The impact of changing the prevalence of overweight/obesity and physical inactivity in Australia

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**The impact of changing the prevalence of
overweight/obesity and physical inactivity in Australia: an
estimate of the proportion of potentially avoidable cancers
2013-2037**

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For Peer Review

The impact of changing the prevalence of overweight/obesity and physical inactivity in Australia: an estimate of the proportion of potentially avoidable cancers 2013-2037.

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Keywords: Neoplasms, risk factors, obesity, exercise, potential impact fraction

Abbreviations:

ABS	Australian Bureau of Statistics
AIHW	Australian Institute of Health and Welfare
BMI	body mass index
CI	confidence interval
IARC	International Agency for Research on Cancer
IGF	Insulin-like growth factor
MET	Metabolic equivalents
PIF	potential impact fraction
RR	relative risk
WCRF	World Cancer Research Fund

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Novelty and Impact:

In Australia, 62% of adults are overweight or obese and 48% are insufficiently physically active. In this study, the authors estimated the proportion of cancers that might be avoidable under different theoretical intervention scenarios to reduce the prevalence of overweight/obesity and physical inactivity. They found that up to 12% of overweight/obesity-related cancers (~ 190,000 cancers) and up to 2% of inactivity-related cancers (~ 19,000 cancers) could be avoided in Australia over the next 25 years.

Abstract

Globally, 39% of the world’s adult population is overweight or obese and 23% is insufficiently active. These percentages are even larger in high-income countries with 58% overweight/obese and 33% insufficiently active. Fourteen cancer types have been declared by the World Cancer Research Fund to be causally associated with being overweight or obese: oesophageal adenocarcinoma, stomach cardia, colon, rectum, liver, gallbladder, pancreas, breast, endometrium, ovary, advanced/fatal prostate, kidney, thyroid and multiple myeloma. Colon, postmenopausal breast and endometrial cancers have also been judged causally associated with physical inactivity. We aimed to quantify the proportion of cancer cases that would be potentially avoidable in Australia if the prevalence of overweight/obesity and physical inactivity in the population could be reduced. We used the simulation modelling software PREVENT 3.01 to calculate the proportion of avoidable cancers over a 25-year period under different theoretical intervention scenarios that change the prevalence of overweight/obesity and physical inactivity in the population. Between 2013 and 2037, ~~910-~~ 13% of overweight/obesity-related cancers in men and 7-11% in women could be avoided if overweight and obesity were eliminated in the Australian population. If everyone in the population met the Australian physical activity guidelines for cancer prevention (i.e. engaged in at least 300 minutes of moderate-intensity physical activity per week), an estimated 2-3% of physical inactivity-related cancers could be prevented in men (colon cancer) and 1-2% in women (colon, breast and endometrial cancers). -This would translate to the prevention of up to ~~189,800~~190,500 overweight/obesity-related cancers and 19,200 inactivity-related cancers over 25 years.

Introduction

Since the mid-twentieth century, the proportion of the global population that is overweight or obese has increased, while the proportion considered physically active has decreased.

Contributing factors include the increasing consumption of cheap, manufactured, energy-dense foods,¹ and growing reliance on the car and other technologies that reduce movement and promote sitting in both the home and workplace.² Globally, 39% of the world's adult population is overweight or obese,³ and 23% is insufficiently active.⁴ These percentages are even larger in high income countries (58% overweight/obese; 33% insufficiently active).^{5, 6}

As at April 2018, both the World Cancer Research Fund (WCRF) and the International Agency for Research on Cancer (IARC) concluded that there was “convincing”/“sufficient” evidence for body fatness causing nine cancers: oesophagus (adenocarcinoma), colon, rectum, liver, pancreas, breast (postmenopausal), endometrium, ovary and kidney.^{7, 8} For cancers of the stomach (cardia) and gallbladder, the WCRF judged the association “probable”⁸ and IARC “sufficient”.⁷ For thyroid cancer and multiple myeloma, the IARC judged the association “sufficient”;⁷ these cancers have not been assessed by the WCRF. In addition, the WCRF also judged the association “probable” for advanced/fatal prostate cancer;⁸ whereas the IARC concluded that the evidence for this cancer was “limited” (Table S1).⁷

Physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure.⁹ Many high income countries recommend adults perform a minimum of 150 minutes of moderate-intensity physical activity per week, or 75 minutes of vigorous-intensity physical activity per week, to improve cardiorespiratory fitness and muscle and bone strength.¹⁰⁻¹² Both the United States and Australian guidelines recommend increasing the duration to 300 minutes of moderate-intensity physical activity or 150 minutes

of vigorous-intensity physical activity per week to prevent cancer and unhealthy weight gain.^{10, 12}

The WCRF concluded that there was convincing evidence that physical activity of all types (recreational, occupational, household and for transport) reduces the risk of colon cancer, and that there is “probable” evidence that it reduces the risk of postmenopausal breast cancer and endometrial cancer (Table S1).⁸ In its most recent review of the evidence for breast cancer,⁸ the WCRF also concluded that vigorous physical activity probably reduces the risk of premenopausal breast cancer.

While the associations between physical activity and cancer may be mediated to some degree through weight loss and changes in body composition,¹³ there is evidence that regular physical activity independently lowers insulin levels and enhances insulin sensitivity;¹⁴ and reduces oestradiol and free oestradiol concentrations.¹⁵ For colon cancer other mechanisms through which physical activity might mediate an effect independently of overweight/obesity include reduced gastrointestinal transit time^{13, 16} and exercise-induced changes to the gut microbiome.¹⁷

Given the high prevalence of overweight/obesity (62%) and physical inactivity (48%) in Australian adults,¹⁸ and the consequent impact on cancer burden, we aimed to quantify the proportion of cancer cases that could potentially be avoided in Australia over a 25-year period (2013-2037) under different theoretical intervention scenarios that reduce the prevalence of overweight/obesity and physical inactivity in the population. For these analyses, we analysed ‘physical inactivity’ (rather than ‘physical activity’) because this is the risk factor targeted in prevention campaigns, and because we can estimate the proportion of the population failing to meet levels recommended by national guidelines.

Methods

We used PREVENT V 3.01 software¹⁹ to calculate the proportion of avoidable cancers under theoretical intervention scenarios aiming to change the prevalence of overweight/obesity and physical inactivity in the Australian population. The following data are required for PREVENT:

Exposure prevalence in the Australian population

We sourced data for both overweight/obesity (measured by body mass index (BMI)) and physical activity (recreational and for transport) from the Australian Bureau of Statistics (ABS) Australian Health Survey 2011-2012 Basic Confidentialised Unit Record Files.¹⁸

Body mass index: BMI was derived using measured height and weight (kg/m^2).²⁰ We created a 17 category BMI variable in $1 \text{ kg}/\text{m}^2$ increments from $<25 \text{ kg}/\text{m}^2$ to $\geq 40 \text{ kg}/\text{m}^2$ ($< 25 \text{ kg}/\text{m}^2$, $25\text{-}25.99 \text{ kg}/\text{m}^2$, $26\text{-}26.99 \text{ kg}/\text{m}^2$... $\geq 40 \text{ kg}/\text{m}^2$). Data were grouped by sex and 105-year age groups (15-19 years, 20-24 years, 25-34 years ... 65+ years). ~~to ensure there were no BMI categories with zero prevalence in any age group.~~

Physical activity for recreation and transport: Physical activity for recreation and transport was self-reported as total minutes spent in the past week doing each of the following mutually exclusive activities: 1) walking for at least 10 minutes (for fitness, recreation, sport, or to get to and from places); 2) moderate exercise; and 3) vigorous exercise.²⁰

To equate the three different types of activity, we weighted the total minutes spent in each activity by its energy requirements defined in metabolic equivalents (METs). One MET is defined as energy expenditure at rest, equivalent to 3.5 millilitres of oxygen uptake per kilogram per minute.²¹ We used MET values of 3.3 for walking, 4.0 for moderate physical activity and 8.0 for vigorous physical activity.²² We summed the MET-minutes for walking, moderate and vigorous activity to derive total MET-minutes of physical activity per week.

We created a 12 category MET-minutes/week variable (0 MET-minutes/week (no activity),

>0 to <100 MET-minutes, 100-<200 MET-minutes, 200-<300 MET-minutes ... $\geq 1,000$ MET-minutes). Anyone falling into a category below the $\geq 1,000$ MET-minutes/week category is considered physically inactive. Data were grouped by sex and five-year age groups (15-19 years, 20-24 years...85+ years). ~~Distribution of the prevalence data allowed for more age groups than for BMI.~~

The WCRF concluded that it was “probable” that vigorous physical activity reduced the risk of premenopausal breast cancer,⁸ so in a supplementary analysis we considered the impact on premenopausal breast cancer of increasing vigorous activity among women under 50. We used the “total minutes undertaken vigorous exercise last week” variable, divided this by seven and dichotomised into <30 minutes and ≥ 30 minutes of vigorous physical activity/day, to align with the relative risks published by the WCRF (see below).

Relative risks

We used relative risks (RRs) from the most recent dose-response meta-analyses of prospective studies conducted by the WCRF Continuous Update Project up until April 2018.^{8, 23} The WCRF has not published dose-response RRs for thyroid cancer and multiple myeloma associated with overweight/obesity, nor for endometrial cancer associated with physical activity, so we used risk estimates from pooled prospective studies²⁴ or recent meta-analyses.^{25, 26} Where available, we used RRs stratified by sex. The RRs for each overweight/obesity-associated cancer are depicted in Fig. 1. As the WCRF and IARC drew different conclusions for advanced/fatal prostate cancer,^{7, 8} we considered prostate cancer in a supplementary analysis. The RRs for recreational physical activity and colon, endometrial and breast cancer are summarised in Table 1.

Body mass index: Published dose-response RRs for a 5 kg/m² or 2 kg/m² increase in BMI were converted to RR per 1 kg/m² increase in BMI by assuming a linear relationship between the exposure and the log of the RR of the outcome, so that:

$$\text{Risk per 1 kg/m}^2 \text{ increase in BMI} = \ln(RR_x)/x$$

Where x is the increase in BMI (in kg/m^2), and RR_x the relative risk for $x \text{ kg/m}^2$ increase in BMI.

We calculated the RR for each BMI category (see Exposure prevalence), assuming a linear dose-response relationship with each cancer outcome. In a sensitivity analysis, we used the RRs from the non-linear dose-response analyses conducted by the WCRF for those cancers where there was evidence of a non-linear relationship (Table S2).

A BMI of 22 kg/m^2 was selected as the Theoretical Minimum Risk level (reference level) as this is the mean BMI in the normal BMI category²⁷ in the Australian population (15+ years),¹⁸ however the increase in risk was only applied to BMI categories of 25 kg/m^2 and above (for BMI categories $22 < 25 \text{ kg/m}^2$, $RR = 1$ was assumed). In a sensitivity analysis, we used a BMI of 25 kg/m^2 as the reference level.

Physical inactivity: We converted each RR to an increased risk due to physical inactivity, with 1,000 MET-minutes/week as the reference level (equivalent to approximately 300 minutes of moderate-intensity physical activity per week as in the relevant Australian guidelines for adults).^{10, 21} We assumed a linear relationship between the exposure and the log of the RR of the outcome, so that:

$$\text{Risk per 100 MET-minutes (~ 30 minutes) deficit per week} = \ln(1/RR_x)/x$$

where x is the decrease in MET-minutes/week and RR_x the relative risk for x decrease in MET-minutes/week. We then calculated the RR for each physical-inactivity category (see Exposure prevalence), assuming a linear dose-response relationship with each cancer outcome.

For the supplementary analysis of vigorous physical activity and premenopausal breast cancer, we used the RR from the WCRF ($RR = 0.91$, 95% confidence interval (CI) 0.83-1.01

per 30 minutes of vigorous physical activity per day),⁸ and considered the impact of increasing vigorous activity among women under 50 to at least 30 minutes per day.

Australian population data

The Estimated Resident Population for 2012 and population projections for 2013-2037 were sourced from the ABS.^{28, 29} We used the ABS population projections that were based on current trends in fertility, life expectancy at birth and net overseas migration (Series B).³⁰ Base year (2012) population data were by sex and one-year age group (required by PREVENT), and by sex and 5-year age group for the period 2013-2037. In 2012 the Australian population was 22.7 million.²⁹ By 2037 the population is projected to increase to 32.8 million; the majority of this growth is expected to occur in Australians aged 65 years and over.²⁸

Cancer data

Cancer incidence rates in Australia in 2012 (the latest year for which national data for all cancer types were available at the time of analysis) by sex and 5-year age group (for each cancer listed in Table S1) were obtained from the Australian Institute of Health and Welfare (AIHW).³¹ We considered the association between overweight/obesity and prostate cancer in a supplementary analysis. As data on the number of advanced prostate cancers diagnosed in Australia was not available at a population level, we restricted our analysis to fatal prostate cancers in Australia in 2012.³¹

Theoretical intervention scenarios

We modelled two intervention scenarios that reduced the prevalence of overweight/obesity (BMI categories ≥ 25 kg/m²) in the Australian population and one scenario where prevalence continued to increase. Scenarios were only applied to the adult population (≥ 15 years).

- 1) Theoretical Maximum Intervention: from year 1 (2013) 100% of the population aged ≥ 15 years reduced their BMI to $<25 \text{ kg/m}^2$.
- 2) Targeted Reduction: over a 10-year period, the proportion of people in each overweight BMI category ($25\text{--}29.99 \text{ kg/m}^2$) declined by 5% each year, and the proportion in each obese BMI category ($\geq 30 \text{ kg/m}^2$) declined by 10% each year.
- 3) Continued Increase: the proportion of people in each obese BMI category ($\geq 30 \text{ kg/m}^2$) continued to increase by 2.3% each year over a 10-year period (2013–2022). This scenario is based on observed prevalence trends between 1995 and 2012 in Australia.³²

Two intervention scenarios were modelled for physical inactivity.

- 1) Theoretical Maximum Intervention: from year 1 (2013) all of the population aged ≥ 15 years performed ≥ 1000 MET-minutes of physical activity/week (≈ 300 minutes of moderate-intensity activity/week). This level of physical activity (in the absence of dietary interventions) may result in modest weight loss ($\sim 3 \text{ kg}$ or a 1 unit reduction in BMI),^{33, 34} so under this scenario we also undertook a supplementary analysis and examined the impact of a 1 unit reduction in BMI in year 1 (2012) in those who were overweight and obese on the additional cancers causally associated with overweight/obesity.
- 2) Everyone Meets Physical Activity Guidelines for Cardiac Health: the proportion of the population (≥ 15 years) performing <500 MET-minutes/week declined linearly to 0 over 10 years while there was a corresponding increase in the proportion in the 500–600 MET-minutes/week category. That is, by 2022 no-one is performing <500 MET-minutes/week and the lowest inactivity category is 500–600 MET-minutes/week, equivalent to 150 minutes of brisk walking per week – the minimum amount recommended in the Australian guidelines for cardiovascular health, but lower than the 1,000 MET-minutes recommended for cancer prevention.¹⁰

Statistical analysis

We used PREVENT 3.01 modelling software¹⁹ to compare projected future cancer incidence assuming no preventive interventions (reference scenario) with projected future cancer incidence under specified intervention scenarios.

In our modelling, the reference scenario assumed no changes in either risk factor prevalence or age- and sex-specific incidence rates for each cancer under study from the base-year (2012 – the year prior to commencement of an intervention) to the end of the study period (2037).

We estimated future numbers of cancers under the reference scenario by multiplying the base-year incidence rate by the projected population in each sex and age category for each year of the study period (2013-2037).²⁸ Thus, all changes in numbers of cancers over the study period in the reference scenario were due solely to demographic changes in the age- and sex-structure of the population.

PREVENT requires two time elements to be incorporated into the model – (LAT and LAG). When summed together, these elements equate to the epidemiologic concept of ‘latency’.

LAT (or lead time) is ~~defined as~~ the number of years that elapse before risk starts to change after the prevalence of an exposure has changed until the relative risk of cancer starts to change. LAG (or latency time) ~~commences after the LAT interval, and is defined as~~ the number of years taken for the relative risk to change from its original magnitude and to reach that of the unexposed (RR=1 if the exposure is removed entirely) or a lower/higher exposure group (if the prevalence of exposure decreases/increases). In our analyses, we assumed a linear ~~decrease~~change in risk over the LAG period. As there is very limited evidence on the true LAT and LAG for each exposure-cancer association, we modelled a ‘rapid’ and ‘slow’ ~~change~~effect on cancer incidence following a change in the prevalence of a causal factor. In the ‘rapid’ change, we modelled a LAT of 1 year and a LAG of 9 years (total latency of 10 years from change in prevalence of exposure to full change in cancer risk), and for the ‘slow’

change we modelled a LAT of 5 years and LAG of 15 years (total latency of 20 years) (Fig. 2).

We then estimated future cancer incidence for each year of the study period (2013-2037) under different intervention scenarios. For each scenario, we assumed that the prevalence of the target factor changed by a precise amount in response to an effective hypothetical intervention, and applied the potential impact fraction (PIF) to the reference scenario estimates for each year to estimate the hypothetical incidence under each intervention. The formula for the PIF is:³⁵

$$PIF = \frac{\sum_{x=1}^n p_x RR_x - \sum_{x=1}^n p_x^* RR_x}{\sum_{x=1}^n p_x RR_x}$$

Where p_x is the proportion of the population in each age and sex and exposure factor category x , RR_x is the RR (LAT/LAG adjusted) for that category compared to the theoretical minimum risk level for each exposure and p_x^* is the proportion in each age, sex and exposure factor category x after the intervention.

For postmenopausal breast cancer, the PIF was only applied to incidence rates in women aged ≥ 50 years. In the supplementary analysis for premenopausal breast cancer and vigorous physical activity, the PIF was only applied to incidence rates in women < 50 years.

To estimate the total proportion of cancers potentially avoidable over the study period (2013-2037), first, for each exposure-cancer couplet we modelled the number of cancers potentially avoided over the 25 year period under each intervention scenario (for both the 'rapid' and 'slow' change LAT and LAG periods). We then summed the estimated number of cancers causally associated with overweight/obesity or physical inactivity expected under the reference scenario and each intervention scenario over the 25-year period and calculated the proportion of cancers potentially avoided under each scenario.

Results

Overweight/obesity

The prevalence of observed overweight and obesity in Australian adults in 2011-2012 and the estimated prevalence of overweight and obesity by the end of the study period (2037), under the different intervention scenarios, is summarised in Table S3.

Under the most optimistic scenario (Theoretical Maximum) in which overweight and obesity were eliminated in the Australian population in Year 1, we estimated between 9-10% (under the ‘slow’ change) and 13% (‘rapid’ change) of overweight/obesity-related cancers could be prevented over the study period in men and 7-11% in women (Table 2). This equates to an estimated 543,000-75,600 avoidable cancers in Australian men and 776,760-114,790 avoidable cancers in Australian women over 25 years (Table 2). We conducted two sensitivity analyses using this scenario. First, we used non-linear dose-response RRs, and found that the overall proportion of avoidable cancers was similar (10-14% men; 9-14% women); however, there were differences by cancer type with some showing an increase in the proportion avoidable (colon, rectum, gallbladder, endometrial) and others a decrease (stomach-cardia, liver, ovary) (Table S4). Second, we used 25 kg/m² as the theoretical minimum risk level (instead of 22 kg/m²) and, as expected, this resulted in a lower proportion of avoidable overweight/obesity-related cancers (6-9% for men; 5-8% women).

Under a more conservative scenario where, over 10 years, the proportion of the population in the overweight and obese categories declined by 5% and 10% each year respectively (Targeted Reduction), we estimated that the proportion of overweight/obesity-related cancers potentially preventable would be 4-6% for men (22,600-35,700 cancers) and 3-5% for women (33,900-56,900 cancers) (Table 2).

Under both the Theoretical Maximum and Targeted Reduction scenarios, the cancers with the highest proportion of potentially avoidable cases were oesophageal adenocarcinoma, liver and kidney cancer for both sexes, and endometrial cancer for women (Table 2). The cancers with the largest absolute numbers potentially avoidable were colon in men (up to 17,000200 cancers over 25 years) and postmenopausal breast in women (up to 48,20047,700 cancers over 25 years) (Table 2).

If the prevalence of obesity continued to rise over the period 2013-2022, we estimated a 1-2% increase in overweight/obesity-related cancers over the 25-year study period (~~5,9006,100-10,1009,900~~ extra cancers men; ~~9,7009,900-17,500-17,300~~ extra cancers women) (Table S5).

In a supplementary analysis we estimated that 7-~~9~~40% of prostate cancer deaths would be potentially preventable under the theoretical maximum scenario (9,~~500200-11,7002,600~~ deaths); this dropped to 3-~~4~~5% under the more conservative scenario (3,~~900800-5,4006,000~~ deaths) (Table S6).

Fig. 3 demonstrates the impact of using different LAT and LAG periods by presenting the proportional difference between the numbers of cancers expected under the reference scenario with those expected under each intervention scenario. It also makes clear the rate of change in the prevalence of overweight/obesity under different scenarios.

Physical inactivity

The prevalence of physical inactivity levels observed in Australian adults in 2011-2012 and the estimated prevalence by the end of the study period (2037), under the intervention scenarios, are summarised in Table S7.

Under the most optimistic scenario (Theoretical Maximum) in which no Australian adults were inactive from year 1 (i.e. fell below the recommended level of $\geq 1,000$ MET-minutes/week), we estimated 2-3% of cancers causally associated with physical inactivity

(inactivity-related cancers) could be prevented over a 25-year period in men (colon cancer $\approx$ 3,700-5,500 avoidable cancers) and 1-2% in women (colon, breast and endometrial cancers $\approx$ 8,800-13,700 avoidable cancers in total) (Table 3). If this scenario also led to weight loss equivalent to a 1 unit reduction in BMI in year 1 in those who were overweight or obese, an additional ~~6,800-9,900~~7,500-9,700 overweight/obesity-related cancers (for those cancer types not also related to physical inactivity) in men and ~~3,000-4,400~~3,200-4,800 in women would also be avoided (Table S8).

Under the scenario which assumed all Australian adults met physical activity guidelines recommended for cardiac health (≥ 150 minutes of physical activity/week), we estimated that ~~0.45%~~ to 1.1% of inactivity-related cancers would be potentially prevented over a 25-year period, and this was similar for men and women (Table 3).

Less than 10% of Australian women ≤ 50 years currently engage in ≥ 30 minutes of vigorous physical activity/day (Table S9). In supplementary analyses, we estimated 1.0-1.4% of all breast cancers (5-7% of premenopausal breast cancers $\approx$ 4,700-6,900 avoidable cancers) were potentially preventable over the period 2013-2037 if all premenopausal women commenced at least 30 minutes of vigorous physical activity daily.

Discussion

We found that up to 13% of overweight/obesity-related cancers in men and 11% in women could be avoided over a 25-year period if overweight and obesity were eliminated from the Australian population ($\approx$ 190,000 cancers avoided). An estimated 3% of colon cancers in men and 2% of colon, breast and endometrial cancers in women could be avoided over a 25-year period if everyone undertook at least 300 minutes of moderate intensity physical activity per week ($\approx$ 19,000 cancers avoided).

Very few studies have used the same approaches to model the potential impact of overweight/obesity and physical activity interventions on cancer incidence. A study of Nordic countries reported that over a 30-year period, 9.5% of overweight/obesity-related cancers could be prevented if overweight/obesity were eliminated in the population (ranging from 8.5% in Norway to 12.6% in Iceland).³⁶ These results, using similar parameters over a slightly longer timeframe, accord quite closely with ours. Another study of seven European countries³⁷ estimated 14-18% of colon cancers (as distinct from colorectal cancers) in men and 2-5% in women could be prevented in 2040 (the final year of a 30-year study period) if they obtained an ideal weight distribution from 2009 onwards. Similarly 3-12% of colon cancers in men and 4-21% in women could be avoided if physical activity guidelines were met from 2009 onwards.³⁷ Our results (9.10% men, 4% women, for overweight/obesity; 3% men, 2% women, for physical inactivity) were mostly lower, though we presented the proportion avoidable over the whole study period rather than in the final year alone, so the results are not directly comparable.

Like all such studies, our findings are based on a number of assumptions and depend upon the validity of the key inputs. We elected to use cancer incidence rates in our base year (2012) as the reference scenario, holding these steady over a 25-year period, with changes in cancer numbers solely due to demographic changes in the population. This approach provides a stable base for comparison across cancers and captures the full impact of the modelled intervention scenarios versus the reference scenario, as the only difference between the two scenarios are due to differences in the prevalence of the exposure. While this approach will likely underestimate future cancer incidence, it does not require assumptions to be made about projected trends in cancer incidence which will vary by cancer type and likely introduce an additional level of uncertainty to these current projections. Moreover it does not have to account for the impacted complex interaction of existing trends in weight change, or

physical activity or other risk factors on future cancer incidence. For example, it is very likely that the proportion of all cancers attributable to overweight/obesity will increase in the future due to the relative decline in infection-related and smoking-related cancers. Modelling the effects of changes in the prevalence of other risk factors was beyond the scope of this analysis, but If we had elected to use projected cancer trends as inputs, the proportion of avoidable cancers would remain essentially the same (as the PIF formula does not include cancer incidence rates), but the estimated numbers of avoidable cancers would differ. Future studies could, however, monitor the impact of these changes.

We used cancer incidence data for 2012 as our base year, as this was the latest year for which national data was available for all relevant cancer types. If more recent data had been available at time of analysis, it is likely that the estimated number of cancers avoided would have been higher for the majority of cancer types; however, the PIF for each cancer would remain unchanged.

When selecting the exposure-cancer associations to include in our model, we used the most up-to-date causality assessments from both the WCRF and IARC, with relative risks sourced from meta-analyses of cohort studies or large pooled analyses. Our exposure prevalence data were from a nationally representative survey;¹⁸ however, we did not have data on other measures of body fatness causally associated with cancer (e.g. waist circumference or waist-hip ratio), and we could only model recreational and transport-related physical activity (and not household or occupational activity).

We tested a number of assumptions in sensitivity analyses. When we explored the nonlinearity of the dose-response relationship between BMI and select cancers we found that the overall proportion of avoidable cancers was similar. The use of a different Theoretical Minimum Risk level when we calculated the RRs for each category of BMI (25 kg/m² instead of 22 kg/m²) resulted in a lower proportion of overweight/obesity-related cancers.

One of the advantages of our modelling approach was the ability to include time elements in the model to reflect delayed changes in risk after a change in exposure prevalence has occurred. Our use of two LAT/LAG sets provides some guidance on the magnitude of uncertainty around how quickly cancer risks might change in populations exposed to broadly based lifestyle interventions.

We could not take into account interactions between overweight/obesity and physical inactivity or with other risk factors in our models; e.g. menopausal hormone therapy and overweight/obesity for reproductive cancers.³⁸⁻⁴⁰ However, we did consider the related reduction in overweight/obesity-related cancer incidence if the Theoretical Maximum physical inactivity intervention scenario resulted in weight loss among those who were overweight and obese.

Conclusions

This study provides policy-relevant information on the magnitude of cancer prevention that might be achieved under interventions that change the prevalence of a specific causal factor by different degrees, and also demonstrates the length of time it takes for interventions to have their full impact. While our estimates of the proportions of cancers avoidable over a 25-year time horizon for the more realistic interventions seem quite modest (3-6% overweight/obesity, 0.4-1% physical-inactivity), the absolute numbers of avoidable cancers are substantial (~~55,600-92,500~~56,500-92,700 overweight/obesity, 3,700-7,000 physical inactivity). In addition, as cancer is only one condition related to overweight/obesity and physical inactivity, any interventions that decrease the prevalence of these factors in the Australian population will also reduce the incidence of other causally-related diseases such as diabetes, cardiovascular disease and dementia.^{41, 42}

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These findings provide further impetus to invest in interventions to mitigate the rising tide of obesity and physical inactivity in the Australian population.

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Conflict of Interest

There are no competing financial interests in relation to this work.

For Peer Review

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Table 1 Summary of relative risks for the association between recreational physical activity and included cancer sites

Cancer (ICD-10 code)	Source of Relative Risk	RR (95% CI)
Colon (C18, C19)	Meta-analysis of 5 cohort studies ($I^2 = 51.7\%$; $p\text{-value} = 0.08$) ¹	P: 0.98 (0.96-1.00) per 5 MET-hours/week
Breast – postmenopausal (C50)	Meta-analysis of 5 cohort studies ($I^2 = 0.0\%$; $p\text{-value} = 0.68$)	F: 0.98 (0.97- 0.99) per 10 MET-hours/week
Endometrium (C54)	Meta-analysis of 3 cohort studies ($I^2 = 0.0\%$; $p\text{-value} = 0.41$)	F: 0.99 (0;98-1.00) per 3 MET-hours/week

ABBREVIATIONS: RR = relative risk; 95% CI = 95% confidence interval; F = females; P = persons; MET-hours = metabolic equivalents (MET) hours

¹Relative risks from the WCRF 2011 Continuous Update Project report for colorectal cancer have been used as the WCRF 2017 Continuous Update Project report for colorectal cancer did not conduct a dose-response meta-analysis as any additional studies with dose-response results (published between 2010 and 2016) were not in MET-hour units.^{8, 23}

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Table 2 Estimated number and proportion of overweight/obesity-related cancers avoided 2013-2037 (25 years) under different theoretical intervention scenarios of future change in body mass index (BMI) prevalence in the Australian population

Cancer site (ICD-10 code)	MEN				WOMEN			
	Intervention scenario 1 Theoretical maximum		Intervention scenario 2 Targeted Reduction		Intervention scenario 1 Theoretical maximum		Intervention scenario 2 Targeted Reduction	
	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹
TOTAL PERIOD 2013-2037								
Oesophagus-adenocarcinoma (C15) ²	<u>6221-</u> <u>87966155-</u> <u>8838</u>	<u>27.0-</u> <u>38.126.7-38.3</u>	<u>2678-</u> <u>42462641-</u> <u>4281</u>	<u>11.6-</u> <u>18.411.5-</u> <u>18.6</u>	<u>1050-15014036-</u> <u>1494</u>	<u>25.0-35.724.6-</u> <u>35.5</u>	<u>470-760464-757</u> <u>18.111.0-18.0</u>	<u>11.2-</u> <u>18.111.0-18.0</u>
Stomach – cardia (C16.0)	<u>2420-</u> <u>33982377-</u> <u>3408</u>	<u>13.6-</u> <u>19.113.4-19.2</u>	<u>1010-</u> <u>1604990-1614</u> <u>9.0</u>	<u>5.6-9.15.7-</u> <u>9.0</u>	<u>748-1081736-</u> <u>1072</u> <u>19.3</u>	<u>13.5-19.513.3-</u> <u>19.3</u>	<u>329-535324-532</u> <u>5.9-9.75.8-9.6</u>	<u>5.9-9.75.8-9.6</u>
Colon (C18, C19)	<u>12475-</u> <u>1704212182-</u> <u>17184</u>	<u>6.4-9.06.6-9.0</u> <u>17.04212182-</u> <u>17184</u>	<u>5150-</u> <u>79605007-</u> <u>8070</u>	<u>2.7-4.22.6-</u> <u>4.2</u>	<u>4547-65734442-</u> <u>6475</u>	<u>2.6-3.82.6-3.8</u> <u>6475</u>	<u>1960-32331908-</u> <u>3185</u>	<u>1.1-1.91.1-1.8</u> <u>3185</u>
Rectum (C20)	<u>1513-</u> <u>21201475-</u> <u>2115</u>	<u>1.41.3-1.9</u> <u>21201475-</u> <u>2115</u>	<u>618-987601-</u> <u>985</u>	<u>0.6-0.90.5-</u> <u>0.9</u>	<u>418-619410-608</u> <u>985</u>	<u>0.6-1.00.6-0.9</u> <u>985</u>	<u>178-301175-299</u> <u>985</u>	<u>0.3-0.5</u> <u>985</u>
Liver (C22)	<u>8945-</u> <u>126838818-</u> <u>12734</u>	<u>22.2-</u> <u>31.421.9-31.6</u> <u>12734</u>	<u>3804-</u> <u>60643737-</u> <u>6111</u>	<u>9.4-15.09.3-</u> <u>15.1</u> <u>6111</u>	<u>3529-51023480-</u> <u>5064</u>	<u>22.5-32.522.2-</u> <u>32.3</u>	<u>1577-25701551-</u> <u>2552</u>	<u>10.0-16.49.9-</u> <u>16.3</u>
Gallbladder (C23,C24)	<u>1755-</u> <u>23721720-</u> <u>2427</u>	<u>13.8-</u> <u>18.613.5-19.0</u> <u>2427</u>	<u>734-1115718-</u> <u>1148</u>	<u>5.8-8.75.6-</u> <u>9.0</u>	<u>2175-31172132-</u> <u>3080</u>	<u>13.9-19.913.6-</u> <u>19.6</u>	<u>954-1552935-</u> <u>1537</u>	<u>6.1-9.96.0-9.8</u> <u>1537</u>
Pancreas (C25)	<u>4467-</u> <u>61044369-</u> <u>6178</u>	<u>8.3-11.48.2-</u> <u>11.5</u>	<u>1848-</u> <u>28541800-</u> <u>2911</u>	<u>3.5-5.33.4-</u> <u>5.3</u>	<u>3226-46263153-</u> <u>4563</u>	<u>6.5-9.36.3-9.2</u> <u>4563</u>	<u>1402-22851363-</u> <u>2256</u>	<u>2.8-4.62.7-4.5</u> <u>2256</u>
Breast (postmenopausal) (C50)	-	-	-	-	<u>32240-</u> <u>4816531907-</u> <u>47674</u>	6.6- <u>9.99.8³</u> <u>4816531907-</u> <u>47674</u>	<u>13927-</u> <u>2366213762-</u> <u>23401</u>	<u>2.9-4.92.8-</u> <u>4.8³</u> <u>23401</u>
Endometrium (C54, C55)	-	-	-	-	<u>19370-</u> <u>2884219235-</u> <u>28621</u>	<u>24.2-36.024.0-</u> <u>35.7</u> <u>28621</u>	<u>8632-</u> <u>145008562-</u> <u>14374</u>	<u>10.8-</u> <u>18.140.7-17.9</u> <u>14374</u>
Ovary (C56)	-	-	-	-	<u>1676-24881653-</u> <u>2467</u>	<u>3.6-5.43.6-5.3</u> <u>2467</u>	<u>723-1221712-</u> <u>1206</u>	<u>1.6-2.61.5-2.6</u> <u>1206</u>
Kidney (C64)	<u>11339-</u>	<u>16.5-</u>	<u>4766-</u>	<u>7.0-11.26.8-</u>	<u>5974-88125898-</u>	<u>16.1-23.715.9-</u>	<u>2632-43942593-</u>	<u>7.1-11.87.0-</u>

	1620911178-	23.616.3-23.7	76844683-	11.2	8714	23.4	4341	11.7
	16219		7711					
Thyroid (C73)	1763-	9.4-14.29.3-	735-1251729-	3.9-6.63.9-	1065-16691064-	2.0-3.22.0-3.2	459-810456-809	0.9-1.60.9-1.5
	26681758-	14.1	1247	6.6	1658			
	2659							
Multiple myeloma (C90)	3067-	9.5-13.19.3-	1274-	3.9-6.13.8-	1568-22841538-	6.3-9.26.2-9.1	679-1125662-	2.7-4.5
	42333008-	13.2	19851244-	6.2	2252		1108	
	4278		2019					
TOTAL 2013-2037	53965-	9.5-13.39.3-	22617-	4.0-6.33.9-	77586-	7.4-10.97.3-10.8 ⁵	33922-	3.2-5.43.2-
	7562553040-	13.4 ⁵	3575022150-	6.4 ⁵	11487976684-		5694832467-	5.3 ⁶
	76040		36097		113742		56357	

ABBREVIATIONS: Est. cancers avoided = estimated number of cancers potentially avoided; % avoided = estimated proportion of cancers potentially avoided

SCENARIOS MODELLED: 1) Theoretical maximum = from year 1 (2013) 100% of the population aged ≥ 15 years reduced their BMI to ≤ 25 kg/m². 2) Targeted reduction = Over a 10-year period, the proportion of people in the each overweight BMI category (25-29.99 kg/m²) declined by 5% each year and the proportion in each obese BMI category (≥ 30 kg/m²) declined by 10% each year.

¹ The lower bound reflects the ‘slow’ change (i.e. LAT= 5 years, LAG=15 years [giving a total latency time of 20 years from change in prevalence of exposure to full change in cancer risk](#)); the upper bound reflects the ‘rapid’ change (i.e. LAT=1 year, LAG=9 years [giving a total latency time of 10 years](#)).

² Oesophageal cancer (adenocarcinoma) with ICD-O-3.1 histology codes 8140–8141, 8143–8145, 8190–8231, 8260–8263, 8310, 8401, 8480–8490, 8550–8551, 8570–8574, 8576

³ Proportion of all breast cancer.

⁴ Proportion of postmenopausal breast cancer (≥ 50 years).

⁵ Proportion of overweight/obesity-related cancers.

Table 3 Estimated number and proportion of inactivity-related cancers avoided 2013-2037 (25 years) under different theoretical intervention scenarios of future change in physical inactivity prevalence in the Australian population

Cancer site	MEN				WOMEN			
	Intervention Scenario 1 Theoretical maximum		Intervention Scenario 2 Everyone meets PA guidelines for cardiac health		Intervention Scenario 1 Theoretical maximum		Intervention Scenario 2 Everyone meets PA guidelines for cardiac health	
	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹	Est. cancers avoided ¹	% avoided ¹
TOTAL PERIOD 2013-2037								
Colon (C18, C19)	366274-5490501	1.9-2.9	11125-20136	0.6-1.1	3669-573842	2.1-3.3	1118-2130	0.6-1.2
Breast (postmenopausal) (C50)	-	-	-	-	38656- 597980	0.8-1.2 ²	1136-21146	0.2-0.4 ²
Endometrium (C54, C55)	-	-	-	-	13067-20067	1.0-1.65 ³	382-70940	0.3-0.5 ³
TOTAL 2013-2037	367624-5490501	1.9-2.9⁴	11125-20136	0.6-1.1⁴	88402- 137239	1.2-1.9⁴	2636-49536	0.4-0.7⁴

ABBREVIATIONS: PA = physical activity; Est. cancers avoided = estimated number of inactivity-related cancers potentially avoided; % avoided = estimated proportion of inactivity related cancers potentially avoided.

SCENARIOS MODELLED: 1) Theoretical maximum = from year 1 (2013) all of the population ≥ 15 years performed ≥ 1000 MET-minutes of physical activity per week.

2) Everyone meets physical activity (PA) guidelines for cardiac health = the proportion of the population (≥ 15 years) performing < 500 MET-minutes/week declined linearly over 10 years while there was a corresponding increase in the proportion in the 500-600 MET-minutes/week category. That is, by 2022 no-one is doing < 500 MET-minutes/week and the lowest physical activity category is now 500-600 MET-minutes/week.

¹ The lower bound reflects the 'slow' change (i.e. LAT= 5 years, LAG=15 years [giving a total latency time of 20 years from change in prevalence of exposure to full change in cancer risk](#)); the upper bound reflects the 'rapid' change (i.e. LAT=1 year, LAG=9 years [giving a total latency time of 10 years](#)).

² Proportion of all breast cancer

³ Proportion of postmenopausal breast cancer (≥ 50 years)

⁴ Proportion of inactivity-related cancers

Figure 1 Summary of summary relative risks from meta-analyses or pooled analyses for the association between body mass index (BMI) and included cancer sites.

ABBREVIATIONS: RR = relative risk; 95% CI = 95% confidence interval; n.p. = not published.

¹ For all cancer sites except thyroid cancer and multiple myeloma, RRs were sourced from the WCRF.⁸ For thyroid cancer RRs were sourced from a pooled analysis;²⁴ for multiple myeloma from a meta-analysis of prospective studies.²⁶

² Oesophageal cancer (adenocarcinoma) with ICD-O-3.1 histology codes 8140–8141, 8143–8145, 8190–8231, 8260–8263, 8310, 8401, 8480–8490, 8550–8551, 8570–8574, 8576.

³ Relative risks are for persons.

⁴ Relative risks are for prostate mortality – in this study this outcome was included as a supplementary analysis and we only calculated the number of prostate cancer deaths potentially avoided as data were not available for advanced prostate cancer incidence in 2012.

Figure 2 Visual explanation of how LAT and LAG periods affect relative risks over time in PREVENT models

Figure 3 Percentage difference in overweight/obesity-related cancers (2013 to 2037) between the reference scenario and different theoretical intervention scenarios and LAT and LAG periods for males and females.

SCENARIOS MODELLED: 1) Theoretical maximum = from year 1 (2013) 100% of the population aged ≥ 15 years reduced their BMI to ≤ 25 kg/m²; 2) Targeted reduction = Over a 10-year period, the proportion of people in the each overweight BMI category (25-29.99 kg/m²) declined by 5% each year and the proportion in each obese BMI category (≥ 30 kg/m²) declined by 10% each year; and 3) Continued increase = The proportion of people in each obese BMI category (≥ 30kg/m²) continued to increase by 2.3% each year over a 10-year period (2013-2022).

Figure 1 Summary of summary relative risks from meta-analyses or pooled analyses for the association between body mass index (BMI) and included cancer sites.

101x66mm (600 x 600 DPI)

Figure 2 Visual explanation of how LAT and LAG periods affect relative risks over time in PREVENT models

97x60mm (600 x 600 DPI)