

Changes in opioid prescribing during the COVID-19 pandemic in England: an interrupted time-series analysis in the OpenSAFELY-TPP cohort



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Summary

Background The COVID-19 pandemic disrupted health-care delivery, including difficulty accessing in-person care, which could have increased the need for strong pharmacological pain relief. Due to the risks associated with overprescribing of opioids, especially to vulnerable populations, we aimed to quantify changes to measures during the COVID-19 pandemic, overall, and by key subgroups.

Methods For this interrupted time-series analysis study conducted in England, with National Health Service England approval, we used routine clinical data from more than 20 million general practice adult patients in OpenSAFELY-TPP, which is a secure software platform for analysis of electronic health records. We included all adults registered with a primary care practice using TPP-SystemOne software. Using interrupted time-series analysis, we quantified prevalent and new opioid prescribing before the COVID-19 pandemic (January, 2018–February, 2020), during the lockdown (March, 2020–March, 2021), and recovery periods (April, 2021–June, 2022), overall and stratified by demographics (age, sex, deprivation, ethnicity, and geographical region) and in people in care homes identified via an address-matching algorithm.

Findings There was little change in prevalent prescribing during the pandemic, except for a temporary increase in March, 2020. We observed a 9·8% (95% CI –14·5 to –6·5) reduction in new opioid prescribing from March, 2020, with a levelling of the downward trend, and rebounding slightly after April, 2021 (4·1%, 95% CI –0·9 to 9·4). Opioid prescribing rates varied by demographics, but we found a reduction in new prescribing for all subgroups except people aged 80 years or older. Among care home residents, in April, 2020, parenteral opioid prescribing increased by 186·3% (153·1 to 223·9).

Interpretation Opioid prescribing increased temporarily among older people and care home residents, likely reflecting use to treat end-of-life COVID-19 symptoms. Despite vulnerable populations being more affected by health-care disruptions, disparities in opioid prescribing by most demographic subgroups did not widen during the pandemic. Further research is needed to understand what is driving the changes in new opioid prescribing and its relation to changes to health-care provision during the pandemic.

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Introduction

In England, 13% of adults received an opioid prescription in 2017–18.¹ Although opioids are effective at treating acute pain, cancer pain, and end-of-life pain, they are commonly overprescribed for chronic non-cancer pain,² in which opioids do not have enough evidence of efficacy^{3,4} and are not recommended.⁵ During the COVID-19 pandemic, there were disruptions to provision of health care, including access to medicines, primary care appointments, and elective procedures. These disruptions were not experienced equally, with women, people living in deprived areas, and older people most affected,⁶ with the same populations disproportionately affected by opioid-related harms.^{7,8}

International studies quantifying opioid prescribing during the COVID-19 pandemic have identified changes not consistent with best practice. A Canadian study⁹ found increases in prescribing to people living in care homes, which is a population known to be at high risk of opioid-related harms. A US study¹⁰ identified a shift from non-pharmacological treatment (eg, physical therapy) towards opioid therapy for people with pain, likely due to increasing remote care during the pandemic. Furthermore, data suggest that rates of opioid-related death and overdose were greater than expected during the pandemic in Canada.¹¹

The National Health Service (NHS) England, the body with national responsibility for care, issued instructions

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See Online for appendix

Research in context

Evidence before this study

We searched PubMed on Jan 8, 2024, using the search terms ("COVID-19" OR "SARS-CoV-2") AND ("United Kingdom" OR "England" OR "Britain" OR "Scotland" OR "Wales") AND ("opioid"). We searched for articles published between March 1, 2020, and Jan 8, 2024, with no language restrictions, and found four relevant publications. We also searched the reference list of relevant articles. We included research studies (excluding conference abstracts and editorials) that quantified opioid prescribing or use in the UK during the COVID-19 pandemic. Studies focused solely on opioid substitution therapy for treatment of opioid use disorder were excluded. We considered that studies using simple before-and-after comparisons provided lower quality evidence than study designs that considered long-term trends such as an interrupted time-series analysis.

From the four identified studies, one performed a before-and-after comparison of opioid use among people on a waiting list for hip or knee arthroplasty in Scotland (n=548) during the COVID-19 pandemic and historical controls and found higher rates of long-term opioid use among people on waiting lists during the pandemic. The second study used a segmented linear regression to quantify changes in opioid prescribing using English Prescription Cost Analysis aggregate prescription data. This study found no changes in opioid prescribing after the start of the COVID-19 pandemic. However, due to no person-level data, this study was not able to identify changes in incident use. The third study of 1.3 million people with rheumatic and musculoskeletal diseases used regression analysis to quantify changes over time and found a decrease in new opioid users among people with certain conditions, but not in the number of overall prescriptions. The last study of 34 711 people newly diagnosed with cancer and 30 256 who died of cancer in Wales found increases in strong opioid prescribing in both populations.

Added value of this study

To our knowledge, this is the largest study (>20 million patients) of opioid prescribing during the COVID-19 pandemic

in a representative sample of the population of England.

We used person-level data to quantify changes in the number of people prescribed opioids and identified that in the general population, prevalent opioid prescribing changed little, except for a temporary increase at the start of the first lockdown. However, we also identified reductions in new opioid prescribing during the lockdown period accompanied by a levelling of the downward trend. Although our findings confirm previous studies quantifying variation in opioid prescribing by sex, ethnicity, region, and deprivation, we showed that changes to new prescribing during the COVID-19 pandemic were experienced approximately similarly across these subgroups. The exceptions were older people and people in care homes who were identified using a previously developed address-matching algorithm. People in care homes experienced substantial temporary increases in opioid prescribing primarily due to parenteral opioids, which are used in palliative care. This coincided with periods of greatest COVID-19 morbidity and mortality in this population.

Implications of all the available evidence

The COVID-19 pandemic resulted in substantial disruptions to the health-care system. Despite concerns that difficulty or delays in providing care during the pandemic could have led to shifts from non-pharmacological treatments to greater opioid prescribing, we observed no increases in prescribing prevalence in most demographic groups in England. The one exception is people living at addresses that matched with care homes residences, whereby the observed prescribing patterns, which suggest use to treat end-of-life symptoms, were consistent with best practice. However, different populations could have been affected differently during the pandemic and these effects could have averaged out. Although we found no evidence that disparities in prescribing by demographic factors widened during the pandemic, a better understanding of the drivers of this variation is needed. Our findings also do not preclude changes in prescribing in high-risk populations, such as increased prescribing to people on procedure waiting lists.

to improve opioid use in 2023, highlighting the need for better use of data to identify, prevent, and reduce opioid harm.¹² Although changes in prescribing have been described during COVID-19 in the UK for different classes of medicines,¹³ for opioids in specific populations^{14,15} and in aggregate prescribing data,¹⁶ there are no studies on changes to opioid prescribing at the person-level in the general population or in high-risk demographic groups. Due to the risks associated with overprescribing of opioids, especially to vulnerable populations, we aimed to quantify changes to the following measures during the COVID-19 pandemic, overall, and by key subgroups: (1) prevalent opioid prescribing; (2) new prescribing; and (3) variation in

COVID-19-related changes by demographic subgroups and people in care homes.

Methods

Study design

We conducted an interrupted time-series analysis study from Jan 1, 2018 to June 30, 2022, using primary care data in England managed by the general practitioner (GP) software provider TPP-SystemOne, linked to Office of National Statistics (ONS) data on death through OpenSAFELY, which is a part of the NHS England OpenSAFELY COVID-19 service. An overview of OpenSAFELY is available from a study by Nab and colleagues.¹⁷ We defined two change points, which were

the start of the lockdown period, defined as March, 2020, as the UK first introduced restrictions on March 23, 2020, and the start of the recovery period, defined as April, 2021. April 1, 2021, was chosen as it coincides with the start of gradual reopening of non-essential services.¹⁸

This study was approved by the Health Research Authority (Research Ethics Committee reference 20/LO/0651) and by the London School of Hygiene & Tropical Medicine ethics board (reference 21863). Consent was not required under the legal basis of the COVID-19 Public Health Directions 2020 and Data Provision Notice that allowed analysis of pseudo anonymised patient data in OpenSAFELY for COVID-19 purposes (appendix pp 13–14).

Participants

We identified all people who were prescribed an opioid in each month of the study period. All people aged at least 18 years, who were alive, and registered with a TPP practice on the first of every month were included in the denominator for the calculation of rates. The TPP population is broadly representative of the full population of England in terms of age, sex, Index of Multiple Deprivation, and ethnicity.¹⁹ We excluded people with missing or impossible values of age and sex (<0.01%) as this is indicative of poor data quality.

Procedures

Opioids were defined as all medicines falling under the British National Formulary (BNF) legacy paragraphs 4.7.2 (Opioid analgesics), opioid medicines falling under 3.9.1 (Cough suppressants), opioid-containing combination medicines under 4.7.1 (Non-opioid analgesics), 1.4.2 (Antimotility drugs), and 10.1.1 (Non-steroidal anti-inflammatory drugs). Opioids used to treat opioid use disorder were not included. Links to the code lists used in this study are openly available for inspection and re-use in this study's Github repository.

Our primary outcome was opioid prescribing prevalence, which was defined as the number of people who were prescribed an opioid and included both new and repeat prescriptions. The secondary outcome was new opioid prescribing, defined as people who were prescribed an opioid without any opioid prescription in the previous year. We also identified the prescribing of two other opioid subtypes. The first subtype is high-dose long-acting opioids that are not recommended for chronic non-cancer pain.³ Among long-acting opioids, high dose opioids were defined as those with at least 120 mg morphine equivalents per day based on the typical total daily dose.²⁰ The second subtype is parenteral opioids (ie, delivered by injection or intravenously), recommended to treat end-of-life symptoms (eg, pain and breathlessness) in the community.²¹ We hypothesised that an increase in COVID-19 mortality would be associated with an increase in medicines used in palliative care.

First, we characterised people who were prescribed an opioid between the last three months of the study period (April–June 2022). Opioid prescribing rates were expressed as the number of people who were prescribed an opioid per 1000 registered adult patients. To prevent disclosure, all counts less than or equal to ten were redacted and rounded to the nearest seven. We included the following demographic categories: sex (male and female); age (18–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, 80–89 years, and ≥90 years); Index of Multiple Deprivation deciles; practice region (east, East Midlands, London, northeast, northwest, southeast, southwest, West Midlands, and Yorkshire and the Humber); and ethnicity (White [British, Irish, or Other]; Asian or British Asian [Bangladeshi, Indian, Pakistani, or Other]; Black or Black British [African, Caribbean, or Other]; Mixed [White and Asian, White and Black African, White and Black Caribbean, Other]; Other [Chinese or Other]). To compare overall prescribing rates within relevant demographic categories, we standardised opioid prescribing rates by age (5-year age bands) and sex using the Office of National Statistics mid-year 2020 English population.²²

As there is no flag in the data to identify people residing in care homes (a vulnerable population during the pandemic), we used a combination of coded events (eg, identification of consultations occurring in care homes) and linking patients' registered address to care homes as held by the Care Quality Commission, refined by applying the algorithm described by the study by Schultze and colleagues. Address-based matching had a good positive predictive value.²³

Statistical analysis

We estimated changes in monthly opioid prescribing during the lockdown period and recovery periods using interrupted time-series analysis. This approach estimates changes accounting for pre-existing trends. We used the crude (unstandardised) rates for these analyses as relative changes, which would not be affected by standardisation, and because of the additional lack of precision of standardised estimates.

We modelled the number of people who were prescribed an opioid using negative binomial log-linear regression which is designed for over-dispersion and included the natural log of the number of registered patients in each month as an offset. The models included variables representing the pre-COVID-19 trend (slope), a level shift (immediate, sustained change) and a slope change (gradual change in trend) after the start of the lockdown and recovery periods. The slope change and level shift after the start of the lockdown represent the changes compared with the predicted values had pre-COVID-19 trends continued. The slope change and level shift after the start of the recovery period represent the changes compared with the predicted values had the changes (if any) observed during the lockdown period

For more on the **study code and codelists** see <https://github.com/opensafely/opioids-covid-research>

continued. Because there was some autocorrelation identified using the Box-Ljung test for white noise of residuals we calculated Newey–West standard errors to account for residual autocorrelation and we included dummy month variables to account for seasonality.

Due to reports of increases in opioid sales in March, 2020, which were probably related to stockpiling followed by decreases in April and May, 2020,²⁴ we tested the model described above for inclusion of dummy variables representing these months to distinguish between temporary and longer-term effects. We retained these dummy variables if they improved model fit

determined by the likelihood ratio test. We estimated incidence rate ratios (IRRs) and 95% CIs, which were expressed as percent changes.

We quantified changes in new prescribing as described earlier. Here the offset was the number of opioid-naive registered patients in each month (ie, people without any opioid prescription in the previous year). We also quantified changes in prescribing among people living in care homes. For the outcome of high-dose long-acting prescribing to people in care homes, we used Poisson log-linear regression (instead of negative binomial) as this was a better fitting model based on the likelihood-ratio test, variance was small and not overdispersed.

To estimate differences in prescribing by demographic subgroups, we created separate models for each variable using the same categories stated earlier for age, sex, Index of Multiple Deprivation decile, ethnicity, and region. People with missing values for Index of Multiple Deprivation and region were excluded from this analysis due to small counts, whereas people with missing (unknown) ethnicity were treated as a separate group. We tested an interaction term between the level shift and change in slope and each category. As inclusion of an interaction with the change in slope did not improve model fit for any of the subgroups, this interaction term was not retained. We therefore assumed a common trend and that the change in slope did not vary across groups, and only the level shift varied.

As most concerns over opioid prescribing focus on use for chronic non-cancer pain, we repeated our primary (prevalent prescribing) and secondary analyses (new prescribing) excluding people with a cancer diagnosis in the past 5 years as a sensitivity analysis.

Role of the funding source

The funders had no role in the study design, data collection, data analysis, and data interpretation, or the writing of the report.

Results

From April 1 to June 1, 2022, there were 20476680 registered patients (aged ≥18 years) with 1445122 patients who were prescribed an opioid, or 70·6 per 1000 registered patients. Opioid prescribing increased with age, ranging from 12·6 per 1000 people aged 18–29 years to 202·8 per 1000 people older than 90 years (table 1). Prescribing also increased with greater deprivation varying more than two-fold, ranging from 47·7 per 1000 for people in the least deprived Index of Multiple Deprivation decile to 102·6 per 1000 for the most deprived. However, after age and sex standardisation, these differences widened further, ranging from 42·0 per 1000 to 120·2 per 1000.

Age and sex standardised rates of opioid prescribing were also high in women (84·9 per 1000), people with Pakistani (95·4 per 1000), Bangladeshi (86·7 per 1000), White British (77·0 per 1000), and White Irish ethnicity

| | Number of registered patients (N [% of total]) | Number of people prescribed opioids (N [% of patients]) | Prevalence per 1000 population | |
|--------------------------------------|--|---|--------------------------------|---------------------------|
| | | | Crude | Age and sex standardised* |
| Total | 20 476 680 (100·0%) | 1 445 122 (7·1%) | 70·6 | .. |
| Sex | | | | |
| Female | 10 278 870 (50·2%) | 898 114 (8·7%) | 87·4 | 84·9 |
| Male | 10 197 810 (49·8%) | 547 001 (5·4%) | 53·6 | 55·2 |
| Age, years | | | | |
| 18–29 | 3 717 679 (18·2%) | 46 886 (1·3%) | 12·6 | 12·8 |
| 30–39 | 3 659 908 (17·9%) | 108 255 (3·0%) | 29·6 | 30·0 |
| 40–49 | 3 276 966 (16·0%) | 165 214 (5·0%) | 50·4 | 51·2 |
| 50–59 | 3 492 216 (17·1%) | 276 024 (7·9%) | 79·0 | 79·7 |
| 60–69 | 2 802 520 (13·7%) | 308 245 (11·0%) | 110·0 | 110·2 |
| 70–79 | 2 248 085 (11·0%) | 307 349 (13·7%) | 136·7 | 136·1 |
| 80–89 | 1 047 270 (5·1%) | 186 088 (17·8%) | 177·7 | 173·8 |
| ≥90 | 232 036 (1·1%) | 47 061 (20·3%) | 202·8 | 190·1 |
| Index of Multiple Deprivation decile | | | | |
| 1 most deprived | 1 928 423 (9·4%) | 197 862 (10·3%) | 102·6 | 120·2 |
| 2 | 1 911 868 (9·3%) | 172 599 (9·0%) | 90·3 | 102·1 |
| 3 | 1 932 042 (9·4%) | 156 940 (8·1%) | 81·2 | 88·8 |
| 4 | 2 026 626 (9·9%) | 149 506 (7·4%) | 73·8 | 77·1 |
| 5 | 2 099 167 (10·3%) | 148 050 (7·1%) | 70·5 | 69·8 |
| 6 | 2 223 221 (10·9%) | 146 265 (6·6%) | 65·8 | 62·9 |
| 7 | 2 009 497 (9·8%) | 125 923 (6·3%) | 62·7 | 58·3 |
| 8 | 2 056 257 (10·0%) | 121 835 (5·9%) | 59·3 | 54·7 |
| 9 | 1 993 831 (9·7%) | 112 651 (5·6%) | 56·5 | 50·5 |
| 10 least deprived | 1 744 274 (8·5%) | 83 202 (4·8%) | 47·7 | 42·0 |
| Missing | 551 460 (2·7%) | 30 289 (5·5%) | 54·9 | 67·0 |
| Region | | | | |
| East | 4 652 396 (22·7%) | 298 844 (6·4%) | 64·2 | 64·0 |
| East Midlands | 3 552 633 (17·3%) | 273 147 (7·7%) | 76·9 | 76·4 |
| London | 1 493 926 (7·3%) | 47 593 (3·2%) | 31·9 | 46·1 |
| Northeast | 938 903 (4·6%) | 83 090 (8·8%) | 88·5 | 89·2 |
| Northwest | 1 766 548 (8·6%) | 160 160 (9·1%) | 90·7 | 86·6 |
| Southeast | 1 360 093 (6·6%) | 84 441 (6·2%) | 62·1 | 59·4 |
| Southwest | 2 926 749 (14·3%) | 198 870 (6·8%) | 67·9 | 63·0 |
| West Midlands | 804 657 (3·9%) | 65 226 (8·1%) | 81·1 | 86·9 |
| Yorkshire and The Humber | 2 911 692 (14·2%) | 229 453 (7·9%) | 78·8 | 79·6 |
| Missing | 69 083 (0·3%) | 4291 (6·2%) | 62·1 | 71·1 |

(Table 1 continues on next page)

(71.8 per 1000), and people living in the northeast (89.2 per 1000) and northwest (86.6 of 1000) of England and West Midlands (86.9 of 1000). Among people residing in care homes (0.8% [168 483 of 20 476 680] of all registered adult patients), nearly one in four patients were prescribed an opioid during this period (228.5 per 1000), which approximately halved after age and sex standardisation (118.7 per 1000).

When looking at trends over time, there were 19 113 668 registered adult patients in Jan 1, 2018, increasing during the study period to 20 510 959 in June 1, 2022 (appendix p 2). The median prevalence of opioid prescribing was 50.9 per 1000 adult patients per month (IQR 49.6 to 51.7) before COVID-19, and was declining by an estimated 0.3% per month (95% CI -0.3 to -0.2; figure 1, table 2). During March, 2020, opioid prescribing prevalence was 7.0% higher than predicted had previous trends continued (95% CI 3.3 to 10.9); this was followed by lower than expected rates in May (-4.7%, 95% CI -7.7 to -1.6). Aside from these temporary pulses, no changes to the level or slope were observed during the lockdown or recovery periods. Similar results were observed when excluding people with a cancer diagnosis in the past 5 years (appendix pp 3-4).

In each month, a median of 9.2% of all opioid prescriptions were new prescriptions. There was a median of 5.7 patients with newly prescribed opioids per 1000 opioid-naïve patients per month (IQR 5.4 to 5.9) and declined by 0.6% per month pre-COVID-19 (95% CI -0.7 to -0.5; figure 1, table 2). In contrast to prevalent prescribing, no increase was observed in March, 2020. Starting during the lockdown period, there was a -9.8% level shift in new prescribing (95% CI -14.5 to -6.5) and a 0.6% increase in slope (0.2 to 1.1) and a small, non-significant, upward shift during the recovery period relative to the lockdown period (4.1%, -0.9 to 9.4; table 2).

High-dose long-acting opioids represented a small minority of opioid prescribing. The median prescribing prevalence was 1.4 per 1000 per month pre-COVID-19 (IQR 1.4 to 1.5) and was declining by 0.8% per month (95% CI -0.9 to -0.8). No changes were observed during the lockdown or recovery periods. For parenteral opioids, the median prevalence was 0.4 per 1000 per month pre-COVID-19 (IQR 0.3 to 0.4). However, there were large increases in prescribing from March to May, 2020, including a 18.0% (95% CI 6.1 to 31.2) increase in March, a 89.4% (76.0 to 103.8) increase in April, and a 16.8% (8.3 to 26.0) increase in May. Even after accounting for these temporary increases, a positive level shift was observed during the lockdown period (10.7%, 95% CI -0.4 to 23.1), which reduced during the recovery period relative to the lockdown period (-8.4%, 95% CI -14.6 to -1.8; table 2; figure 1).

There was a median of 155 943 registered adult patients living in a care home per month (IQR 151 298 to 158 774).

| | Number of registered patients (N [% of total]) | Number of people prescribed opioids (N [% of patients]) | Prevalence per 1000 population | |
|--------------------------------|--|---|--------------------------------|---------------------------|
| | | | Crude | Age and sex standardised* |
| (Continued from previous page) | | | | |
| Ethnicity | | | | |
| White | 13 732 257 (67.1%) | 1 087 471 (7.9%) | 79.2 | 73.7 |
| British | 11 702 222 (57.1%) | 1 003 373 (8.6%) | 85.7 | 77.0 |
| Irish | 99 127 (0.5%) | 8 211 (8.3%) | 82.8 | 71.8 |
| Other | 1 930 908 (9.4%) | 75 887 (3.9%) | 39.3 | 56.2 |
| Asian or British Asian | 1 371 685 (6.7%) | 58 639 (4.3%) | 42.7 | 64.3 |
| Bangladeshi | 90 923 (0.4%) | 4 431 (4.9%) | 48.7 | 86.7 |
| Indian | 580 874 (2.8%) | 20 188 (3.5%) | 34.8 | 51.2 |
| Pakistani | 374 626 (1.8%) | 23 282 (6.2%) | 62.1 | 95.4 |
| Other | 325 269 (1.6%) | 10 738 (3.3%) | 33.0 | 51.4 |
| Black or Black British | 460 236 (2.2%) | 20 440 (4.4%) | 44.4 | 62.9 |
| African | 287 581 (1.4%) | 10 493 (3.6%) | 36.5 | 63.7 |
| Caribbean | 97 790 (0.5%) | 6 447 (6.6%) | 65.9 | 63.4 |
| Other | 74 865 (0.4%) | 3 500 (4.7%) | 46.8 | 65.0 |
| Mixed | 244 097 (1.2%) | 9 401 (3.9%) | 38.5 | 62.0 |
| White and Asian | 50 351 (0.2%) | 1 687 (3.4%) | 33.5 | 57.2 |
| White and Black African | 48 160 (0.2%) | 1 764 (3.7%) | 36.6 | 61.2 |
| White and Black Caribbean | 54 397 (0.3%) | 2 807 (5.2%) | 51.6 | 73.3 |
| Other | 91 182 (0.4%) | 3 143 (3.4%) | 34.5 | 56.6 |
| Other | 411 992 (2.0%) | 11 340 (2.8%) | 27.5 | 48.1 |
| Chinese | 160 958 (0.8%) | 1 008 (0.6%) | 6.3 | 17.6 |
| Other | 251 034 (1.2%) | 10 332 (4.1%) | 41.2 | 64.6 |
| Missing | 4 256 413 (20.8%) | 257 838 (6.1%) | 60.6 | 66.5 |
| Living in a care home | 168 483 (0.8%) | 38 493 (22.8%) | 228.5 | 118.7 |

All counts rounded to nearest 7. *Age (5-year age bands) and sex-standardised using the Office of National Statistics English mid-year 2020 population.

Table 1: Registered adult patients (aged ≥18 years) who were prescribed an opioid April-June, 2022

Before the start of COVID-19, a median of 182.4 people were prescribed an opioid per 1000 patients in a care home (IQR 180.2 to 185.1), which declined by 0.2% per month (95% CI -0.3 to -0.2; figure 2, table 2). An increase in prevalent prescribing was observed in March (2.9%, 95% CI 0.3 to 5.6) and April (13.3%, 11.2 to 15.4), and there was a small negative level shift during the recovery period (-1.5%, -3.0 to -0.01). Prescribing of high dose, long-acting opioids also declined by 1.3% per month (95% CI -1.4 to -1.1), with an increasing slope starting in the recovery period (1.5%, 1.3 to 1.8; table 2).

Median new opioid prescribing was 25.4 per 1000 opioid-naïve patients in a care home pre-COVID-19 (IQR 24.5 to 27.3) and was stable. Increases in new prescribing were observed in April (112.5%, 95% CI 92.2 to 134.9) and May (26.0%, 14.6 to 38.5). After accounting for these changes, no other changes were observed during the lockdown period. There was a -10.2% level shift (95% CI -18.7 to -0.7) in new prescribing starting in the recovery period. Prescribing

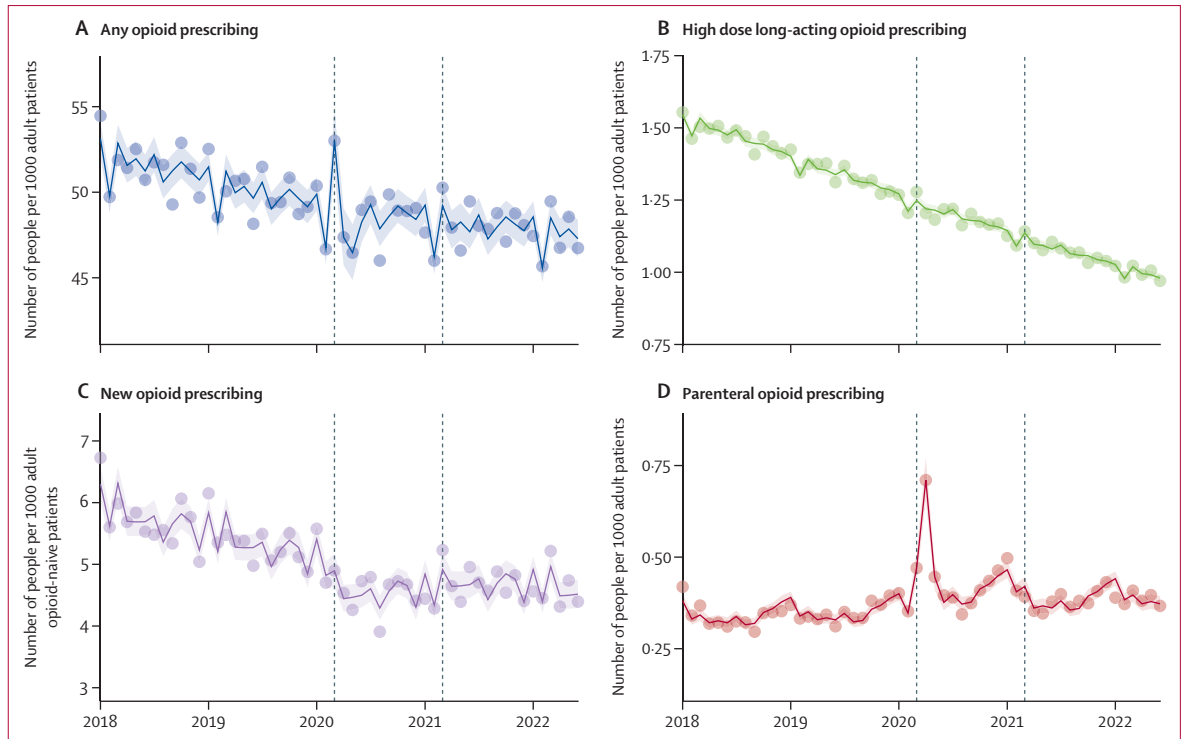


Figure 1: Number of people prescribed opioids per 1000 population per month (Jan 1, 2018, to June 30, 2022) among all registered adult patients. Solid lines are fitted values, dots are observed values, and vertical dashed lines represent start of lockdown period (March 1, 2020) and recovery period (April 1, 2021).

| | Pre-COVID-19 monthly slope | Changes during the lockdown period relative to pre-COVID-19 | | | | | Changes during recovery period relative to lockdown period | |
|-------------------------------------|----------------------------|---|-------------------------|-------------------------|----------------------------|-------------------------|--|-------------------------|
| | | Level shift | Change in slope | March, 2020 | April, 2020 | May, 2020 | Level shift | Change in slope |
| Full adult population | | | | | | | | |
| Any opioid | -0.3% (-0.3 to -0.2) | -0.6% (-3.4 to 2.5) | 0.2% (-0.1 to 0.6) | 7.0% (3.3 to 10.9) | -2.0% (-4.2 to 0.3) | -4.7% (-7.7 to -1.6) | -0.6% (-3.0 to 1.9) | -0.03% (-0.4 to 0.3) |
| New opioid | -0.6% (-0.7 to -0.5) | -9.8% (-14.5 to -6.5) | 0.6% (0.2 to 1.1) | * * | * * | * * | 4.1% (-0.9 to 9.4) | -0.3% (-0.8 to 0.2) |
| High dose long-acting opioid | -0.8% (-0.9 to -0.8) | -1.1% (-2.6 to 0.5) | 0.03% (-0.1 to 0.2) | * * | * * | * * | -1.2% (-2.5 to 0.1) | -0.03% (-0.2 to 0.1) |
| Parenteral opioid | 0.2% (-0.1 to 0.5) | 10.7% (-0.4 to 23.1) | 0.2% (-0.8 to 1.3) | 18.0% (6.1 to 31.2) | 89.4% (76.0 to 103.8) | 16.8% (8.3 to 26.0) | -8.4% (-14.6 to -1.8) | -0.2% (-1.5 to 1.1) |
| People living in care homes† | | | | | | | | |
| Any opioid | -0.2% (-0.3 to -0.2) | 0.2% (-2.1 to 2.4) | 0.09% (-0.2 to 0.3) | 2.9% (0.3 to 5.6) | 13.3% (11.2 to 15.4) | 0.3% (-2.3 to 2.9) | -1.5% (-3.0 to -0.01) | 0.05% (-0.2 to 0.3) |
| New opioid | -0.3% (-0.6 to 0.04) | 4.4% (-9.4 to 20.4) | 0.5% (-1.0 to 2.1) | 12.9% (-2.3 to 30.6) | 112.5% (92.2 to 134.9) | 26.0% (14.6 to 38.5) | -10.2% (-18.7 to -0.7) | -0.06% (-1.8 to 1.7) |
| High dose long-acting opioid | -1.3% (-1.4 to -1.1) | 1.7% (-1.0 to 4.5) | -0.4% (-0.7 to -0.2) | * * | * * | * * | -0.6% (-2.9 to 1.7) | 1.5% (1.3 to 1.8) |
| Parenteral opioid | 0.03% (-0.5 to 0.5) | -4.1% (-21.1 to 16.6) | 1.2% (-1.1 to 3.6) | 35.9% (11.6 to 65.5) | 186.3% (153.1 to 223.9) | 54.2% (37.0 to 73.7) | -14.3% (-26.7 to 0.2) | -0.8% (-3.5 to 2.0) |

Data are %, 95% CI. *Not included in the model. †Identified using an address-matching algorithm.

Table 2: Relative changes in the number of people prescribed opioids per 1000 population during the COVID-19 lockdown (March, 2020–March, 2021) and recovery (April, 2021–June, 2022) periods among all registered adult patients and people living in care homes

of parenteral opioids was much higher in care homes than in the general population (16.2 per 1000 pre-COVID-19) and there were large increases in prescribing

from March to May, 2020, including a 35.9% (95% CI 11.6 to 65.5) increase in March, 186.3% (153.1 to 223.9) in April, and 54.2% (37.0 to 73.7) in May. Aside from

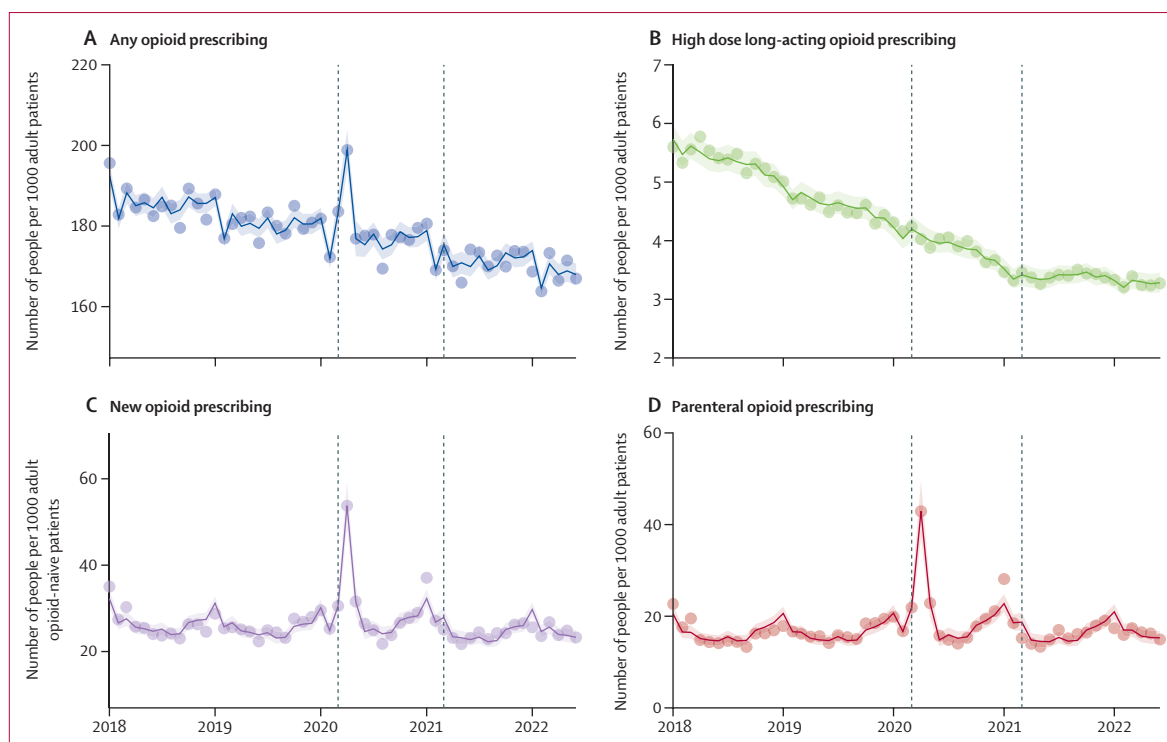


Figure 2: Number of people prescribed opioids per 1000 population per month (Jan 1, 2018 to June 30, 2022) among all registered adult patients living in care homes
Solid lines are fitted values, dots are observed values, and vertical dashed lines represent start of lockdown period (March 1, 2020) and recovery period (April 1, 2021).

these temporary changes, there was also a level shift during the recovery period relative to the lockdown period of -14.3% (-26.7 to 0.2 ; table 2).

Demographic variation in prevalent and new opioid prescribing by month (appendix pp 5–6) mirrored those observed in table 1. During the lockdown period, there was a negative shift in overall opioid prescribing for people aged 18–29 years (-5.2% , 95% CI -8.8 to -1.4) compared with predicted values had previous trends continued, but no change for all other age groups (figure 3; appendix pp 7–8). Other differences include a decrease in people with Asian or British Asian ethnicity (-5.7% , 95% CI -8.5 to -2.8), Other ethnicity (-4.2% , -7.2 to -1.2) and people living in London (-5.8% , -8.9 to -2.5). These decreases did not reverse during the recovery period. For people aged 18–29 years, there was a further level shift of -4.2% (-7.2 to -1.2) during the recovery period compared with the lockdown period. There was little variation by sex or Index of Multiple Deprivation decile (appendix pp 7–8).

For new opioid prescribing, no significant differences were observed by sex. The change in new prescribing associated with the lockdown period varied most dramatically by age (figure 3; appendix pp 9–10). There were negative shifts in new prescribing ranging from -7.0% to -13.0% in age categories younger than 80 years; these decreases reversed in the recovery period compared with the lockdown period for people aged 60–79 years, but not in younger age groups. For most other

demographic categories, there were similar decreases in new prescribing during the lockdown period, with minimal evidence of rebounding during the recovery period.

Discussion

Although the COVID-19 pandemic was associated with minimal changes in prevalent opioid prescribing in England, we found decreases in people who had newly prescribed opioids, with a levelling of the downward trend and some evidence that the reduction reversed slightly during the recovery period. And although our findings confirm previously identified differences in opioid prescribing by deprivation, ethnicity, and geography,^{7,20} we found only minimal differences in how the pandemic affected opioid prescribing by sex, Index of Multiple Deprivation decile, region, and ethnicity. The exception was older people and people living in care homes in which temporary increases in prescribing of parenteral opioids coincided with the peak in COVID-19 morbidity and mortality, strongly suggesting use in treating end-of-life COVID-19 symptoms.²¹

Our work also confirms continuation of the downward trend in opioid prescribing in England starting in 2016 seen in aggregate prescribing data,²⁰ coinciding with a policy focus on reducing opioid prescribing for chronic non-cancer pain.²⁵ One other study also found a decrease in new opioid users among people with certain

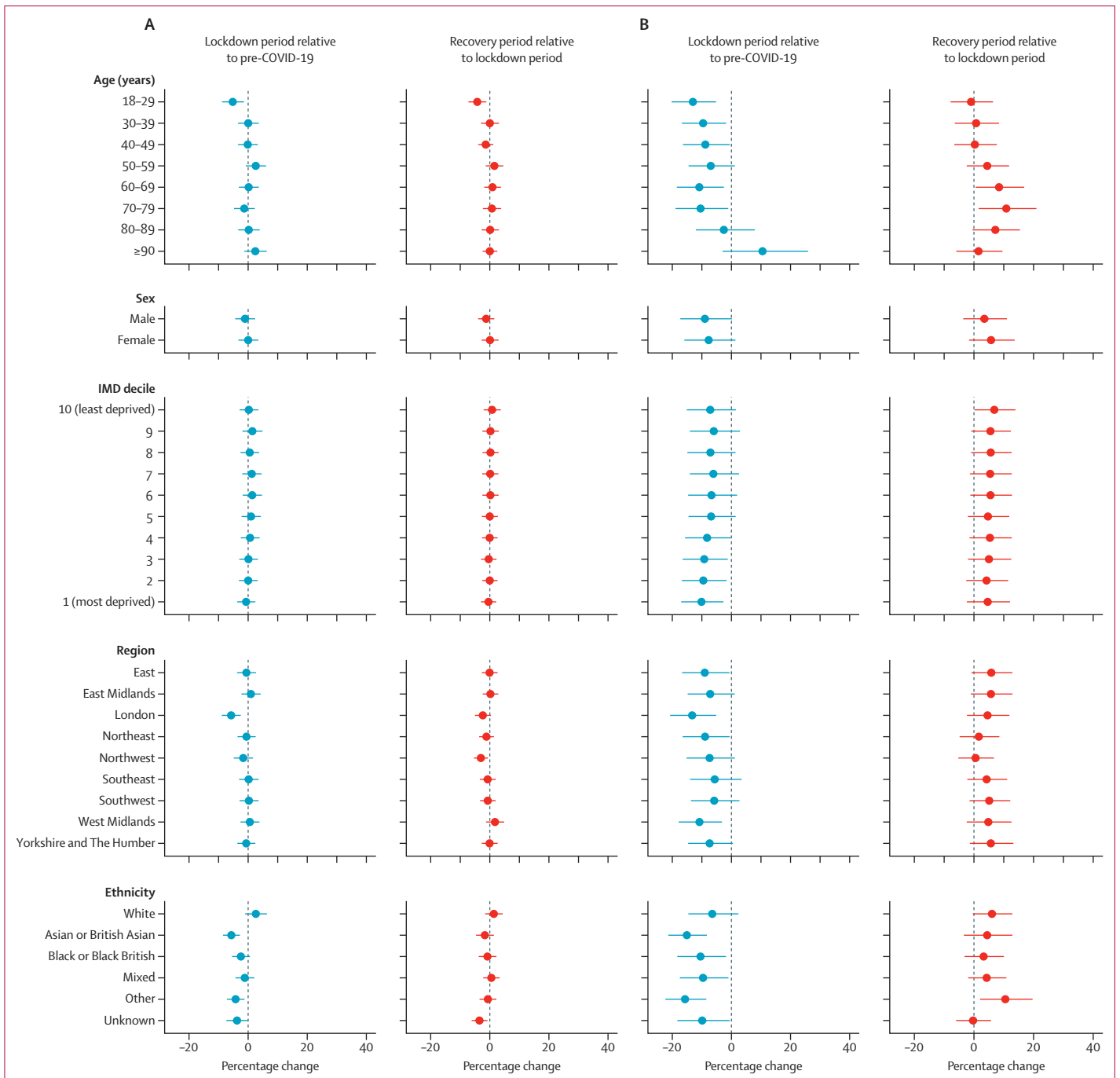


Figure 3: Level shift changes in number of people prescribed opioids during the lockdown and recovery periods by demographics

(A) shows the change in all people prescribed with opioids and (B) shows the change in people newly prescribed with opioids. All estimates adjusted for long-term trends and seasonality.

musculoskeletal or rheumatic conditions, but not in the number of overall prescriptions.¹⁴ This reduction was attributed by the authors of the study to caution from GPs in newly prescribing opioids during the pandemic when monitoring was more difficult. Early in the pandemic, there was also a decrease in elective medical procedures that often require prescribed analgesia;²⁶

however, opioids would typically be supplied by the hospital and are not captured in our data. Therefore, reduced new opioid prescribing is more likely related to decreased primary care contacts and fewer opportunities for opioids to be initiated.²⁷

We identified higher prescribing rates among women compared with men, although both groups were affected

similarly during the pandemic. Higher rates of analgesic use among women have been consistently found in UK studies,^{28,29} although rates of long-term use tend to be more similar between the sexes.²⁸ The cause is likely multifactorial, including differences in the prevalence of chronic pain, pain tolerance, sensitivity to analgesia, and propensity to seek or receive treatment.^{30–32} Similarly, prescribing varied substantially by ethnicity, region, and Index of Multiple Deprivation. People living in areas of greater deprivation have higher rates of suboptimal opioid prescribing such as long-term use^{7,8} in part related to variation in rates of chronic pain.³³ Although people living in deprived areas experienced greater health-care disruption and worse outcomes during the pandemic,^{5,34} the disparity in opioid prescribing did not widen further.

We could not definitely identify people who were at end of life, however, parenteral opioids are recommended in palliative care including for treating severe COVID-19, and the spikes in parenteral opioid prescribing, both in the general population and people in care homes, coincide with the peak in mortality during the pandemic (appendix p 11)³⁵ strongly suggesting this is related to treatment of people at the end of life.³⁶ Most of the peak in parenteral opioid prescribing was attributable to people in care homes who were greatly affected during the pandemic; in the first 12 weeks, one-third of all deaths in care homes were attributable to COVID-19.³⁷ A similar pattern was observed with antipsychotic prescribing.³⁸ Although opioid prescribing for treatment of patients at the end of life is best practice,³⁹ other studies have identified increases in prescribing of sedating medicines (opioids, antidepressants, antipsychotics, and benzodiazepines) to people in care homes,⁹ to deal with the psychological symptoms resulting from increased social isolation during the pandemic.⁴⁰

Our data capture primary care records for approximately 42.6% of patients registered with a practice in England on June 30, 2020, via the OpenSAFELY platform, and these data are broadly representative of the wider English population.¹⁹ Still, there might be regional differences in TPP patients that could limit the generalisability of the findings for the full population in England. This study, to our knowledge, is the largest to quantify person-level changes in opioid prescribing during the COVID-19 pandemic in England, allowing us to identify changes by demographic groups and in new prescribing, which is not possible with aggregate data. Although understanding how opioid prescribing has changed is important, it is limited in what it tells us about the quality of prescribing. We do not know the reason for prescribing as is common with many large database studies. We did not have information on prescribed dose or duration, which could identify more nuanced changes such as dose escalation as this is not currently captured in a structured format on prescriptions in England. Although we included all opioids (including non-analgesia), most prescribing in

England is for weak opioids for pain (eg, codeine). Weak opioids are generally less harmful than stronger opioids, but there are still risks if used inappropriately.⁴¹

There is no gold standard to identify people living in care homes in England, and we have relied on a previously developed algorithm that uses a combination of coded procedures and address-matching.²³ Algorithms based on address have good positive predictive value for identifying care home residents,⁴² and the prevalence in our study is similar to ONS data.⁴³ Our data also only includes prescriptions in primary care and not in secondary care, and some people could have been admitted to hospital in which opioid prescribing would not be captured. However, nearly one in four deaths in people older than 70 years during the pandemic was in a care home.³⁶ Although there will be some under-ascertainment of opioid prescribing in care homes residents, the relative changes observed are likely to still hold.

Although electronic health records are a rich source of data, there is potential for misclassification related to under-recording, inaccuracies in coding, or incorrect linkage with mortality data. The extent of these errors is not quantifiable in this study, but likely to be small.

Even though we saw no change in prevalent prescribing during the pandemic, there were multiple pressures that could have resulted both in decreased (eg, fewer interactions with the health-care system) and increased prescribing (eg, less availability of non-pharmacological pain treatment). Decreases in new prescribing (which represents a minority of all prescribing) could have been offset by increases in other subgroups. For instance, the COVID-19 pandemic led to worsening of the backlog in elective procedures with nearly 7.0 million people on waiting lists as of August, 2022,⁴⁴ putting people at increased risk of long-term opioid use, and quantifying this effect is vital. Further, although we found no evidence that disparities in prescribing by demographic factors widened during the pandemic, identifying the drivers of these observed differences can help inform strategies to reduce suboptimal use in high-risk populations.

A better understanding of the changes observed in this study is needed. A 2019 report by Public Health England has raised concerns about the high prevalence of opioid prescribing, and has emphasised the need for quality, contemporary, and detailed data on predictors of long-term use and dependence¹ and NHS England has highlighted the need for better use of data to reduce opioid harm.¹² We are developing tools to facilitate near real-time audit and feedback in the context of rapidly evolving pressures on the health service readily extendable to other clinical areas and challenges and can include any measures on opioids needed to support NHS England's ambition on safe opioid use.

In conclusion, we found little change in overall opioid prescribing apart from temporary changes at the start of the first lockdown, with changes in new opioid

prescribing that rebounded slightly during the recovery period. Disparities in opioid prescribing by demographic factors did not widen during the pandemic. However, we observed a substantial temporary increase in parenteral opioid prescribing and new opioid prescribing for people living at addresses linked to care homes, coinciding with the peak in COVID-19 morbidity and mortality and likely representing use to treat end-of-life COVID-19 symptoms.

OpenSAFELY collaborators

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Contributors

Conceptualisation: ALS, BM, and AJW. Data curation: ALS, CDA, SCJB, CB, BG, JM, and PI. Formal analysis: ALS, CDA, and MW. Funding acquisition: BG. Investigation: ALS. Methodology: ALS, BM, CW, and RC. Project administration: AJW, BM, AM, and BG. Resources: AM, SCJB, and PI. Software: ALS, CDA, MW, JM, and PI. Supervision: AJW, BM, AM, and BG. Validation: ALS, CDA, and MW. Visualisation: ALS. Writing of the original draft: ALS. Writing, review, and editing: all authors. ALS, JM, and PI directly accessed and verified the underlying data reported in the manuscript. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work. All authors confirm that they had full access to all the data in the study and accept responsibility to submit for publication. Members of the OpenSAFELY group also contributed to the paper as follows: data curation: SD, ID, DE, GH, RMS, TW, TO, SM, LB, BFCB-C, CB, JC, JP, and FH. Resources: SD, ID, DE, GH, RMS, TW, TO, SM, LB, BFCB-C, CB, JC, JP, and FH. Software: SCJB, SD, ID, DE, GH, RMS, TW, TO, SM, LB, and BFCB-C.

Declaration of interests

BG has received research funding from the Bennett Foundation, the Laura and John Arnold Foundation, the National Health Service (NHS), The National Institute for Health and Care Research (NIHR), the NIHR School of Primary Care Research, NHS England, the NIHR Oxford Biomedical Research Centre, the Mohn–Westlake Foundation, NIHR Applied Research Collaboration Oxford and Thames Valley, the Wellcome Trust, the Good Thinking Foundation, Health Data Research UK, the Health Foundation, WHO, UK Research and Innovation Medical Research Council, Asthma UK, the British Lung Foundation, and the Longitudinal Health and Wellbeing strand of the National Core Studies programme; has previously been a Non-Executive Director at NHS Digital; and has received personal income from speaking and writing for lay audiences on the misuse of science. BM is employed by NHS England working on medicines policy and is clinical lead for primary care medicines data. AM has represented the Royal College of General Practitioners in the health informatics group and the Profession Advisory Group that advises on access to GP Data for Pandemic Planning and Research, of which the latter was a paid role. AM is a former employee and interim Chief Medical Officer of NHS Digital; and has consulted for health-care vendors, the last time being in 2022. The companies consulted in the last 3 years have no relationship to OpenSAFELY.

Data sharing

Primary care records managed by the general practitioner (GP) software provider TPP were linked to Office of National Statistics (ONS) death data through OpenSAFELY and were linked, stored, and analysed securely within the OpenSAFELY platform via <https://opensafely.org> as part of the NHS England OpenSAFELY COVID-19 service. Data include pseudonymised data such as coded diagnoses, medications, and physiological parameters. No free text data are included. Detailed pseudonymised patient-level data is potentially re-identifiable and therefore not shared. The process for external users to request access to

the data is available on the OpenSAFELY website (<https://www.opensafely.org>). The public Github repository for this project (<https://github.com/opensafely/opioids-covid-research>) includes all codes used in this study, shared openly for review and re-use under Massachusetts Institute of Technology open license, all code lists used in this study and the study protocol. Detailed information on how each code list was compiled is available at <https://codelists.opensafely.org> for inspection and re-use by the wider research community.

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References

- Public Health England. Prescribed medicines review: report. 2020. <https://www.gov.uk/government/publications/prescribed-medicines-review-report> (accessed Dec 16, 2022).
- Ashaye T, Hounsome N, Carnes D, et al. Opioid prescribing for chronic musculoskeletal pain in UK primary care: results from a cohort analysis of the COPERS trial. *BMJ Open* 2018; 8: e019491.
- Els C, Jackson TD, Hagtveldt R, et al. High-dose opioids for chronic non-cancer pain: an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2017; 10: CD012299.
- Busse JW, Wang L, Kamaleldin M, et al. Opioids for chronic noncancer pain: a systematic review and meta-analysis. *JAMA* 2018; 320: 2448–60.
- National Institute for Health and Care Excellence. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. 2021. <https://www.nice.org.uk/guidance/NG193> (accessed Aug 9, 2022).
- Maddock J, Parsons S, Di Gessa G, et al. Inequalities in healthcare disruptions during the COVID-19 pandemic: evidence from 12 UK population-based longitudinal studies. *BMJ Open* 2022; 12: e064981.
- Nowakowska M, Zghebi SS, Perisi R, Chen LC, Ashcroft DM, Kontopantelis E. Association of socioeconomic deprivation with opioid prescribing in primary care in England: a spatial analysis. *J Epidemiol Community Health* 2021; 75: 128–36.
- Macfarlane GJ, Beasley M, Jones GT, Stannard C. The epidemiology of regular opioid use and its association with mortality: prospective cohort study of 466 486 UK biobank participants. *EclinicalMedicine* 2020; 21: 100321.
- Campitelli MA, Bronskill SE, Maclagan LC, et al. Comparison of medication prescribing before and after the COVID-19 pandemic among nursing home residents in Ontario, Canada. *JAMA Netw Open* 2021; 4: e2118441–2118441.
- Lee B, Yang KC, Kaminski P, et al. Substitution of nonpharmacologic therapy with opioid prescribing for pain during the COVID-19 pandemic. *JAMA Netw Open* 2021; 4: e2138453.
- Gomes T, Kitchen SA, Murray R. Measuring the burden of opioid-related mortality in Ontario, Canada, during the COVID-19 pandemic. *JAMA Netw Open* 2021; 4: e2112865.
- NHS England. Optimising personalised care for adults prescribed medicines associated with dependence or withdrawal symptoms: Framework for action for integrated care boards (ICBs) and primary care. 2023. <https://www.england.nhs.uk/long-read/optimising-personalised-care-for-adults-prescribed-medicines-associated-with-dependence-or-withdrawal-symptoms> (accessed Feb 15, 2024).
- Frazer JS, Frazer GR. Analysis of primary care prescription trends in England during the COVID-19 pandemic compared against a predictive model. *Fam Med Community Health* 2021; 9: e001143.

- 14 Huang YT, Jenkins DA, Yimer BB, et al. Trends for opioid prescribing and the impact of the COVID-19 pandemic in patients with rheumatic and musculoskeletal diseases between 2006–2021. *Rheumatology* 2023; **63**: 1093–1103.
- 15 Han J, Rolles M, Torabi F, et al. The impact of the COVID-19 pandemic on community prescription of opioid and antineuropathic analgesics for cancer patients in Wales, UK. *Support Care Cancer* 2023; **31**: 531.
- 16 Sindi NO, Alshaikh FS, Godman B, Kurdi A. The impact of the COVID-19 pandemic lockdown measures on the prescribing trends and utilization of opioids in the English primary care setting: segmented-linear regression analysis. *Expert Rev Clin Pharmacol* 2022; **15**: 787–93.
- 17 Nab L, Schaffer A, Hulme WJ, et al. OpenSAFELY: a platform for analysing electronic health records designed for reproducible research. *Pharmacoepidemiol Drug Saf* 2024; **33**: e5815.
- 18 Institute for Government. Timeline of UK government coronavirus lockdowns and restrictions. 2021. <https://www.instituteforgovernment.org.uk/charts/uk-government-coronavirus-lockdowns> (accessed Nov 4, 2022).
- 19 Andrews C, Schultze A, Curtis H, et al. OpenSAFELY: Representativeness of electronic health record platform OpenSAFELY-TPP data compared to the population of England. *Wellcome Open Res* 2022; **7**: 191.
- 20 Curtis HJ, Croker R, Walker AJ, Richards GC, Quinlan J, Goldacre B. Opioid prescribing trends and geographical variation in England, 1998–2018: a retrospective database study. *Lancet Psychiatry* 2019; **6**: 140–50.
- 21 National Institute for Health and Care Excellence (NICE) in collaboration with NHS England and NHS Improvement. Managing COVID-19 symptoms (including at the end of life) in the community: summary of NICE guidelines. *BMJ* 2020; **369**: m1461.
- 22 Office for National Statistics. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2020. 2020. <https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2020> (accessed Dec 6, 2022).
- 23 Schultze A, Bates C, Cockburn J, et al. Identifying care home residents in electronic health records—an OpenSAFELY short data report. *Wellcome Open Res* 2021; **6**: 90.
- 24 Gomes T, Kim KC, Suda KJ, Garg R, Tadrus M. International trends in prescription opioid sales among developed and developing economies, and the impact of the COVID-19 pandemic: a cross-sectional analysis of 66 countries. *Pharmacoepidemiol Drug Saf* 2022; **31**: 779–87.
- 25 Faculty of Pain Medicine of the Royal College of Anaesthetists. Opioids aware. 2022. <https://fpm.ac.uk/opioids-aware> (accessed Dec 12, 2022).
- 26 Dobbs TD, Gibson JAG, Fowler AJ, et al. Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study. *Br J Anaesth* 2021; **127**: 196–204.
- 27 Mansfield KE, Mathur R, Tazare J, et al. Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: a population-based study. *Lancet Digit Health* 2021; **3**: e217–30.
- 28 Marsden J, White M, Annand F, et al. Medicines associated with dependence or withdrawal: a mixed-methods public health review and national database study in England. *Lancet Psychiatry* 2019; **6**: 935–50.
- 29 Scott IC, Whittle R, Bailey J, et al. Analgesic prescribing in patients with inflammatory arthritis in England: observational studies in the Clinical Practice Research Datalink. *Rheumatology* 2023; published online Oct 12. <https://doi.org/10.1093/rheumatology/kead463>.
- 30 Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth* 2019; **123**: e273–83.
- 31 Mazure CM, Fiellin DA. Women and opioids: something different is happening here. *Lancet* 2018; **392**: 9–11.
- 32 Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth* 2013; **111**: 52–58.
- 33 Todd A, Akhter N, Cairns JM, et al. The Pain Divide: a cross-sectional analysis of chronic pain prevalence, pain intensity and opioid utilisation in England. *BMJ Open* 2018; **8**: e023391.
- 34 Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020; **584**: 430–36.
- 35 Schultze A, Nightingale E, Evans D, et al. Mortality among care home residents in England during the first and second waves of the COVID-19 pandemic: an observational study of 4.3 million adults over the age of 65. *Lancet Reg Health Eur* 2022; **14**: 100295.
- 36 Nuffield Trust. Deaths at home during the COVID-19 pandemic and implications for patients and services. 2023. <https://www.nuffieldtrust.org.uk/research/deaths-at-home-during-the-covid-19-pandemic-and-implications-for-patients-and-services> (accessed Feb 15, 2024).
- 37 Office for National Statistics. Deaths involving COVID-19 in the care sector, England and Wales: deaths registered between week ending 20 March 2020 and week ending 21 January 2022. <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/deathsinvolvingcovid19-inthecaresectorenglandandwales/deathsregisteredbetweenweekending20march2020andweekending21january2022> (accessed Nov 8, 2022).
- 38 Macdonald O, Green A, Walker A, et al. Impact of the COVID-19 pandemic on antipsychotic prescribing in individuals with autism, dementia, learning disability, serious mental illness or living in a care home: a federated analysis of 59 million patients' primary care records in situ using OpenSAFELY. *BMJ Ment Health* 2023; **26**: e300775.
- 39 National Institute for Clinical Excellence. COVID-19 rapid guideline: managing COVID-19. 2024. <https://www.nice.org.uk/guidance/ng191> (accessed Dec 21, 2022).
- 40 Suárez-González A, Rajagopalan J, Livingston G, Alladi S. The effect of COVID-19 isolation measures on the cognition and mental health of people living with dementia: a rapid systematic review of one year of quantitative evidence. *EClinicalMedicine* 2021; **39**: 101047.
- 41 Crush J, Levy N, Knaggs RD, Lobo DN. Misappropriation of the 1986 WHO analgesic ladder: the pitfalls of labelling opioids as weak or strong. *Br J Anaesth* 2022; **129**: 137–42.
- 42 Housley G, Lewis S, Usman A, Gordon AL, Shaw DE. Accurate identification of hospital admissions from care homes: development and validation of an automated algorithm. *Age Ageing* 2018; **47**: 387–91.
- 43 Office for National Statistics. Care homes and estimating the self-funding population, England: 2019 to 2020. 2022. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/socialcare/articles/carehomesandestimatingtheselffundingpopulationengland/2019to2020> (accessed Nov 10, 2022).
- 44 British Medical Association. NHS backlog data analysis. 2024. <https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/nhs-backlog-data-analysis> (accessed Jan 31, 2024).