Opioid prescribing trends and geographical variation in England, 1998–2018: a retrospective database study

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Summary

Background There is a call for greater monitoring of opioid prescribing in the UK, particularly of strong opioids in chronic pain, for which there is little evidence of clinical benefit. We aimed to comprehensively assess trends and variation in opioid prescribing in primary care in England, from 1998 to 2018, and to assess factors associated with high-dose opioid prescribing behaviour in general practices.

Methods We did a retrospective database study using open data sources on prescribing for all general practices in England. For all standard opioids we calculated the number of items prescribed, costs, and oral morphine equivalency to account for variation in strength. We assessed long-term prescribing trends from 1998 to 2017, patterns of geographical variation for 2018, and investigated practice factors associated with higher opioid prescribing. We also analysed prescriptions for long-acting opioids at high doses.

Findings Between 1998 and 2016, opioid prescriptions increased by 34% in England (from 568 per 1000 patients to 761 per 1000). After correcting for total oral morphine equivalency, the increase was 127% (from 190 000 mg to 431 000 mg per 1000 population). There was a decline in prescriptions from 2016 to 2017. If every practice prescribed high-dose opioids at the lowest decile rate, 543 000 fewer high-dose prescriptions could have been issued over a period of 6 months. Larger practice list size, ruralness, and deprivation were associated with greater high-dose prescribing rates. The clinical commissioning group to which a practice belongs accounted for 11·7% of the variation in high-dose prescribing. We have developed a publicly available interactive online tool, OpenPrescribing.net, which displays all primary care opioid prescribing data in England down to the individual practice level.

Interpretation Failing to account for opioid strength would substantially underestimate the true increase in opioid prescribing in the National Health Service (NHS) in England. Our findings support calls for greater action to promote best practice in chronic pain prescribing and to reduce geographical variation. This study provides a model for routine monitoring of opioid prescribing to aid targeting of interventions to reduce high-dose prescribing.

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For more on
OpenPrescribing.net see
https://openprescribing.net/

Introduction

Opioids are commonly and appropriately prescribed to reduce the intensity of acute, end-of-life, and cancer pain. However, they can cause harm such as addiction and abuse, particularly at higher doses.[1,2] The UK has seen a rising number of opioid-related deaths,[3] while the USA has severely restricted access to prescribed opioids.[4] Concerns have particularly been raised about the use of strong opioids in chronic pain, for which there is little evidence of clinical benefit.[5]

There has been a call for greater monitoring of opioid prescribing in the UK.[6] Guidelines released in 2010 promoted a cautious approach to any planned long-term prescribing of opioids.[7] The Opioids Aware resource, launched in 2016, was formed through collaborations among many of the UK's relevant major regulatory bodies, and gives guidance about the hazards associated with opioid prescribing.[8]

Several reports have been published about trends in non-cancer opioid prescribing in the UK National Health Service (NHS), with research to date examining only a subset of treatments, practices, and conditions.[9,10] For example, a widely reported paper explored prescribing trends in the Clinical Practice Research Datalink (CPRD) up to 2015;[6] however, this study did not account for opioid strength, analysed only the five most commonly prescribed drug–dose pairs in detail, and is likely to be unrepresentative of the full picture. A study from 2018 reported increased opioid prescribing for a limited period from 2010 to 2014.[11]

We therefore aimed to use the full NHS England primary care prescribing dataset to assess trends and variation in prescribing of opioids in primary care from 1998 to 2018 robustly and comprehensively, and to assess factors associated with high-dose opioid prescribing behaviour in general practices. We also provide an open tool at OpenPrescribing.net where readers can find the latest data about opioid prescribing for each of England's general practices and clinical commissioning groups (CCGs).

Research in context

Evidence before this study
Concerns have been raised about the use of strong opioids and at high doses, especially in management of chronic pain; better monitoring and audit has been advocated. We reviewed the literature published in English on PubMed describing the trends and variation in opioid prescribing for chronic non-cancer pain in the UK since Jan 1, 2010, onwards. We screened abstracts for relevance after using combinations of the search terms "opioid" AND/OR "opiate", "prescribing", "chronic pain", and "NHS" AND/OR "UK". We also reviewed relevant reports from public bodies. The consensus is for an increase in prescribing of opioids in primary care in England, but most data are several years out of date at publication and very few correct for opioid strength or analyse high-dose prescriptions separately. Few publications cover the entire country or contain robust statistical analyses. None provides detailed data or tools to allow readers to investigate detailed prescribing information for their local area.

Added value of this study
There has been a substantial increase in opioid prescribing in the National Health Service (NHS) in England between 1998 and 2016; failing to account for the different potencies of opioid being prescribed would underestimate this increase by a factor of 3·7. We provide detailed prescribing data at the individual practice level, available to all through an interactive online tool at OpenPrescribing.net.

Implications of all the available evidence
Our study provides a framework for monitoring of primary care opioid prescribing in routinely available data and provides a tool for anyone to use for further research, such as local audits and improvement projects. Future work with patient-level data could reveal more detailed high-dose opioid prescribing patterns.

Methods

Data sources and preparation

We used two sources of data: monthly practice-level data covering October, 2010, to August, 2018; and annual prescription cost analysis data, aggregated nationally, covering 1998 to 2017.

The monthly prescribing datasets published by NHS Digital contain one row for each different medication and dose, in each prescribing organisation in NHS primary care in England, describing the number of prescriptions issued and the total cost. These data are sourced from community pharmacy claims data and therefore contain all items that were dispensed. We extracted all available prescribing data, limited to institutions with setting code 4—general practices, according to the NHS Digital dataset of practice characteristics.[12] We excluded all other organisations such as prisons and out-of-hours services as they are not represented fully or consistently in our dataset since many of these prescriptions would not be dispensed in community pharmacies. Practices were excluded for any month in which they had no registered patients or no prescribing. For analyses involving the latest 6 months, practices were also excluded if their current status was closed or dormant, as these practices are likely to have low and unusual patterns of prescribing. Numbers of patients registered at each practice were obtained from NHS Digital.[13]

The annual prescription cost analysis datasets contain one row for each different medication and dose, for all items dispensed in community settings in England, describing the number of prescriptions and the total cost. Prescription cost analysis data were processed as previously described.[14] Briefly, data for each year between 1998 and 2017 were obtained from NHS Digital or archive locations, compiled, and loaded into Google BigQuery. Full British National Formulary (BNF) codes were obtained from the latest BNF for each drug name where possible. Any remaining drugs were matched to the most similar item in the current BNF. Data were normalised by converting the number of items prescribed and costs to relative figures per 1000 population, by use of mid-year population estimates for England.[15] We also corrected costs for inflation using the consumer price index compared to 2017.[16] Full data processing details are available.[17] Ethical approval was not required for this study.

Data extraction and classification

We extracted prescribing data for all drugs in paragraph 4.7.2 (Opioid Analgesics), as well as opioid-containing combination drugs from paragraphs 4.7.1 (Non-Opioid Analgesics and Compound Preps) and 10.1.1 (Non-Steroidal Anti-Inflammatory Drugs; appendix). We excluded preparations from section 4.10 (Drugs used for substance dependence) as these are less commonly used in pain; this section includes some formulations of methadone and buprenorphine that are normally used for treatment of opioid dependence. Drugs were assigned to the appropriate class according to their chemical name (appendix). We calculated oral morphine equivalency (OME) for each drug using conversion tables available from various sources (conversion factors and sources are listed in the appendix).

Long-acting opioids are those used on a regular basis to control pain, whereas short-acting preparations act quickly and for a short duration. Long-acting formulations include modified release morphine and oxycodone tablets, and fentanyl and buprenorphine transdermal patches, but exclude preparations used for breakthrough pain, such as Oramorph, and opioid injections, which are more commonly used in palliative care. Of the long-acting opioids, high-dose opioids were defined as those with 120 mg or greater morphine (or equivalent) per day based

See **Online** for appendix

on the estimated total daily dose. For example, for morphine sulfate modified release tablets, usually taken as one tablet twice daily, we assumed 60 mg tablets are high dose (probable total daily dose 120 mg), whereas 30 mg tablets are not (probable total daily dose 60 mg). A full list of opioids classified as high dose is given in the appendix.

Long-term time trends
We created stacked charts to display the number of items, OME, and cost of all opioid-containing items dispensed each year. We repeated this process for opioids that were long acting and those that were high dose.

Geographical variation
We used practice-level data, aggregated to CCGs, to create choropleth maps of current prescribing for all CCGs in England, for the latest available 6 months combined (March to August, 2018). For each CCG we calculated the total items, OME, and cost of all opioids prescribed per 1000 registered patients; the percentage of long-acting OMEs prescribed that were high dose; and the percentage of high-dose OMEs prescribed that were each of fentanyl, morphine, and oxycodone. We also calculated and plotted the change from 2016 to 2017 in total OMEs prescribed per 1000 registered patients for each CCG in England.

We assessed variation in prescribing among general practices in England by calculating deciles for each month (October, 2010, to August, 2018) for total OMEs per 1000 registered patients, percentage of OMEs prescribed that were high dose (of all long-acting OMEs prescribed), and total cost of all opioids and high-dose opioids per 1000 registered patients. We display these data as time-trend charts.

We estimated potential savings that could be made in opioid prescribing by taking the total high-dose items per 1000 patients for practices ranked at the 10th centile, for the latest available 6 months combined (March to August, 2018), and applying this rate to every practice prescribing above this level. Similarly, we calculated possible financial savings from more cost-effective prescribing, taking the 10th centile average cost per item (for high-dose items) and applying this to all items prescribed by practices with a higher cost per item.

Statistical analysis
To measure factors most associated with prescribing of high-dose opioids, we created a mixed-effects logistic regression model, using publicly available practice demographic data to define various fixed-effects variables, and included CCG as a random effect to assess its impact on prescribing variation. The fixed-effects variables included were the proportion of registered patients aged older than 65 years, proportion of patients with a long-term health condition, Index of Multiple Deprivation, and Quality and Outcomes Framework score (each of which

were obtained from Public Health England[18]), as well as practice list size (NHS Digital) and extent of ruralness or urbanisation of practice postcode.[19] Where possible, we tried to use variables that to some extent matched previous models of opioid prescribing.[6,11,20,21] Continuous variables were categorised a priori into quintiles to allow for non-linearity of effects and to enhance the intelligibility of results.

The main outcome was high-dose, long-acting opioid prescriptions as a proportion of all long-acting opioid prescriptions. This proportion was transformed with a conditional logit transformation.[22] The model was used to calculate odds ratios and 95% CI for each of the fixed-effects variables, as well as an R-squared value (along with the significance level) to describe the degree of variance associated with CCG membership.

A second model was also run, on the outcome of total OME prescribing per 1000 patients. This model used mixed-effects linear regression, and the same fixed-effects and random-effects variables, to ascertain the degree to which each variable was associated with the volume of opioid prescribing.

Data were extracted with SQL in Google BigQuery, including OME conversions. Further calculations and aggregations were done in Python, with regression analysis done with Stata, version 13.1. Charts and maps were produced with Python matplotlib.pyplot, seaborn and geopandas modules. Complete codes are provided online.

Role of the funding source

Results
From the practice-level data available between October, 2010, and August, 2018, 8123 standard general practices were included. For analyses relating to the latest 6 months (7194 practices), we excluded practices with a current status of closed (n=0) or dormant (n=166) according to NHS Digital organisation datasets, and those with non-standard CCG codes (n=1), leaving 7026 practices included from all 195 CCGs. All prescription cost analysis data were extracted successfully.

Between 1998 and 2016, there was a 34% increase in opioid items prescribed (from 568 per 1000 to 761 per 1000 population; figure 1; appendix). However, after correcting for OME, the total volume prescribed increased by 127% (from 190000 mg to 431000 mg OME per 1000 population). There was a decline in both items

A Total items for all opioid-containing preparations

B Total OME (mg) for all opioid-containing preparations

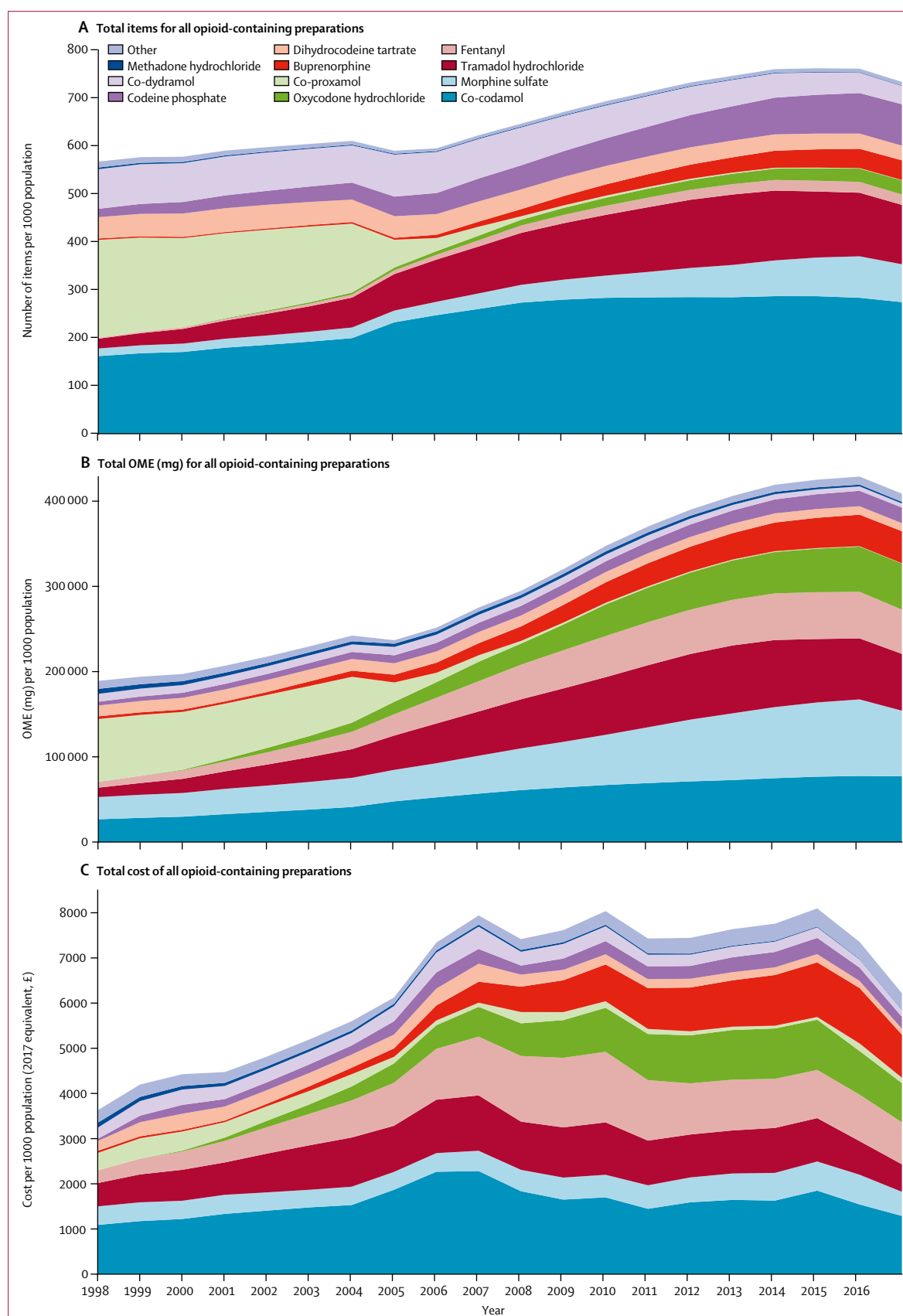**C Total cost of all opioid-containing preparations**

Figure 1: **Trends in all opioid-containing products dispensed in in England, 1998–2017**
(A) Total items per 1000 population. (B) Total oral morphine equivalency (OME) per 1000 population. (C) Total cost per 1000 population (2017 equivalent, £). Summary data and details of the "Other" group are provided in the appendix.

prescribed and OME from 2016 to 2017, largely accounted for by a reduction in morphine.

Morphine, fentanyl, oxycodone, and buprenorphine made up relatively more of the total opioid prescribing by OME than by number of items, indicating these opioids are subject to some high-dose prescribing (figure 1). Among the lesser-prescribed opioids within the "Other" category, the use of tapentadol has been increasing most rapidly since it became available in 2011 (appendix), more by OME than by number of items, indicating a tendency towards high-dose prescribing. We have supplied information about the earliest prescribing date of each opioid for context (appendix).

Fentanyl, oxycodone, and buprenorphine contributed a greater proportion of overall prescribing costs relative to the number of items prescribed. Prescribing of co-proxamol (a previously popular opioid), reduced drastically following its withdrawal,[23] but spending remained stable as it continued to be prescribed as an unlicensed special at a high unit cost.

Figure 2 shows trends in high-dose (>120 mg OME), long-acting opioids between 1998 and 2017 (with long-acting opioids of all doses and non-high doses shown in the appendix). There was a large, rapid increase in the volume of high-dose, long-acting opioid prescribing, seen in both the crude and OME data (figure 2A, B). The number of prescriptions increased from three per 1000 population in 1998 to 23 per 1000 in 2016 (corresponding to a 581% increase, or 457% by OME (from 17800 mg to 99300 mg OME per 1000 population). The greatest contributors in 2016 were fentanyl, morphine, and oxycodone, together accounting for more than 90% of high-dose long-acting opioid prescribing (appendix). Oxycodone prescribing increased the most since becoming available in 2000. The number of long-acting opioids not prescribed at high doses also increased substantially but showed a similar decline from 2016 to 2017, largely in morphine use (appendix). The overall spend on high-dose preparations has reduced since 2010, mainly due to decreased spend on fentanyl and, more recently, oxycodone (figure 2C).

Maps indicate the range of prescribing behaviour across CCGs in England over the latest 6-month period (figure 3). Total OME differed almost eight-fold (from 52700 mg per 1000 to 416000 mg per 1000 registered patients; figure 3A), whereas total items prescribed varied 6·1 times (119–727 items per 1000; appendix). Total spend on opioids closely reflected the total OME prescribed, with a 5·9-fold variation (£859–5050 per 1000, figure 3B). High-dose items prescribed varied 15 times (from 1·73 per 1000 to 26·4 per 1000; figure 3C). The lowest prescribers of opioid OMEs and high-dose items were mainly around the Greater London regions, with high prescribers in northern and coastal areas. The CCGs with the greatest percentage of items prescribed as high dose were more dispersed across England (figure 3D). For OMEs prescribed in high-dose formulations, there was wide variation between CCGs on which opioid groups were the most frequently prescribed (figure 3E–G). We also show the change in total opioid prescribing between 2016 and 2017 for all CCGs in England (appendix), ranging from a decrease of almost 60000 OME per 1000 (–10·5%) to an increase of 20000 per 1000 (3·5%).

Figure 4 shows the range and time-course of variation in prescribing behaviour across practices in England since 2010. Although there is wide variation, there has been relatively little change in the extent of this variation during the time period analysed. The range (10th–90th percentiles) of total OMEs prescribed per patient has increased, mostly due to an increase among the highest prescribers. The increasing trend appears to have stabilised since 2015. The percentage of long-acting opioid items prescribed in high-dose preparations has reduced in range, with the highest decile decreasing (from 68% to 60%) and the lower deciles increasing. The overall cost of opioid prescribing per 1000 patients ranged from £150 to £700 in August, 2018, having declined since 2015; for high-dose preparations it was £10–£120.

If every practice in the country prescribed high-dose opioids at the same rate as the lowest decile (0·17 items, or £6·56, per 1000 patients per month) over the latest 6 months, we estimate that overall 543000 fewer high-dose prescriptions could have been issued from a total of 601000, or a cost saving of £24·8 million achieved from a total £27·0 million. If each practice prescribed at the lowest decile cost per item for high-dose opioids over the latest 6 months (£25·64 per item), without reducing the number of items prescribed, in total they could have collectively saved £12·0 million (44·4%) of £27·0 million.

We modelled the practice factors associated with the proportion of long-acting opioids prescribed as high dose (table). Practice list size had the strongest and most consistent effect size, with larger practices being more likely than smaller ones to prescribe high-dose opioids (multivariable odds ratio for smallest vs largest 1·53, 95% CI 1·44–1·64). Greater ruralness and deprivation scores were both associated with increased high-dose prescribing, with practices in the "Urban with major conurbation" category less likely to prescribe high-dose opioids than those in "Mainly rural" areas (multivariable odds ratio 0·77, 95% CI 0·68–0·86), and practices in the most deprived areas more likely to prescribe high-dose opioids than those in the least deprived areas (multivariable odds ratio 1·24, 95% CI 1·13–1·36). Practices that had a higher proportion of patients with a long-term health condition had slightly higher odds of prescribing high-dose opioids (multivariable odds ratio for lowest vs highest 1·19, 95% CI 1·11–1·28). The proportion of patients aged older than 65 years registered at a practice was not associated with prescribing of high-dose opioids in multivariable modelling, although there was some effect in the univariable analysis. Practice Quality and Outcomes Framework score was only marginally associated with high-dose opioid prescribing, with much of the observed effect in the univariable
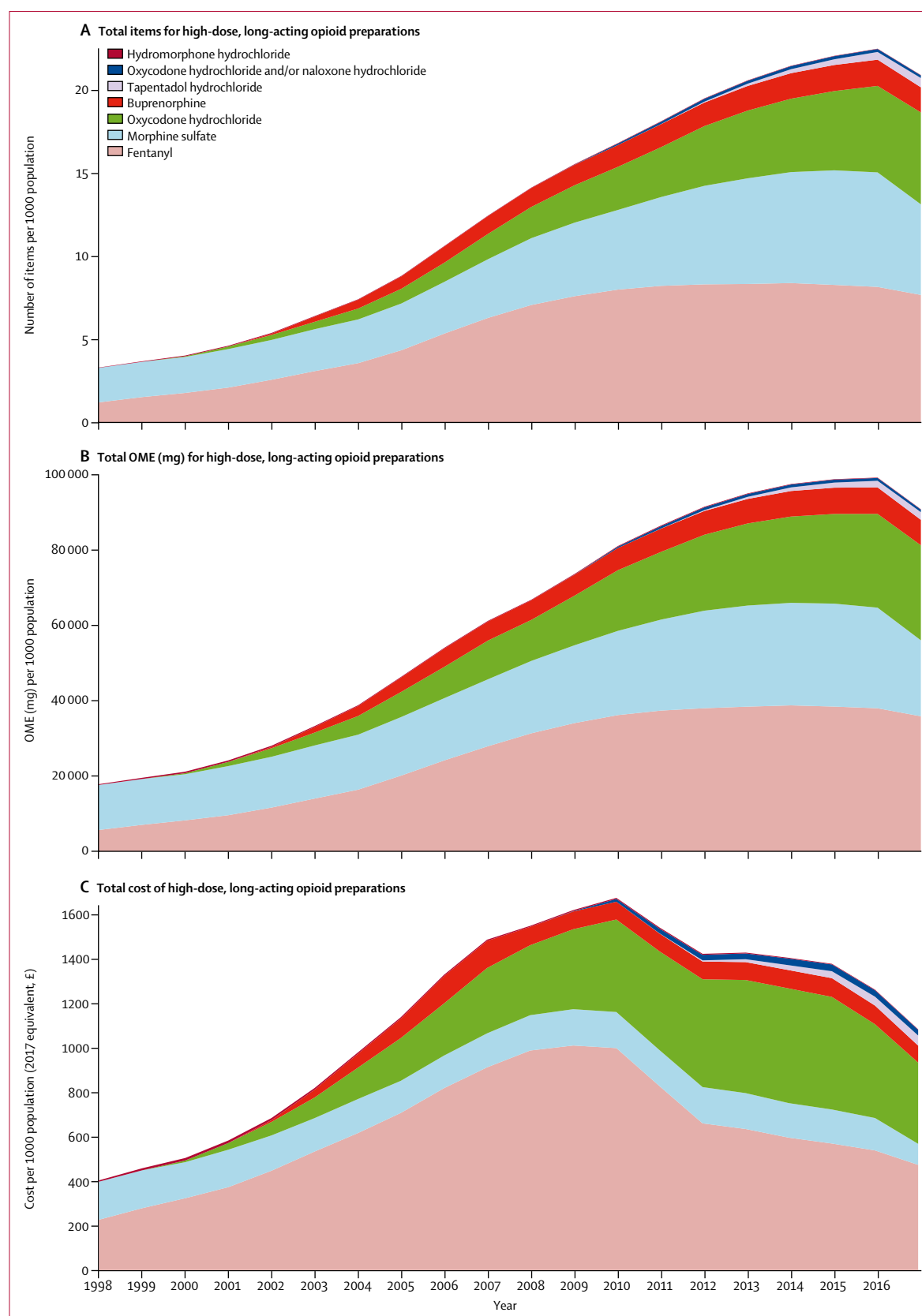
A Total items for high-dose, long-acting opioid preparations

Legend:
- Hydromorphone hydrochloride
- Oxycodone hydrochloride and/or naloxone hydrochloride
- Tapentadol hydrochloride
- Buprenorphine
- Oxycodone hydrochloride
- Morphine sulfate
- Fentanyl

Number of items per 1000 population

B Total OME (mg) for high-dose, long-acting opioid preparations

OME (mg) per 1000 population

C Total cost of high-dose, long-acting opioid preparations

Cost per 1000 population (2017 equivalent, £)

Year

***Figure 2*: Trends in high-dose (≥120 mg OME per day), long-acting opioid prescribing in England, 1998–2017**
(A) Total items per 1000 population. (B) Total mg oral morphine equivalency (OME) per 1000 population. (C) Total cost per 1000 population (2017 equivalent, £). OME data are shown in the appendix.
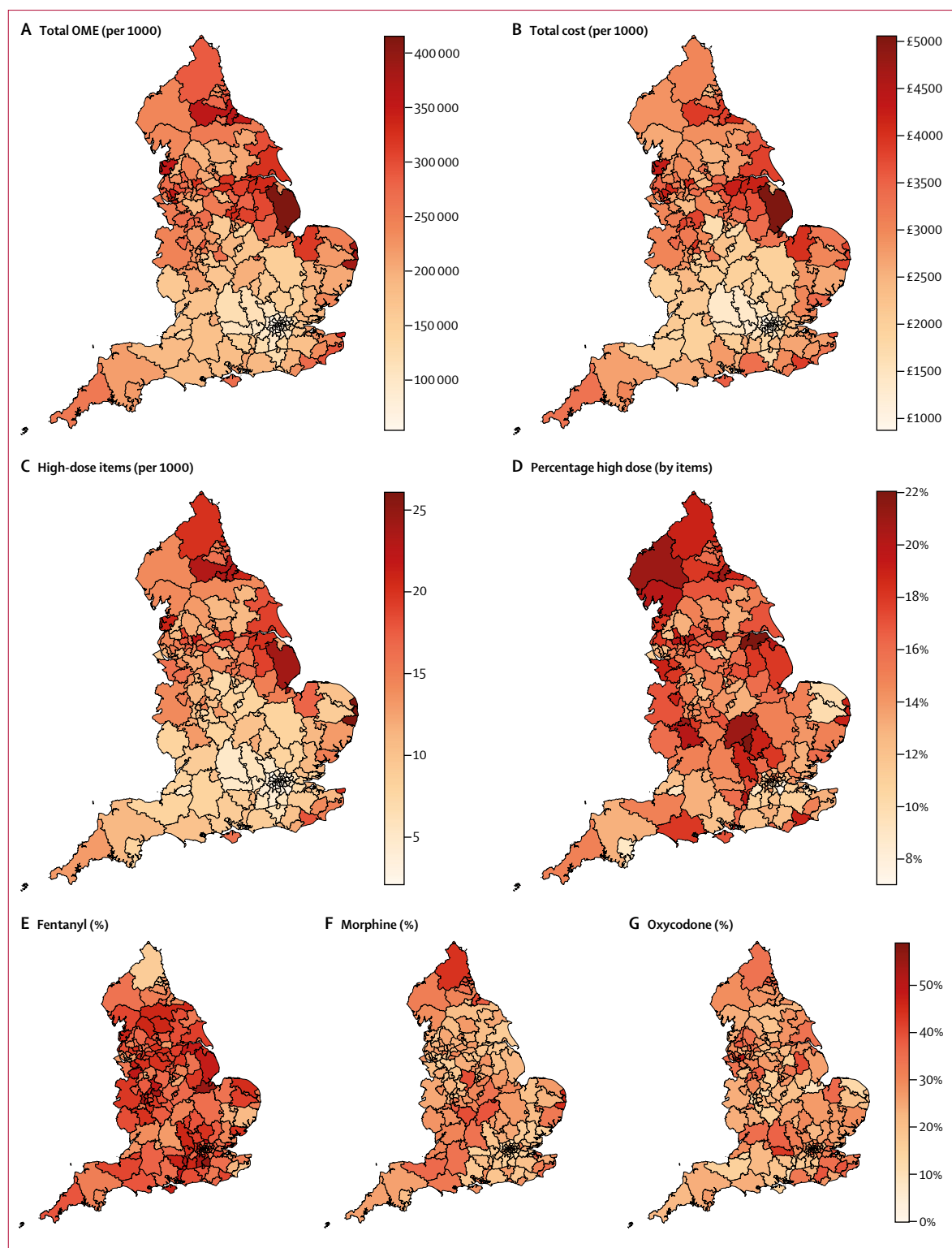
Figure 3: Variation in opioid prescribing by clinical commissioning groups in England, March to August, 2018

(A) Total oral morphine equivalency (OME) for all opioid-containing preparations per 1000 registered patients. (B) Total cost of opioid prescribing per 1000 registered patients. (C) Total opioid items prescribed as high dose per 1000 registered patients. (D) Percentage of long-acting opioid items prescribed as high dose (≥120 mg OME per day). (E) Percentage of high-dose OME prescribed as fentanyl. (F) Percentage of high-dose OME prescribed as morphine. (G) Percentage of high-dose OME prescribed as oxycodone. Data are summarised in the appendix.
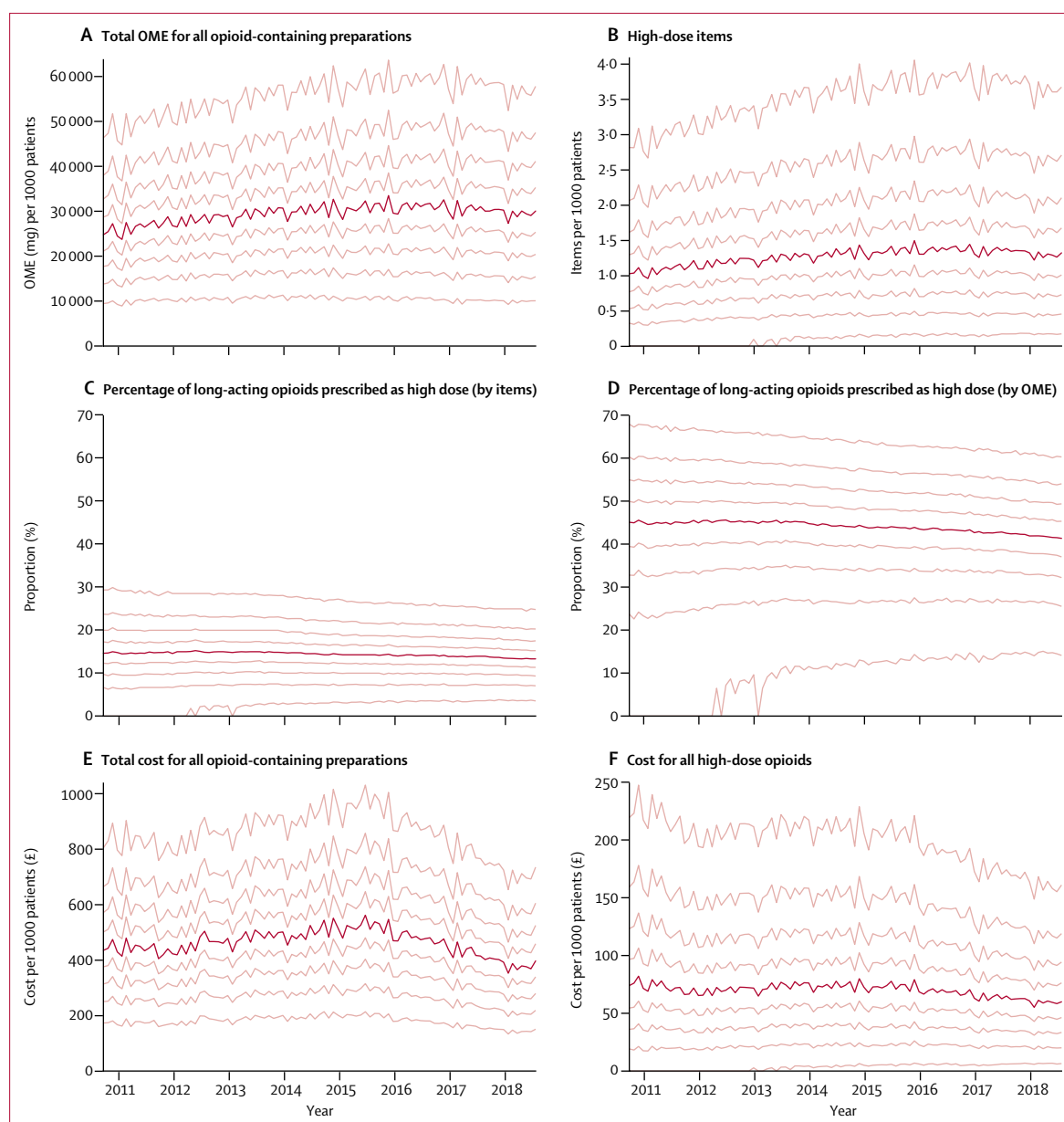
Figure 4: Trends over time in opioid prescribing by general practices in England, from October, 2010, to August, 2018
Dark red line shows median, light red lines are deciles. (A) Total oral morphine equivalency (OME) for all opioid-containing preparations per 1000 registered patients.
(B) Total opioid items prescribed as high dose per 1000 registered patients. (C) Percentage of long-acting opioid items prescribed as high dose (≥120 mg OME per day).
(D) Percentage of long-acting opioid OME prescribed as high dose. (E) Total cost of all opioids per 1000 registered patients. (F) Total cost of high-dose opioids per
1000 registered patients.

analysis absent in the multivariable analysis. The CCG to which a practice belongs (as a random effect) was associated with high-dose prescribing (p<0·0001) and accounted for 11·7% of the variation in high-dose opioid prescribing.

We also modelled the factors associated with total OME prescribing rate per 1000 patients (appendix). These results were broadly similar to the first model in terms of the factors associated with prescribing, but the magnitude of association could not be directly compared.

Discussion

In this retrospective database study, we found a substantial increase in opioid prescribing between 1998 and 2016. We also found that measuring opioid prescribing in terms of number of items, without correcting for OME, would underestimate the true increase in prescribing between 1998 and 2016 by a factor of 3·7 (34% vs 127%). We report wide variation in opioid prescribing across general practices and CCGs in England, particularly in costs, but with relatively little change in variation over

	Median high dose	Univariable logistic regression	Multivariable logistic regression
Patients older than 65 years (%)			
0 to 11·0	12·3%	1 (ref)	1 (ref)
>11·0 to 15·5	13·4%	1·16 (1·09–1·24)	1·06 (0·99–1·14)
>15·5 to 18·9	14·3%	1·33 (1·25–1·42)	1·09 (1·01–1·18)
>18·9 to 22·5	14·0%	1·33 (1·24–1·42)	1·05 (0·97–1·14)
>22·5 to 92·2	13·2%	1·26 (1·18–1·35)	0·98 (0·89–1·08)
Patients with a long-term health condition (%)			
16·5 to 47·0	11·9%	1 (ref)	1 (ref)
>47·0 to 51·4	13·1%	1·13 (1·06–1·20)	1·06 (1·00–1·14)
>51·4 to 55·3	14·2%	1·30 (1·22–1·39)	1·15 (1·08–1·23)
>55·3 to 59·6	13·8%	1·30 (1·22–1·39)	1·15 (1·07–1·23)
>59·6 to 96·0	14·3%	1·40 (1·31–1·50)	1·19 (1·11–1·28)
Practice list size (thousands)			
0 to 3900	11·7%	1 (ref)	1 (ref)
>3900 to 5900	12·9%	1·25 (1·17–1·34)	1·26 (1·18–1·34)
>5900 to 8100	13·6%	1·40 (1·31–1·49)	1·42 (1·33–1·51)
>8100 to 11 300	13·8%	1·47 (1·38–1·57)	1·47 (1·38–1·57)
>11 300 to 60 600	14·4%	1·55 (1·45–1·66)	1·53 (1·44–1·64)
Urban or rural			
Mainly rural	14·1%	1 (ref)	1 (ref)
Largely rural	13·9%	0·97 (0·88–1·07)	0·92 (0·82–1·03)
Urban with significant rural	14·2%	0·99 (0·90–1·09)	0·97 (0·87–1·09)
Urban with city and town	14·3%	0·96 (0·88–1·05)	0·92 (0·83–1·02)
Urban with minor conurbation	12·6%	0·83 (0·73–0·94)	0·83 (0·67–1·03)
Urban with major conurbation	12·6%	0·74 (0·69–0·80)	0·77 (0·68–0·86)
Index of Multiple Deprivation			
1 (least deprived)	12·1%	1 (ref)	1 (ref)
2	13·6%	1·13 (1·06–1·21)	1·13 (1·06–1·21)
3	14·1%	1·14 (1·07–1·22)	1·22 (1·13–1·31)
4	14·1%	1·08 (1·01–1·15)	1·18 (1·09–1·27)
5 (most deprived)	13·7%	1·07 (1·00–1·14)	1·24 (1·13–1·36)
Quality and Outcomes Framework score			
14 to 523	13·3%	1 (ref)	1 (ref)
>523 to 541	12·9%	1·05 (0·98–1·12)	0·99 (0·93–1·06)
>541 to 550	13·8%	1·14 (1·07–1·22)	1·04 (0·97–1·11)
>550 to 557	13·6%	1·18 (1·10–1·26)	1·06 (1·00–1·14)
>557 to 559	13·7%	1·17 (1·10–1·25)	1·02 (0·96–1·09)

Data are % or odds ratio (95% CI).

Table: Median proportion of long-acting opioid items prescribed in high-dose formulations, stratified by various practice factors, along with odds ratios from univariable and multivariable logistic regression models

dose, course length, and continual prescribing period for each individual; and to separate indications by identifying patients with cancer diagnoses.[24] However, these datasets currently cover only a subset of all NHS prescribers, and do not identify individual CCGs and practices; furthermore, data about diagnosis and indication for each individual prescription in datasets such as the CPRD are commonly incomplete.[25]

We accounted for variation in opioid strength and listed our sources of conversion figures. These will not apply equally to all patients and prescriptions because of variation in drug formulations, patient tolerability, and type of pain.[26] However, these conversions are appropriate for calculation of totals, long-term trends, and comparison of overall prescribing behaviours. We made general assumptions about common dosing schedules to classify high-dose prescriptions, but some low-dose formulations could also represent high doses if taken more frequently or in combination with short-acting formulations.

We included all opioids likely to be prescribed for chronic pain. Although most prescriptions are probably for non-cancer pain,[24] we could have included some used in cancer, for short-term or end-of-life pain (eg, patches for patients unable to swallow[27]). The gradually increasing need for end-of-life pain relief might have contributed slightly to the increases in prescribing shown in our study.[28] Secondary care prescribing is not included; however, ongoing care is largely managed in primary care. Our data originate from pharmacy claims and therefore do not include prescriptions that are issued but not presented to a pharmacist.

Our savings estimates indicate the possible extent of savings if all practices were able either to reduce their high-dose opioid prescribing to the level of the lowest 10% of prescribers or to match the 10% most cost-effective prescribers on cost per item. A more detailed analysis would be required to adjust fully for the extent of patient need in each practice.

Our results are consistent with another study in CPRD, which reported a large increase in prescribing of four strong opioids in the UK between 2000 and 2010.[24] The results of this previous study indicate that the increase in high-dose opioids is largely attributable to prescribing for non-cancer patients, through both increasing numbers of recipients and prescriptions per patient. We show that the increase in national opioid prescribing levels off from 2014 onwards; similarly, the report commissioned by the National Institute for Health Research (NIHR) Policy Research Programme showed that the proportion of patients prescribed opioids has declined since 2012, with the mean duration of opioid prescribing periods levelling off in 2014.[6]

Another study, looking at musculoskeletal conditions, showed a trend towards opioids being prescribed sooner and in longer-acting forms between 2002 and 2013, but a decline in prescribing overall after 2011.[9]

time. If every practice prescribed high-dose opioids at the lowest decile rate, this could have saved 543 000 high-dose prescriptions over 6 months. Larger list size, ruralness, and higher deprivation scores were associated with greater rates of high-dose prescribing. The CCG to which a practice belongs accounted for 11·7% of the variation in high-dose opioid prescribing behaviour.

Our study covers complete prescribing data for all practices in England. Our work could be complemented by analysis of patient-level data to ascertain the number of different recipients per practice; the total combined

Our study also builds on the findings of a 2018 publication showing increasing opioid prescribing up to February, 2014.[11] We include all classes of opioid and more recent data showing that the increase is now slowing. We detail high-dose prescribing, present time trends for the most-prescribed opioids, and include our full data and codes.

We report wide variation across practices and CCGs, with CCG membership accounting for 11·7% of practice-level variation in high-dose prescribing. A similar CCG-level pattern (for total OME, 2010–14) was previously reported, with highest prescribers in northern areas,[11] but that study did not have access to practice-level data. The NIHR report based geographical patterns on a single presentation (tramadol 50 mg), which is unlikely to represent the full extent of variation.[6] We also show that the decreases in opioid prescribing rates between 2016 and 2017 are not evenly distributed across CCGs, with some having increased prescribing.

Greater practice list size, rurality, and deprivation were associated with high-dose prescribing. Less optimal opioid prescribing has previously been associated with deprivation in England[6,11] and in Scotland;[29] with rurality in Australia and the USA;[20,21] and with age, but not including adults aged older than 65 years.[20] However, a previous cohort study in one region in England (Leeds and Bradford) found no practice-level factors associated with opioid prescribing behaviour.[10] The limited geographical area might have been unable to capture the level of variation we found across the country.

It is important to interpret data on opioid prescribing thoughtfully and cautiously. A large increase in opioid prescribing could represent better pain management for patients with acute or palliative pain, or unwarranted and dangerous prescribing in chronic pain. The prolonged prescribing periods reported elsewhere[9] suggest the increase is due to unwarranted and dangerous prescribing. Currently, there is no evidence to support the routine prescription of high-dose opioid analgesics,[2] and there are clear guidelines to limit opioid prescribing for chronic pain.[7] Thus, our findings support calls for greater action to promote best practice: lower doses, for shorter durations, and ceasing opioids if they are not beneficial.[10] This approach could reduce adverse events,[2] prescribing costs, and the costs of managing dependency.

The geographical variation highlights where interventions can best be targeted—for example, rural areas. Our map of changes in CCG-level prescribing between 2016 and 2017 indicates that some regions are substantially reducing their opioid prescribing. Reviewing patients on high doses can lead to improved prescribing: a recent study in 41 general practices in England led to modification of treatment for 85 (23%) of 363 non-cancer patients prescribed high-dose opioids.[30] Some geographical variation might be driven by the availability and quality of clear chronic pain pathways with multidisciplinary services involving pain psychologists, which are recommended to help patients manage chronic pain.[31] For patients requiring specialist help with prescribed opioid addiction, most publicly funded addiction services generally address illicit drug use and so might not be well equipped to help patients with pain. Local guidelines and formularies can also influence prescribing patterns,[32] and the complex decision-making processes in opioid prescribing[33] could contribute to variation between individual clinicians. Additionally, some GPs might not have adequate understanding of the strength of the widely used fentanyl and buprenorphine patches.[34] The best methods to reduce inappropriate opioid prescribing in chronic pain warrant further study, particularly those that have led to the greatest reductions in CCG-level prescribing.

Better access to comparative data can have a valuable role in monitoring and improving clinical practice.[35] Findings from qualitative studies suggest there is scope to prevent dose escalation within primary care[36] and that educational interventions can improve clinical decision making.[33] Therefore, routine monitoring and feedback on opioid prescribing at a practice level is likely to be beneficial. Previous systematic review data on audit and feedback across a range of targeted clinical behaviours show a modest impact,[35] and when clinicians in the USA were informed of the death of one of their patients from an opioid overdose, their opioid prescribing subsequently reduced.[37] The measures used in our study provide easy and accessible tools to monitor opioid prescribing routinely. The measures presented in this study are also displayed on our OpenPrescribing.net website, an openly accessible data tool displaying the latest 5 years of NHS England prescribing data. For every practice in England, the site displays the number of high-dose opioid (≥120 mg daily) items prescribed, both per 1000 population and as a proportion of all opioids prescribed, as well as the total OME (mg) prescribed per 1000 population. We will maintain these live charts for all practices and CCGs as long as our team has funding and these data remain relevant to patient care.

In conclusion, overall levels of opioid prescribing have increased substantially since 1998 but despite a slowing of this trend, wide geographical variation exists across England. Our study results and OpenPrescribing.net tool provide a current picture of opioid prescribing. Monitoring data nationally and locally for potentially problematic prescribing might help to highlight areas where action is most required.

For the **complete codes** see https://figshare.com/s/787e8e94347c11a62762

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