<td>118</td>
<td>0.88 (0.76 - 1.02)</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>EXPCAT 220 119</td>
<td>0.93 (0.74 - 1.16)</td>
<td>220</td>
<td>119</td>
<td>0.93 (0.74 - 1.16)</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>EXPLIV 220 119</td>
<td>0.90 (0.70 - 1.16)</td>
<td>220</td>
<td>119</td>
<td>0.90 (0.70 - 1.16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPCRP 220 119</td>
<td>1.10 (0.96 - 1.26)</td>
<td>220</td>
<td>119</td>
<td>1.10 (0.96 - 1.26)</td>
</tr>
<tr>
<td><strong>OP Pesticides</strong></td>
<td>Sheep</td>
<td>OPNEW 218 118</td>
<td>0.96 (0.79 - 1.17)</td>
<td>218</td>
<td>118</td>
<td>0.96 (0.79 - 1.17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPSHAPE 218 118</td>
<td>0.97 (0.70 - 1.34)</td>
<td>218</td>
<td>118</td>
<td>0.97 (0.70 - 1.34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXPSH 218 118</td>
<td>0.91 (0.75 - 1.11)</td>
<td>218</td>
<td>118</td>
<td>0.91 (0.75 - 1.11)</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>OPEXPCAT 220 119</td>
<td>0.93 (0.75 - 1.16)</td>
<td>220</td>
<td>119</td>
<td>0.93 (0.75 - 1.16)</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>OPEXPLIV 220 119</td>
<td>1.00 (0.69 - 1.44)</td>
<td>220</td>
<td>119</td>
<td>1.00 (0.69 - 1.44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXCRP 220 119</td>
<td>1.11 (0.91 - 1.37)</td>
<td>220</td>
<td>119</td>
<td>1.11 (0.91 - 1.37)</td>
</tr>
</tbody>
</table>

a n = number of all farmers and UM = number of farmers with memory scores under median.  
b Adjusted for age

c Table. App. 19-1: Association between depression and pesticide exposure in different farming sectors

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Farming sector</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Pesticides</strong></td>
<td>Sheep</td>
<td>NEW 222 31</td>
<td>1.06 (0.77 - 1.47)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SHAPE 222 31</td>
<td>1.10 (0.68 - 1.76)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TASK 223 31</td>
<td>1.06 (0.79 - 1.43)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPSH 222 31</td>
<td>1.04 (0.83 - 1.31)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>EXPCAT 224 32</td>
<td>0.91 (0.67 - 1.24)</td>
<td>66 7</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>EXPLIV 224 32</td>
<td>1.05 (0.75 - 1.46)</td>
<td>66 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPCRP 224 32</td>
<td>1.04 (0.86 - 1.27)</td>
<td>66 7</td>
</tr>
<tr>
<td><strong>OP Pesticides</strong></td>
<td>Sheep</td>
<td>OPNEW 222 31</td>
<td>0.89 (0.67 - 1.18)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPSHAPE 222 31</td>
<td>0.86 (0.54 - 1.36)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXPSH 222 31</td>
<td>0.91 (0.75 - 1.11)</td>
<td>65 7</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>OPEXPCAT 224 32</td>
<td>0.95 (0.70 - 1.28)</td>
<td>66 7</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>OPEXPLIV 224 32</td>
<td>0.64 (0.28 - 1.45)</td>
<td>66 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXCRP 224 32</td>
<td>1.09 (0.81 - 1.46)</td>
<td>66 7</td>
</tr>
</tbody>
</table>

a n = number of all farmers and NS = number of screen-positive farmers  
b Adjusted for age  
c All screen-positive farmers were unexposed
### Table.App. 19-2: Association between neuropathy and pesticide exposure in different farming sectors

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Farming sector</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>General Pesticides</td>
<td>Sheep</td>
<td>NEW</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SHAPE</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TASK</td>
<td>223</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPSPH</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>EXPCAT</td>
<td>224</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Other Livestock</td>
<td>EXPLIV</td>
<td>224</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>EXPCRP</td>
<td>224</td>
<td>28</td>
</tr>
<tr>
<td>OP Pesticides</td>
<td>Sheep</td>
<td>OPNEW</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPSHAPE</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXPSH</td>
<td>222</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>OPEXPCAT</td>
<td>224</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Other Livestock</td>
<td>OPEXPLIV</td>
<td>224</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>OPEXPCRP</td>
<td>224</td>
<td>28</td>
</tr>
</tbody>
</table>

* a n = number of all farmers and NS = number of screen-positive farmers
* b Adjusted for age

### Table.App. 19-3: Association between Parkinsonism and pesticide exposure in different farming sectors

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Farming sector</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>General Pesticides</td>
<td>Sheep</td>
<td>NEW</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SHAPE</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TASK</td>
<td>223</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EXPSH</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>EXPCAT</td>
<td>224</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Other Livestock</td>
<td>EXPLIV</td>
<td>224</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>EXPCRP</td>
<td>224</td>
<td>27</td>
</tr>
<tr>
<td>OP Pesticides</td>
<td>Sheep</td>
<td>OPNEW</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPSHAPE</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OPEXPSH</td>
<td>222</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>OPEXPCAT</td>
<td>224</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Other Livestock</td>
<td>OPEXPLIV</td>
<td>224</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>OPEXPCRP</td>
<td>224</td>
<td>27</td>
</tr>
</tbody>
</table>

* a n = number of all farmers and NS = number of screen-positive farmers
* b Adjusted for age
Table.App. 19-4: Association between dementia and pesticide exposure in different farming sectors

<table>
<thead>
<tr>
<th>Pesticide type</th>
<th>Farming sector</th>
<th>Exposure estimates</th>
<th>Phase 1 definition</th>
<th>Phase 2 definition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>NS</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>General Pesticides</td>
<td>Sheep</td>
<td>NEW</td>
<td>222</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>SHAPE</td>
<td>222</td>
<td>42</td>
<td>0.77 (0.53 - 1.12)</td>
</tr>
<tr>
<td></td>
<td>TASK</td>
<td>223</td>
<td>42</td>
<td>0.83 (0.66 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>EXPSH</td>
<td>222</td>
<td>42</td>
<td>0.93 (0.78 - 1.11)</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>EXPCAT</td>
<td>224</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>EXPLIV</td>
<td>224</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>EXPCRP</td>
<td>224</td>
<td>43</td>
</tr>
<tr>
<td>OP Pesticides</td>
<td>Sheep</td>
<td>OPNEW</td>
<td>222</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>OPSHAPE</td>
<td>222</td>
<td>42</td>
<td>0.64 (0.43 - 0.96)</td>
</tr>
<tr>
<td></td>
<td>OPEXPSH</td>
<td>222</td>
<td>42</td>
<td>0.87 (0.74 - 1.03)</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>OPEXPCAT</td>
<td>224</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Other livestock</td>
<td>OPEXPLIV</td>
<td>224</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Crops</td>
<td>OPEXPCRP</td>
<td>224</td>
<td>43</td>
</tr>
</tbody>
</table>

\( \text{a} \) n = number of all farmers and NS = number of screen-positive farmers

\( \text{b} \) Adjusted for age