BMJ Open  Medication use and comorbidities in an increasingly younger osteoarthritis population: an 18-year retrospective open-cohort study

Jove Graham 1, Tonia Novosat 2, Haiyan Sun 3, Brian J Piper 1,4, Joseph A Boscarino 5, Melissa S Kern 1, Vanessa A Hayduk 1, Craig Beck 6, Rebecca L Robinson 7, Edward Casey 6, Jerry Hall 7, Patricia Dorling 6, Eric Wright 1

ABSTRACT

Objectives As understanding of the pathogenesis and treatment strategies for osteoarthritis (OA) evolves, it is important to understand how patient factors are also changing. Our goal was to examine demographics and known risk factors of patients with OA over time.

Design Open-cohort retrospective study using electronic health records.

Setting Large US integrated health system with 7 hospitals, 2.6 million outpatient clinic visits and 97,300 hospital admissions annually in a mostly rural geographic region.

Participants Adult patients with at least two encounters and a diagnosis of OA or OA-related surgery between 2001 and 2018. Because of geographic region, over 96% of participants were white/Caucasian.

Interventions None.

Primary and secondary outcome measures Descriptive statistics were used to examine age, sex, body mass index (BMI), Charlson Comorbidity Index, major comorbidities and OA-relevant prescribing over time.

Results We identified 290,897 patients with OA. Prevalence of OA increased significantly from 6.7% to 33.5% and incidence increased 37% (from 3772 to 5142 new cases per 100,000 patients per year, p<0.0001). Percentage of females declined from 65.3% to 60.8%, and percentage of patients with OA in the youngest age bracket (18–45 years) increased significantly (6.2% to 22.7%, p<0.0001). The percentage of patients with OA with BMI ≥30 remained above 50% over the time period. Patients had low comorbidity overall, but anxiety, depression and gastro-oesophageal reflux disease showed the largest increases in prevalence. Opioid use (tramadol and non-tramadol) showed peaks followed by declines, while most other medications increased slightly in use or remained steady.

Conclusions We observe increasing OA prevalence and a greater proportion of younger patients over time. With better understanding of how characteristics of patients with OA are changing over time, we can develop better approaches for managing disease burden in the future.

INTRODUCTION

Osteoarthritis (OA) is a severe disease resulting in substantial clinical and economic burden to society and large humanistic tolls on sufferers and their families.1,2 The global rate of OA has increased 9.5% over the last two decades, with prevalence in North America increasing over 22.5%.3 Although OA inflicts its greatest burden on the growing age population,4–6 it is important to understand the impacts on all segments of the population, including younger patients. In 2013, the US population with arthritis between the ages of 16 and 64 years lost an average of $4040 in earnings directly attributable to their disease,7 and in Spain from 2010 to 2018, the total cost incurred by the disease including both direct healthcare costs and lost wages was estimated at €690.4 million or $839 million.8 In

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Primary strength was our ability to leverage records on a large cohort of over 290,000 patients over almost two decades to study the trends in osteoarthritis (OA).

⇒ We are not aware of any similar US-based study combining demographics, comorbidities and prescribing trends in OA over such a long time period.

⇒ As an observational study of information collected during routine clinical care, patient information was only collected when patients sought medical care.

⇒ We identified patients with OA based on diagnosis and procedure codes that could have been assigned by any provider based on his/her clinical judgement, so we may have overestimated the absolute size of the OA population; however, the relative changes and trends are less likely to have been affected.

⇒ As an open-cohort study, we did not follow the same group of patients over the entire time period; this approach, however, more accurately represented the reality that providers face in treating new patients each year, and the mean observation time per patient was approximately 6 years.
addition, there is overwhelming evidence that obesity is a risk factor for OA, though the mechanism is not fully understood since OA is now correctly studied as a systemic disease rather than just isolated degenerations of weight-bearing joints. Similarly, postmenopausal women are also at higher risk of OA but no simple causal relationship between oestrogen and OA has been found, and men suffer from OA as well.

Understanding the burden of OA and whether patient factors are changing over time is important for implementing preventative strategies. While several other studies have used panel surveys or other data sources to document the growing global burden of OA, more population-level information on how patients with OA have been changing over time is helpful for clinicians and researchers to maintain understanding of underlying changes in the populations they treat. Our objective was to use electronic health records (EHRs) from a large, mostly rural integrated US health system in which we could simultaneously examine trends in demographics (eg, age, sex), physical characteristics (body mass index, BMI), comorbid conditions and relevant medication use. We performed this study using a retrospective, open-cohort design, and we are not aware of another trend study that has been able to examine these different aspects of patients with OA over an almost two-decade interval in a comparably large population.

METHODS

Setting and study design

All data for this study originated from Geisinger, an integrated health system in Pennsylvania with approximately 2.6 million outpatient clinic visits and 97 300 hospital admissions annually. Geisinger comprised seven hospitals, a network of 138 primary and specialty clinic sites and a single EHR platform (Epic, Verona, Wisconsin) encompassing inpatient and outpatient care across its network since 2001. It serves a 45-county area of central and northeastern Pennsylvania (with 35 counties designated as rural) with 18% of the population aged 65 or older, and a median household income ($60 500) that was 14.5% lower than the US median in 2021. Geisinger Health Plan, an affiliated insurance company, provides insurance to approximately one-third of the patients receiving care at Geisinger, though insurance claims were not used for this analysis. We note that the total size of the health system also increased in 2014 due to acquisition of a new hospital system. This was a retrospective, open-cohort study using EHRs at Geisinger. Patients were initially identified as belonging to the health system’s adult population if they were aged 18 years or older when they had at least two ambulatory encounters at a Geisinger facility between 1 January 2001 and 31 December 2018. From this population, we then identified patients as having OA if they received a diagnosis code for OA in the EHR from any provider during an encounter, or if they underwent an OA-relevant procedure (hip/knee replacement, arthroscopy or injection; list of procedure codes is provided in online supplemental table X1). We realise that there have been many published algorithms for identifying patients with OA in the EHR, and that this definition was similar to several of those, but not identical due to our desire to leverage procedure as well as diagnosis codes. The first occurrence of an OA diagnosis or procedure was defined as the patient’s index date, recognising that in a retrospective study like this one, patients may have been diagnosed with OA prior to the study period or prior to entering the health system. OA was defined using the International Classification of Diseases Ninth/Tenth Revisions, Clinical Modification (ICD-9/10) codes ICD-9: 715.* or ICD-10 M15–19. During each calendar year (2001–2018), patients were defined as active during that year if they had an outpatient visit, emergency department visit or inpatient admission where review of all medications took place; patients with only a prescription order or refill in a year were not considered active. Patients were defined as an active patient with OA if they were active and had been diagnosed with OA in that year or a previous year.

Statistical analysis

Descriptive statistics were used to report the per cent of patients with OA (prevalence) in each year (1 January to 31 December) beginning in 2001, and the number of new patients with OA per 100 000 patients in the population (incidence) in each subsequent year. Patients who died were still included in prevalence and incidence counts for the year of death if they had been active. Estimates of prevalence and incidence that were age and sex adjusted based on the US census were also calculated. Descriptive statistics were then used to examine patient characteristics (age, sex, BMI) among the active patients with OA in each year. We examined the percentage of patients in each year with the comorbidities in the Charlson Comorbidity Index (CCI) and percentage of patients with anxiety or depression, based on whether a relevant ICD-10 or ICD-9 code (for those conditions) appeared on their problem list or on two separate encounters before or during the year in question.

Finally, we examined the percentages of patients in each year who had used nine categories of medications: acetaminophen, serotonin and norepinephrine reuptake inhibitors (SNRI), homeopathic medications, injectable OA medications, non-steroidal anti-inflammatory drugs (NSAID, including continuous or as needed), tramadol, non-tramadol opioids, salicylates or other topical OA medications. The generic drug names included in these nine categories are provided in online supplemental table X2. For prescription drugs, we examined prescription orders from 2001 to 2018 and counted patients with at least one order in a given year. For non-prescription (ie, over-the-counter) drugs, we were unable to assess use over the entire time period, but medication reconciliation records (ie, self-reported use) were examined from 2007 to 2017, and we counted patients with at least one...
self-reported use of each medication in a given year. For acetaminophen and NSAID, our primary interest was non-prescription acetaminophen and prescription NSAIDs.

This was primarily a descriptive study of a population without a priori hypotheses; however, since it was a longitudinal study, we constructed 95% CIs around all estimates and used Cochran-Armitage (two categories) or Cochran-Mantel-Haenszel (more than two categories) test of trend for statistically significant changes in percentages over time. All statistical analyses were completed using SAS software (SAS V.9.4).

**Patient and public involvement**
The research was designed and conducted without patient or public involvement.

**RESULTS**
There were 290,897 patients identified in the EHR with a diagnosis of OA during the study period. The total observation time was 1.73 million patient-years for a mean observation time per patient of 5.96 years. The prevalence of OA increased from 6.7% in the first year (2001) to 33.5% in the final year (2018), which was a statistically significant increasing trend (p<0.0001). After age-sex standardisation, this increase in prevalence was 5.3% to 30.9%, which was also significant (p<0.0001). In the four age categories (18–44, 45–64, 65–79 and 80+), the prevalence of OA from 2001 to 2018 increased from 1.6% to 21.2%, 11.0% to 37.6%, 22.3% to 45.0% and 26.9% to 51.5%, respectively. The incidence of OA similarly showed a significant increase from 3772 new cases per 100 000 in 2002 to 5142 new cases per 100 000 in 2018 (p<0.0001).

Figure 1 presents data on prevalence and incidence.

The patient characteristic that showed the most noticeable difference over time was age: the percentage of patients with OA in the youngest age category (18–44 years) increased from 6.2% in 2001 to 22.7% in 2018, while the percentages in the oldest two age categories (65–79 and 80+) declined over the same period (44.0% to 27.7% and 15.7% to 11.7%, respectively). These changes occurred despite the fact that the overall age distribution of patients in the health system did not change appreciably, as seen in figure 2A. The percentage of patients with OA who were female declined from 65.3% in 2001 to 60.8% in 2018. Percentage of current tobacco smokers increased from 12.5% in 2001 to 18.1% in 2018. The percentage of patients in the BMI 30–35 range decreased slightly from 29.1% to 25.0%, and the percentage of patients with BMI >35 also decreased slightly from 29.9% to 28.3%. All of the increases and decreases referenced above were statistically significant trends as per the Cochran-Armitage or Cochran-Mantel-Haenszel test (p<0.0001). Table 1 presents the patient demographics for the OA population over time, while figure 2A,B show the age distribution over time of the total system patient population and OA population, respectively.

![Figure 1](http://bmjopen.bmj.com/)

**Figure 1** Total active patients in the health system, total patients with osteoarthritis (OA), new OA cases, prevalence and incidence over time for selected years in the study period. Prevalence was defined as the percentage of active patients diagnosed with OA in the health system, and incidence was defined as the number of new OA cases per 100 000 active patients per year. Note that 95% CIs have been shaded in grey on the figures but in most cases are too small to see.
present the sex and BMI distribution of the OA population, respectively.

While comorbidity was low overall (mean CCI scores between 0.9 and 2.9), the percentage of patients with CCI score greater than zero (ie, at least one Charlson comorbidity) increased significantly from 47.5% in 2001 to 64.0% in 2018. There were six comorbid conditions that either maintained or had reached greater than 20% prevalence in the OA population by the end of the study. Hypertension was consistently present in over 50% of the patients with OA every year, and diabetes mellitus (without complication) was present in 19%–21% of patients each year. Two other conditions (anxiety disorders and gastroesophageal reflux disease (GORD)) affected over 30% of the OA population by 2018 and significantly increased over time (p<0.0001), and prevalence of depression increased from 14.4% to 29.5% (p<0.0001). Chronic obstructive pulmonary disease (COPD) also significantly increased from 14.5% to 23.9% in prevalence over the period (p<0.0001). These data are presented in table 2.

Online supplemental table X3 and figure 3 present the percentages of patients using nine categories of OA-relevant medication in each year, based on prescription records. (Online supplemental table X4 presents this information for self-reporting of non-prescription medications in a different table because it was available over a different time range of 2007–2017.) Non-tramadol opioids showed a peak usage around 2009–2010 followed by a decline; tramadol opioids similarly displayed a peak in use slightly after that timeframe (2014–2015) and then declined. NSAIDs showed an initial sharp decline followed by usage by approximately 17%–20% of patients for most of the timeframe. Of the remaining medication types examined, acetaminophen use increased from 9.6% to 16.7%, and injectable OA medications, SNRIs and topical OA medications showed increases but with much lower absolute frequency (<8% of patients per year). Salicylates showed a relatively steady use from 31.2% to 36.2%, and homeopathic medications showed a low, steady use overall (4.0%–6.7% of patients).

**DISCUSSION**

In this retrospective study of EHRs at a single large health system from 2001 to 2018, prevalence and incidence of OA increased over time, some population characteristics remained relatively constant, but other patient characteristics appeared to be changing. Female sex and obesity, both known risk factors for OA, were present in the majority of patients over the entire time. Results showed, however, that younger patients in the age range of 18–44 years made up an increasingly larger proportion of the OA population over time. In addition to comorbid conditions like hypertension and diabetes that consistently remained highly prevalent, we also observed significant increases in the diagnoses of anxiety, depression, GORD and COPD. Finally, we saw peaks followed by declines in the use of opioids, increased use of injectable OA medication, an early decline in NSAID use and a relatively constant frequency of use of the other medications.

The primary strength of this study was its ability to leverage records on a large cohort of over 290,000 patients over almost two decades to study trends in OA. There are several limitations to acknowledge, however. First, this was an observational study of information collected during routine clinical care, so patient information was only collected when patients sought medical care. Second, due to the nature of the study and large cohort size, we identified patients with OA based on diagnosis codes that could have been assigned by any provider based on his/her clinical judgement, not by an American College of Rheumatology (ACR) clinical classification.
This simplistic definition is likely to have overestimated the absolute size of the OA population; however, the relative changes and trends reported on here are less likely to have been affected. Third, some of the medications discussed here (such as salicylates for cardiovascular disease) and procedures (eg, knee arthroscopy) could have been used for indications other than OA, something we were not able to discern from the data, which could lead to misclassification of patients with OA being treated for other conditions. With respect to this concern for procedures, we noted that the volume of these ‘ambiguous’ procedures that could have been related to injuries was much lower than that of joint replacement and other procedures known to be indicative of OA. We also examined the procedure frequency over time, which did not show an increase that would suggest oversampling of young patients over time, but a stable procedure volume over the period (data not shown). Fourth, as an open-cohort study, we did not follow the same group of patients over the entire time period; this approach, however, more accurately represented the reality that providers face in treating new patients each year, and the median observation time per patient was over 7 years. Finally, these results reflect a single health system in a largely rural geographic area with over 96% of patients who are white/Caucasian. This low racial and ethnic diversity may not represent trends seen in other more diverse regions, and is particularly important here because black or African

Table 1  Patient demographics for the OA population in selected years, with 95% CIs

<table>
<thead>
<tr>
<th>Year</th>
<th>Age (years), % (95% CI)</th>
<th>Sex*, % (95% CI)</th>
<th>Race, % (95% CI)</th>
<th>Ethnicity, % (95% CI)</th>
<th>BMI* (kg/m²), % (95% CI)</th>
<th>Smoking status, % (95% CI)</th>
<th>Charlson Comorbidity Index (CCI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>18–44: 6.2 (5.9, 6.6)</td>
<td>Females: 65.3 (64.6, 66.1)</td>
<td>White/Caucasian: 99.2 (99.0, 99.3)</td>
<td>Non-Hispanic: 99.6 (99.5, 99.7)</td>
<td>&lt;30: 41.0 (40.1, 41.8)</td>
<td>Never: 52.0 (51.2, 52.7)</td>
<td>Mean: 0.9 (0.88, 0.92)</td>
</tr>
<tr>
<td></td>
<td>45–64: 34.0 (33.3, 34.8)</td>
<td>Males: 34.6 (33.9, 35.4)</td>
<td>African American: 0.3 (0.2, 0.4)</td>
<td>Hispanic: 0.4 (0.3, 0.5)</td>
<td>30–35: 29.1 (28.3, 29.9)</td>
<td>Current: 12.5 (12.0, 13.0)</td>
<td>0.9 (0.88, 0.92)</td>
</tr>
<tr>
<td></td>
<td>65–79: 44.0 (43.2, 44.8)</td>
<td>Asian: 0.2 (0.2, 0.3)</td>
<td></td>
<td>BMI: 0.7 (0.6, 0.8)</td>
<td>&gt;35: 29.9 (29.2, 30.7)</td>
<td>Quit: 25.0 (24.3, 25.7)</td>
<td>With CCI&gt;0: 47.5 (46.7, 48.2)</td>
</tr>
<tr>
<td></td>
<td>80+: 15.7 (15.1, 16.3)</td>
<td>Other: 0.3 (0.2, 0.4)</td>
<td></td>
<td></td>
<td></td>
<td>Not asked: 10.5 (10.1, 11.0)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>18–44: 6.2 (5.9, 6.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
American individuals are more likely to have radiographic and symptomatic OA than white individuals. We acknowledge, therefore, that our study was unable to examine this group that is disproportionately impacted by OA at the national level.26

Our finding that OA is affecting a proportionately larger number of younger patients (aged 18–44) over time is important for predicting future burden worldwide. Age strongly correlates with risk of OA,6 27 28 and OA is often thought of as primarily affecting older patients; even so, by 2030, it is projected that approximately 25% of American adults will have disability due to OA, and approximately 50% of these sufferers will be younger than 65 years of age.29 We are not aware of similar studies reporting the age of patients with OA outside the USA with which to fully compare these data: we note that an approximate 1% prevalence in patients aged 18–29 years but the study did not report trends over time.30

The scope of our data did not allow us to fully explore the mechanism behind why our prevalence of OA increased among younger people, but two possible explanations could be continuing issues with obesity in younger adults accelerating OA-related joint degradation, or younger

### Table 2

<table>
<thead>
<tr>
<th>Prevalence (%) in active patients with OA</th>
<th>2001 (n=15 714)</th>
<th>2005 (n=45 777)</th>
<th>2010 (n=88 057)</th>
<th>2015 (n=141 681)</th>
<th>2018 (n=186 315)</th>
<th>Absolute change, 2001–2018 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety disorders</td>
<td>18.4 (17.8, 19.0)</td>
<td>26.7 (26.3, 27.1)</td>
<td>31.5 (31.2, 31.8)</td>
<td>36.1 (35.8, 36.3)</td>
<td>40.6 (40.4, 40.8)</td>
<td>22.2 (21.5, 22.8)</td>
</tr>
<tr>
<td>Depression</td>
<td>14.4 (13.8, 14.9)</td>
<td>21.8 (21.4, 22.2)</td>
<td>24.8 (24.5, 25.0)</td>
<td>27.7 (27.4, 27.9)</td>
<td>29.5 (29.3, 29.8)</td>
<td>15.2 (14.6, 15.7)</td>
</tr>
<tr>
<td>GORD</td>
<td>20.9 (20.3, 21.6)</td>
<td>30.8 (30.3, 31.2)</td>
<td>34.5 (34.2, 34.9)</td>
<td>36.9 (36.7, 37.2)</td>
<td>35.4 (35.1, 35.6)</td>
<td>14.4 (13.7, 15.1)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1.3 (1.1, 1.5)</td>
<td>3.1 (2.9, 3.3)</td>
<td>11.0 (10.8, 11.2)</td>
<td>13.5 (13.3, 13.7)</td>
<td>13.7 (13.5, 13.8)</td>
<td>12.4 (12.1, 12.6)</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>0.9 (0.7, 1.0)</td>
<td>2.5 (2.3, 2.6)</td>
<td>5.9 (5.7, 6.0)</td>
<td>8.6 (8.4, 8.7)</td>
<td>12.7 (12.6, 12.9)</td>
<td>11.9 (11.6, 12.1)</td>
</tr>
<tr>
<td>COPD</td>
<td>14.5 (14.0, 15.1)</td>
<td>18.9 (18.5, 19.2)</td>
<td>21.2 (21.0, 21.5)</td>
<td>23.1 (22.8, 23.3)</td>
<td>23.9 (23.7, 24.1)</td>
<td>9.3 (8.7, 9.9)</td>
</tr>
<tr>
<td>Solid tumour</td>
<td>7.3 (6.9, 7.7)</td>
<td>12.1 (11.8, 12.4)</td>
<td>14.5 (14.3, 14.7)</td>
<td>14.9 (14.7, 15.1)</td>
<td>15.5 (15.4, 15.7)</td>
<td>8.2 (7.8, 8.7)</td>
</tr>
<tr>
<td>Metastatic tumour</td>
<td>0.3 (0.2, 0.4)</td>
<td>1.5 (1.4, 1.6)</td>
<td>1.9 (1.8, 2.0)</td>
<td>3.1 (3.0, 3.2)</td>
<td>7.5 (7.4, 7.6)</td>
<td>7.2 (7.0, 7.3)</td>
</tr>
<tr>
<td>AIDS</td>
<td>0.0 (0.0, 0.0)</td>
<td>0.0 (0.0, 0.1)</td>
<td>0.1 (0.1, 0.1)</td>
<td>1.4 (1.3, 1.4)</td>
<td>6.9 (6.8, 7.0)</td>
<td>6.9 (6.8, 7.0)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>4.5 (4.2, 4.8)</td>
<td>8.8 (8.5, 9.0)</td>
<td>10.2 (10.0, 10.4)</td>
<td>10.4 (10.2, 10.5)</td>
<td>10.7 (10.6, 10.9)</td>
<td>6.2 (5.9, 6.6)</td>
</tr>
<tr>
<td>Diabetes, with organ failure</td>
<td>3.3 (3.0, 3.6)</td>
<td>5.8 (5.6, 6.0)</td>
<td>7.7 (7.5, 7.9)</td>
<td>7.4 (7.3, 7.5)</td>
<td>8.6 (8.5, 8.8)</td>
<td>5.3 (5.0, 5.6)</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>3.4 (3.1, 3.7)</td>
<td>5.8 (5.6, 6.1)</td>
<td>6.0 (5.8, 6.2)</td>
<td>6.3 (6.2, 6.4)</td>
<td>7.7 (7.6, 7.8)</td>
<td>4.3 (4.0, 4.6)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>7.0 (6.6, 7.4)</td>
<td>10.3 (10.0, 10.6)</td>
<td>11.5 (11.3, 11.7)</td>
<td>11.2 (11.1, 11.4)</td>
<td>10.9 (10.8, 11.1)</td>
<td>4.0 (3.6, 4.4)</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>0.3 (0.2, 0.3)</td>
<td>0.6 (0.5, 0.6)</td>
<td>1.0 (0.9, 1.0)</td>
<td>1.6 (1.5, 1.7)</td>
<td>3.9 (3.9, 4.0)</td>
<td>3.7 (3.6, 3.8)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2.3 (2.0, 2.5)</td>
<td>4.1 (4.0, 4.3)</td>
<td>4.5 (4.4, 4.7)</td>
<td>4.6 (4.5, 4.7)</td>
<td>4.7 (4.6, 4.8)</td>
<td>2.5 (2.2, 2.7)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0.3 (0.2, 0.4)</td>
<td>0.9 (0.8, 1.0)</td>
<td>1.1 (1.0, 1.2)</td>
<td>1.5 (1.4, 1.5)</td>
<td>2.7 (2.6, 2.8)</td>
<td>2.4 (2.2, 2.5)</td>
</tr>
<tr>
<td>Severe liver disease</td>
<td>0.1 (0.0, 0.1)</td>
<td>0.1 (0.1, 0.2)</td>
<td>0.3 (0.3, 0.4)</td>
<td>0.8 (0.8, 0.9)</td>
<td>1.9 (1.9, 2.0)</td>
<td>1.9 (1.8, 2.0)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>6.8 (6.4, 7.2)</td>
<td>9.0 (8.8, 9.3)</td>
<td>8.4 (8.3, 8.6)</td>
<td>8.4 (8.3, 8.6)</td>
<td>8.6 (8.4, 8.7)</td>
<td>1.8 (1.4, 2.2)</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>3.4 (3.1, 3.7)</td>
<td>3.3 (3.1, 3.5)</td>
<td>3.3 (3.2, 3.4)</td>
<td>3.4 (3.3, 3.5)</td>
<td>5.2 (5.1, 5.3)</td>
<td>1.8 (1.5, 2.1)</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>0.2 (0.1, 0.3)</td>
<td>0.4 (0.3, 0.4)</td>
<td>0.4 (0.4, 0.5)</td>
<td>0.5 (0.5, 0.6)</td>
<td>1.0 (1.0, 1.1)</td>
<td>0.8 (0.7, 0.9)</td>
</tr>
<tr>
<td>Dementia</td>
<td>1.5 (1.3, 1.6)</td>
<td>1.9 (1.7, 2.0)</td>
<td>2.0 (1.9, 2.1)</td>
<td>2.1 (2.0, 2.2)</td>
<td>2.0 (1.9, 2.0)</td>
<td>0.5 (0.3, 0.7)</td>
</tr>
<tr>
<td>Diabetes, uncomplicated</td>
<td>19.6 (19.0, 20.2)</td>
<td>20.5 (20.1, 20.9)</td>
<td>20.8 (20.5, 21.0)</td>
<td>20.3 (20.1, 20.5)</td>
<td>19.5 (19.3, 19.7)</td>
<td>−0.1 (−0.7, 0.6)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>56.7 (55.9, 57.5)</td>
<td>56.3 (55.9, 56.8)</td>
<td>53.8 (53.5, 54.2)</td>
<td>54.4 (54.2, 54.7)</td>
<td>55.8 (55.6, 56.0)</td>
<td>−0.9 (−1.7, −0.1)</td>
</tr>
</tbody>
</table>

Items are ranked by absolute per cent change from 2001 to 2018.

COPD, chronic obstructive pulmonary disease; GORD, gastro-oesophageal reflux disease; OA, osteoarthritis.
patients increasingly seeking care. Our estimate that 22%–23% of patients with OA were in the age range of 18–44 years was slightly higher but very close to the weighted nationally representative estimate of 16% in the 2015 Medical Expenditure Panel Survey.1 That same survey also estimated that for working age adults, missed workdays resulted in an approximately twofold higher wage loss among adults with OA versus those without, in addition to higher total annual healthcare costs. Another age-related consideration is that currently, there is no ‘cure’ for end-stage OA except for total joint replacements, and these devices have a finite life expectancy, with an expected revision rate of 12% within 10 years for total knees.31 The implication here is that even with this cure, younger patients who receive them will likely require additional revision surgeries, adding to the cost and burden of the disease.

The active OA population remained predominantly female (61%–65%) over the time period, and predominantly overweight or obese (53%–59% with BMI ≥30). The stability of the female versus male breakdown was not surprising given prior studies showing that females, and particularly postmenopausal females, are at higher risk of OA.14 Females over the age of 55 have a risk three times greater for radiologic OA than their male counterparts,32 and the female to male ratio of the world’s population is not likely to change over time. Obesity, on the other hand, has the potential to change the worldwide landscape of OA. The USA is recognised as having higher rates of overweight and obese citizens than most other countries (70.9% of men, 61.9% of women), but overweight rates have now risen to over 50% in over half of the world’s most developed countries,33 suggesting that increases in global OA burden will follow. The Framingham Study established a causal relationship between weight and knee OA,10 and that relationship poses a specific challenge for treatment. Total joint replacement, especially of the knee, is not expected to be as successful or complication free in patients who are more obese,34 and total joint recipients often do not lose weight or become more active after replacement, either.35–37 Our results add to the evidence, therefore, that both these epidemics—obesity and OA—are expected to continue and create challenges into the future. Perhaps the most important actions that can be taken now based on this evidence are for providers and healthcare systems to continue their efforts to prevent and/or reduce patient obesity in order to lessen the burden of OA.

Anxiety and depression more than doubled in prevalence over this time period, affecting 40.6% and 29.5% of the OA population in 2018, respectively. Prior research has established links between pain, OA and depression,38 though we also acknowledge that some of these increases could be due to greater recognition and identification of mental health conditions by providers over this timeframe. GORD and COPD, two comorbid conditions that are not traditionally thought of as related to the musculoskeletal system, were also frequently observed (35.4% and 23.9% in 2018, respectively) and were surprising. We note that the prevalence of tobacco smoking was fairly high in this population (12%–18% current smokers), though not much higher than the estimated national average of

Figure 3  Percentage of active patients with osteoarthritis (OA) in each year using OA-related medication. Note that acetaminophen, topical OA medication, salicylate and homeopathic medication are based on self-reported data of over-the-counter use from 2007 to 2017; all other medications are based on prescription orders from 2001 to 2018. APAP, acetaminophen; NSAID, non-steroidal anti-inflammatory drug.
14%,

which increases the risk of COPD. In addition, obesity is recognised as a major risk factor for GORD, which may explain this indirect association with OA.

Results suggest that the nationally recognised opioid epidemic has affected prescribing practices and that physicians have worked to reduce the amount of opioids, both tramadol and non-tramadol, being ordered. Otherwise, non-prescription medications such as salicylates and acetaminophen showed stable use, and NSAIDs showed an initial decline as opioid prescribing increased in the earlier years but then reached a stable level. Besides the rise of opioids, the decline in prescription NSAIDs in the early 2000s we believe may have had a number of other contributing factors, including changing expectations around pain management, increasing use of physical therapy and safety-related market withdrawals of COX-2 inhibitors such as rofecoxib in 2004. Another recent study examining newly diagnosed patients with knee OA at Geisinger from 2010 to 2018 described first-line and second-line treatment selections, with intra-articular corticosteroids and opioids being most frequent, but we are not aware of any similar US-based study examining prescribing trends over this long time period. DeMik et al reported stable rates of OA-relevant opioid prescribing from 2007 to 2014 but noted geographic disparities, and we agree that opioid prescribing may depend highly on the environment and health system efforts to deprecate, given the national media attention in recent years. Spitaels et al studied prescribing rates over a wider variety of drugs in Belgium over a timeframe similar to ours, from 1996 to 2015, and showed similar significant positive trends in use of acetaminophen, weak opioids, glucosamine (ie, homeopathic medications) and high but steady levels of oral NSAIDs.

CONCLUSION

In conclusion, this study provides new long-term data on how OA continues to disproportionately affect women and overweight individuals, and is increasingly affecting younger patients under the age of 45. Additionally, associations with other conditions such as anxiety and depression are on the rise, creating new complexity for treating providers. As OA costs rise, it is important to understand what to expect from future disease burden and design new preventative and treatment strategies accordingly.

Author affiliations

1Center for Pharmacy Innovation and Outcomes, Geisinger, Danville, Pennsylvania, USA
2Interventional Pain, Geisinger, Danville, Pennsylvania, USA
3Biostatistics Core, Geisinger, Danville, Pennsylvania, USA
4Department of Medical Education, Geisinger Commonwealth School of Medicine, Scranton, Pennsylvania, USA
5Department of Population Health Sciences, Geisinger, Danville, Pennsylvania, USA
6Pfizer, New York, New York, USA
7Eli Lilly and Company, Indianapolis, Indiana, USA

Twitter Eric Wright @nericwright

Contributors JG, TN, HS, BJ, JAB, MSK, VAH, CB, RLR, EC, JH, PD and EW contributed substantially to the planning, conception and design of the study, and provided a critical review of this manuscript during its writing. JG, TN, HS, BJ, JAB, MSK, VAH, CB, RLR, EC, JH, PD and EW provided final approval of this manuscript version to be published. JG and HS were directly responsible for the analysis of data. JG was responsible for the initial draft of this manuscript and is the guarantor of this work.

Funding The study was supported by Pfizer and Eli Lilly and Company (Award/Grant No CP208546).

Competing interests CB and EC are employees of Pfizer and have stock options. RLR and JH are employees and stockholders of Eli Lilly and Company. JG, BJ, MSK, VAH and EW are employees of Geisinger. During the study period, TN, HS and JAB were employees of Geisinger. Geisinger received institutional funding from Pfizer and Eli Lilly and Company for the study and in connection with the development of this manuscript. PD was an employee of Pfizer with stock options.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was reviewed and approved by Geisinger Institutional Review Board (IRB).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations, including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs

Jove Graham http://orcid.org/0000-0002-7881-8588
Brian J Piper http://orcid.org/0000-0002-2295-445X
Eric Wright http://orcid.org/0000-0003-1721-4104

REFERENCES


