Regional variation and increasing gabapentinoids prescribing in England

Document Version
Final published version

Link to publication record in Manchester Research Explorer

Citation for published version (APA):

Published in:
Pharmacoepidemiology and drug safety

Citing this paper
Please note that where the full-text provided on Manchester Research Explorer is the Author Accepted Manuscript or Proof version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version.

General rights
Copyright and moral rights for the publications made accessible in the Research Explorer are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Takedown policy
If you believe that this document breaches copyright please refer to the University of Manchester’s Takedown Procedures [http://man.ac.uk/04Y6Bo] or contact uml.scholarlycommunications@manchester.ac.uk providing relevant details, so we can investigate your claim.
Treatment patterns were captured at the class level and included selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), anxiolytics, hypnotics/sedatives, and antipsychotics. Treatment patterns were captured during all available follow-up, a minimum of 3 years.

**Results:** We identified 102,738 patients diagnosed with depression. The median patient age was 58 years [interquartile range = 35 to 70 years] and 66% were female. One quarter (26%) of patients did not receive any pharmacological treatment during follow-up. Of the treated, 56% received ≥2 different classes of therapy, while 25% received ≥3 classes and 8% received 4 or more. Sixty-four percent of patients first received an SSRI or SNRI, however 34% received an anxiolytic, hypnotic/sedative, or antipsychotic as the first treatment prior to any antidepressive treatment. Anxiolytics and SNRIs were the most common 2nd and 3rd treatments received, while anxiolytics and SNRIs were the most common 4th treatment, received by 24% of patients with at least 4 different treatments. Patients remained on their first treatment for an average of nine months.

**Conclusions:** More than a third of patients received a non-antidepressant as their first treatment. More than half of patients received more than one type of antidepressant or a completely different treatment class - anxiolytics, hypnotics, or antipsychotics - during the study follow up, suggesting that the first treatment received may not be optimal for most patients.

**567 | Levodopa misuse/abuse among patients with Parkinson’s disease**

Richard S. Swain; Patty Greene; Sara Karami; Travis Ready; Tamra Meyer

*Food and Drug Administration, Silver Spring, MD*

**Background:** Levodopa, often combined with carbidopa or with carbidopa/entacapone to improve its bioavailability, is indicated to treat symptoms of Parkinson’s disease (PD). A small portion of PD patients are thought to misuse/abuse levodopa, developing a pattern of compulsive self-medication called Dopamine Dysregulation Syndrome (DDS), in which patients increase their dosage despite experiencing harmful consequences of high levodopa dosage.

**Objectives:** To describe prevalence, risk factors, and trends of levodopa misuse/abuse among PD patients.

**Methods:** We extracted published epidemiologic studies on DDS or misuse/abuse of levodopa using PubMed on June 18, 2018 using search terms related to [Parkinson’s disease] and [levodopa] and [[dopamine dysregulation syndrome] or (misuse) or (abuse)]. We analyzed patterns of US poison center exposure calls (2008–2017) related to levodopa from the National Poison Data System (NPDS) and U.S. outpatient retail utilization patterns for levodopa-containing products from IQVIA™ (2013–2017) to provide context for misuse/abuse calls over time.

**Results:** Twenty-eight studies reported incidence, prevalence, or risk factors for misuse/abuse of levodopa among PD patients. Among the general PD population, reports of levodopa misuse/abuse prevalence ranged from 0–7.4%. High-risk sub-populations, including patients with compulsive behavior disorders (4–58.8%) and candidates for surgical subthalamic stimulation (0–20.6%), reported higher prevalence of misuse/abuse. Patient characteristics associated with levodopa misuse/abuse included: male gender, early onset PD, history of drug abuse or compulsive behaviors, mood disorders, and high daily dose of levodopa. U.S. retail drug utilization data showed the number of patients taking levodopa in the outpatient setting ranged from an estimated 541,000 patients in 2013 to 580,000 in 2017; including long-term care pharmacies, the number of tablets dispensed increased from 570 to 721 million tablets during the same span. We identified 11,985 NPDS exposure calls related to levodopa from 2008–2017, including 230 (1.9%) misuse/abuse calls. From 2013 to 2017, the years with available drug utilization data, the rate of levodopa misuse/abuse calls increased from 3.5 to 5.7 calls per 100,000 patients with a prescription for levodopa.

**Conclusions:** The epidemiologic literature and epidemiologic data suggest misuse/abuse of levodopa occurs among some PD patients. However, one summary estimate for PD patients may not be appropriate, as prevalence varies substantially based on patient characteristics.

**568 | Regional variation and increasing Gabapentinoids prescribing in England**

G.U. Xinchun; Teng-Chou Chen; Douglas Steinke; Li-Chia Chen

*Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK*

**Background:** Gabapentinoids (GPNs; i.e. gabapentin and pregabalin) will be classified as controlled substances in the United Kingdom (UK) from April 2019, due to increasing concerns of probable drug misuse deaths. Medication use is often linked with geographical variation and health inequality, but variations of GPN utilization is still not fully understood in the UK.

**Objectives:** This study aimed to quantify the amount and trend of prescription GPNs in England and identify the geographical variation in use.

**Methods:** This cross-sectional study applied practice-level dispensing data from the UK National Health Service Digital and the estimated population sizes from the Office for National Statistics between January 2011 and December 2017. GPNs prescribed by general practitioners in England were identified from the dispensing data. The annual utilization of GPNs dispensed in England was calculated in the number of defined daily doses (DDD)/1000 registrants. In 2017, the 7467 general practices were grouped into 207 clinical commissioning groups (CCGs) and ranked by the GPN utilization. Descriptive statistics were used to report annual utilization and its trend from 2011 to 2017. The CCG regions with top GPN utilization in 2017 were identified.

**Results:** The annual DDD/1000 registrants of prescribed GPNs significantly increased 140% from 1847 in 2011 to 4450 in 2017, with an
increasing annual rate of 442 DDD/1000 registrants per year. The increasing trend is consistent when stratified into gabapentin and pregabalin. In 2017, the median DDD/1000 registrants across the 207 CCGs was 4247 (interquartile range: 2857, 5302). The majority of CCGs with the highest GPNs utilization was in the North of England. Five of the top 10 ranking CCGs of GPN utilization were situated in the North West.

Conclusions: The prescribing of GPNs markedly and steadily increased in England. There is a North–South divide in prescribing GPNs with the North having a larger use than the South, which is potentially related to socioeconomic status. Further study is needed to identify the determinants of increasing GPNs prescribing and the associated harms.

569  |  Characterization of gabapentin use in Kentucky

GYeon Oh1,2; Svelta Slavova2,3; Patricia R. Freeman4,5

1 Department of Epidemiology, University of Kentucky, Lexington, KY; 2 Kentucky Injury Prevention and Research Center, University of Kentucky, Lexington, KY; 3 Department of Biostatistics, University of Kentucky, Lexington, KY; 4 Department of Pharmacy Practice and Science, University of Kentucky, Lexington, KY; 5 Institute for Pharmaceutical Outcomes and Policy, University of Kentucky, Lexington, KY

Background: Due to high prevalence of gabapentin among Kentucky (KY) drug overdose decedents and concerns for possible misuse in communities, gabapentin was reclassified as a Schedule V controlled substance (CS) in KY, effective July 2017.

Objectives: The purpose of this study was to characterize gabapentin use in KY.

Methods: We used Kentucky All Schedule Prescription Electronic Reporting (KASPER) data (Oct 2017-Sep 2018). Gabapentin use was defined as having received at least one gabapentin prescription during the study period. Gabapentin use rates, including by age, sex, and region, were calculated based on 2017 annual estimates of the resident population. Choropleth maps were created to examine regional variations in county-level gabapentin rate. Concurrent use of gabapentin with opioids, pregabalin, and benzodiazepines (BDZ) with 7+ continuous overlapping days was assessed.

Results: The overall state rate of gabapentin use was 66.3 per 1,000 residents, with highest rates among residents 55–64 years of age (133.4/1,000). Rates of gabapentin use were significantly higher in females vs. males [rate ratio (RR): 1.47; 95% confidence interval (CI): 1.46–1.48]. The prevalence of gabapentin use was significantly higher in eastern Kentucky counties, Appalachian region vs. Central region [RR: 1.73; 95% CI: 1.72–1.75] and Appalachian region vs. Delta region [RR: 1.36; 95% CI: 1.34–1.37]. The median days’ supply of gabapentin during study period was 179 days and the median daily dose was 911.0 mg. The median days’ supply of gabapentin and the median daily dose was significantly higher in Appalachian region [227 days; 1200 mg] than Central region [153 days (p-value: <0.001); 900 mg (p-value: <0.001)] and Delta region [170 days (p-value: <0.001); 900 mg (p-value: <0.001)]. Among gabapentin users, 44.6%, 19.5%, and 1.8% had 7+ continuous overlapping days with opioids, BDZ, and pregabalin, respectively.

Conclusions: Given that gabapentin use is more frequent in vulnerable populations (older age, female, and eastern Kentucky counties), further studies should examine the factors related to gabapentin prescribing and risk of having overlapping days with other CS.

570  |  New treatments for comorbidities after diagnosis with multiple sclerosis (MS): A study in the UK clinical practice research datalink (CPRD) GOLD

Rebecca Persson1; Sally Lee2; Neil Minton2; Steve Niemcryk2; Anders Lindholm2; Susan Jick1,3

1 Boston Collaborative Drug Surveillance Program, Lexington, MA; 2 Celgene Corporation, Summit, NJ; 3 Boston University School of Public Health, Boston, MA

Background: Patients with MS have an elevated risk of many comorbid conditions. Few studies have examined patterns of new treatment use for these conditions after MS diagnosis.

Objectives: To describe the patterns of new treatments for comorbid conditions in MS patients compared with matched non-MS patients.

Methods: We conducted a cohort study in the UK CPRD GOLD. Each MS patient diagnosed from 2001–2015 with ≥1 year of pre-diagnosis history was matched with up to 10 non-MS patients on age, sex, general practice and record history length before cohort entry (MS diagnosis/matched date). We compared new use of treatments for comorbid conditions in years 0 to <2 and 2 to <4 after cohort entry using a chi-square test. Prevalent users (patients with at least one prior prescription in the year before cohort entry) were excluded separately from each treatment category.

Results: 6932 MS patients were identified and compared with 68,526 non-MS patients (female, 70%; median age at cohort entry, 43 years). In both time periods, MS patients had higher use of antihypertensives (years 0–2: 7.9% vs. 5.3% [p < 0.0001] and years 2–4: 5.9% vs. 5.1% [p = 0.03]), immuno-suppressants for non-MS autoimmune disorders (years 0–2: 1.2% vs. 0.5% [p < 0.0001] and years 2–4: 0.6% vs. 0.4% [p = 0.01]), proton pump inhibitors (PPIs) (years 0–2: 14.9 vs. 7.6% [p < 0.0001] and years 2–4: 10.8 vs. 7.7% [p < 0.0001]), antibiotics (years 0–2: 39.1 vs. 31.7% [p < 0.0001] and years 2–4: 30.2 vs. 24.9% [p < 0.0001]) and sexual dysfunction treatments (males) (years 0–2: 6.2 vs. 1.8% [p < 0.0001] and years 2–4: 5.9% vs. 5.1%). MS and non-MS patients had similar new use of asthma/COPD treatments, but the percentage of new users changed over time (years 0–2: 5.2 vs. 5.0% [p = 0.66] and years 2–4: 3.2 vs. 3.6% [p = 0.10]). Use of the following drug categories were similar for MS and non-MS patients and percentage of new users was consistent over time: statins (~2.5%),