

Regional variation in longitudinal trajectories of primary care opioids prescribing across Health Boards in Scotland: A population-based study

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Authorship: Teng-Chou Chen ¹, Amanj Kurdi ^{2, 3,4}, Ting-Li Su ⁵, Li-Chia Chen ¹

Full names, affiliation and email address for each author:

Teng-Chou Chen

Email: teng-chou.chen@manchester.ac.uk

1. Centre for Pharmacoepidemiology and Drug Safety, Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom

Amanj Kurdi

Email: amanj.baker@strath.ac.uk

2. Strathclyde Institute of Pharmacy and Biomedical Science, University of Strathclyde, Glasgow, United Kingdom
3. Department of Pharmacology, College of Pharmacy, Hawler Medical University, Erbil, Iraq
4. Division of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, South Africa

Ting-Li Su

Email: ting-li.su@manchester.ac.uk

5. Division of Dentistry, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom

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Li-Chia Chen

Email: li-chia.chen@manchester.ac.uk

1. Centre for Pharmacoepidemiology and Drug Safety, Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom

Corresponding author contact information:

Teng-Chou Chen

Email address: teng-chou.chen@manchester.ac.uk

Telephone: +44(0)161 306 2307

ORCID iD: <https://orcid.org/0000-0002-9491-0421>

Abstract

Background

This study aims to describe the longitudinal trajectory of opioid prescribing at the practice level and assess factors associated with utilisation, including Health Boards and socioeconomic status.

Research design and methods

This drug utilisation research used practice-level dispensing data from 2016 to 2018. Practice-level prescription opioids dispensed were quantified by the defined daily doses (DDDs) per 1000 registrants. Group-based trajectory models were used to identify groups of practices with similar trajectories based on the difference in monthly opioid utilisation. Characteristics of registrants were associated with the trajectory by a conditional logistic regression and the prescription opioids dispensed by a random-effect regression model.

Results

Of the 798 practices, 29.5% increased opioid prescription by an additional 100 DDDs/1000 registrants/month during 2017 and 2018. Practice in southwest Scotland tended to be categorised into the group with increasing opioid utilisation. Deprived socioeconomic status was associated with increasing opioid utilisation (odds ratio: 2.2; 95% confidence interval: 1.5, 3.2) or higher annual opioid utilisation (coefficient: 358.2;

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95% confidence interval: 327.6, 388.8) in 2018.

Conclusions

Increasing opioid utilisation over time was related to deprived socioeconomic status associated with chronic pain conditions and inequality in pain services. Further strategies to balance inequality are needed, which needs further investigation.

Keywords: longitudinal trajectory, opioid analgesics, primary health care, Scotland, socioeconomic factors, spatial mapping

1. Introduction

Opioid analgesics were traditionally used for acute pain or cancer pain as recommended by the World Health Organization analgesic ladder [1]. However, increasing opioid prescribing for patients with chronic non-cancer pain has been associated with the growing opioid-related harms and mortality in many developed countries [2-5]. In Scotland, the number of **opioid prescriptions increased by 1.6 times from 2003 to 2015** [6]. Meanwhile, the incidence of drug-related death increased more than three times, of which more than 85% involved any opiate [7]. In 2018, Scotland had the highest incidence of opioid-related deaths among the countries in the European Union [7,8].

Scotland initiated strategies to mitigate opioid analgesic prescribing for non-cancer pain and its associated dependence and harm. Since 2014, opioids have been included in the National Therapeutic Indicators, which provides a measure of prescribing activity across the 14 National Health Service (NHS) Health Boards and general practitioner (GP) practices peers [9]. **Each Health Board sets up its own opioid optimisation strategies and targets. To benchmark their prescribing with peers, interventions to mitigate inappropriate or overprescribing opioids were initiated through the Pharmacy and Prescribing Support Units, which oversee, monitor, and support**

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prescribing across GP practices within the corresponding Health Boards using regional dispensing data. Besides, NHS Scotland developed guidance to provide suggestions to clinicians, GP practices, and Health Boards on developing action plans to improve the quality of pain management, including analgesic prescribing [10].

As each Health Board has its healthcare priority, and this guidance has not been linked to any active implementation strategies, such as financial incentives, various action plans and care models have been adopted across the Health Boards [10]. The variation in the utilisation of opioids between Health Boards has been identified from published statistics, and 9% and 13% of the variance in prescribing strong and weak opioids can be explained by deprivation and urban/rural classification [6]. However, opioid prescribing was associated with multiple factors, such as demographic characteristics [11], deprived socioeconomic status (SES) [12-14], and pain-related comorbidities, such as depression and fibromyalgia [15]. The association between Health Boards and opioid prescribing at GP practices after considering the variation of those factors is still unclear.

Moreover, chronic pain conditions and persistent opioid prescribing were often found in more deprived areas [16,17], and limited policy impacts on controlling opioid

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prescribing might be found in more deprived areas. Although previously published studies have taken a cross-sectional approach to explore the association between opioid prescribing and characteristics, no study examined the longitudinal change of opioid prescribing over time and its associated factors at GP practices in Scotland.

Therefore, this study aimed to build a hypothesis to explain increased opioid prescribing at general practices in Scotland. The objectives are to (1) quantify and associate opioid utilisation across GP practices in different Health Boards after considering relevant factors, such as SES at the population level; (2) explore the longitudinal trajectory of change in opioid utilisation **and categorise general practices based on its longitudinal trajectory**; (3) identify factors associated with increased opioid prescribing across GP practices.

2. Participants and methods

2.1. Study design and data sources

This drug utilisation research **was conducted in June 2019** using publicly available practice-level data from the NHS National Services Scotland between January 2016 to December 2018 **(the most recent data available)**, including monthly opioid prescriptions dispensed, annual socio-demographic data, and the prevalence of

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selected diseases (Table 1) [18-25].

The monthly practice-level dispensing data obtain all the prescriptions issued by GPs and dispensed in the community setting in Scotland [18]. The practice-level socio-demographic data include the annual total number of registered people (registrants), females, registrants over 65 years [19,22], registrants from each Scottish Index of Multiple Deprivation (SIMD) quintile [20,25] and registrants from the settlements with a population more than 10000 residents [21,23].

The numbers of registrants with characteristics that have been reported to be associated with opioid prescribing, such as depression, cancer, and mental health diseases in each practice, were also retrieved from the Quality of Outcomes Framework (QOF) indicators in 2016, the Transitional Quality Arrangements (TQA) measures in 2017 and 2018 [24]. Ethical approval was not required as all the datasets are publicly available aggregate-level data.

2.2. Study subjects

General practices in Scotland, which had records of opioid prescriptions dispensed and the number of registrants from January 2016 to December 2018, were identified

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as study subjects. Practices with a practice code for administrative purposes but do not have patients registered, such as the Out of Hours Services, were excluded.

Practices with the identifiable socio-demographic characteristics in each calendar year were included in the analysis to associate relevant factors with the quantity of prescription opioids dispensed (Supplementary 1, A). Furthermore, to examine the trajectory of the change in prescription opioids dispensed, 798 practices with the identifiable socio-demographic factors in 2016 and issued opioids in 2017 and 2018 were selected (Supplementary 1, B).

2.3. Opioid utilisation

The monthly and annual opioid utilisation for each practice between January 2016 and December 2018 was measured as the number of Defined Daily Doses (DDD) per 1000 registrants. For each practice, opioid preparations which can be assigned a DDD and indicated for pain relief were extracted from the monthly practice-level dispensing data, including codeine, tramadol, dihydrocodeine, tapentadol, meptazinol, hydromorphone, pethidine, dextropropoxyphene, morphine, fentanyl, oxycodone and buprenorphine. **Buprenorphine products categorised as analgesics according to the British National Formulary (BNF; code 0407020B0) were included** [26]. On the contrary,

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Opioids generally prescribed for opioid dependence, such as buprenorphine sublingual (BNF code 0410030A0 and 0410030B0) and methadone, were excluded.

The strength was multiplied by the dispensed quantity for each preparation to calculate the total amount and then divided by the DDD. For each practice, we added up the DDD of each preparation prescribed in each calendar month and then divided it by the total number of registrants to calculate the monthly DDDs per 1000 registrants in 2016, 2017 and 2018. Similarly, we calculated the annual DDDs per 1000 registrants for each practice.

To quantify the change in monthly utilisation in 2017 and 2018 when compared to 2016, the monthly utilisation in each calendar month in 2017 and 2018 was subtracted by the utilisation in each corresponding calendar month in 2016 (e.g. January 2018-January 2016) to control the seasonal effect and derive the marginal opioid utilisation in each calendar month in 2017 and 2018.

2.4. Study covariates

In each practice, the characteristics of registrants, which have been found associated

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with prescription opioids dispensed, were identified annually [27-32]. In each calendar year, the proportion of females, registrants aged over 65 years, registrants living in a settlement with a population of more than 10000 residents and registrants from the most deprived SIMD quintile in each practice was calculated [33,34]. The SIMD is the Scottish Government's standard approach to identify deprivation across the 6979 data zones in Scotland. SIMD is calculated according to weighted domains, including income, employment, health, crime, housing, geographic access to services and education, skills, and training [33].

At each practice, the proportion of registrants diagnosed with cancers, depression, and mental illnesses, including schizophrenia, bipolar affective disorder and other psychoses, was directly extracted from the QoF indicators in 2016 and TQA measures in 2017 and 2018. Cancer includes all registered cancer excluding non-melanotic skin cancers. These conditions were selected according to published studies indicating the association with prescription opioids dispensed [24,35]. QoF indicators, pay-for-performance indicators, were introduced as a significant part of the General Medical Service contract to improve the quality of care in Scotland and were replaced by TQA measures in 2016 [24,35].

2.5. Data analysis

2.5.1. Quantify and associate opioid utilisation across general practices in different health boards

A random-effect regression model was applied to estimate the association between annual opioid utilisation and characteristics of registrants in the practices and considered the Health Boards cluster random intercept effect [36]. The likelihood ratio test was used for model selection, and the random effect of the Health Board on opioid prescribing was presented graphically after adjusting for the characteristics of registrants.

The regression model was conducted in 2016, 2017, and 2018 respectively, and the results were presented as a coefficient (CE) and 95% confidence interval (95%CI). The marginal annual opioid utilisation (with 95%CI) for practices with different proportions of registrants residing in the most deprived areas were reported. The annual opioid utilisation across practices in Scotland in 2018 was smoothly mapped by Spline regression to highlight the geographical distribution of opioid utilisation [37]. A sensitivity analysis was conducted by including buprenorphine products categorised for opioid dependence to examine the impacts of discarding these products.

2.5.2. The longitudinal trajectory of marginal opioid utilisation and its associated factors

A group-based trajectory model was applied to identify practice groups with a similar evolution of monthly marginal opioid utilisation (January 2017 to December 2018) [38].

Practices were assigned to each trajectory according to the highest estimated probability, and 2 to 5 groups of trajectory models with the polynomial function of time were generated and compared [38]. As the marginal opioid utilisation was a continuous variable, the censored normal distribution model was used to analyse the probability of group membership. **The final model was determined to have the lowest Bayesian information criterion value, an estimated probability of group membership of $\geq 5\%$, and an average posterior probability of above 0.7 with consideration on its implication** [38].

A conditional logistic regression was used to associate the trajectory of increased monthly opioid utilisation and the characteristics of registrants in 2016. The regression results were reported as the odds ratio (OR) and 95%CI. Besides, to investigate the geographical distribution in the trajectories of marginal opioid utilisation, the practices categorised into the four trajectories of monthly marginal opioid utilisation were highlighted on the map. STATA 14 (Stata-Corp, Texas, USA, 2015) and R (version 3.6.0) were applied for data analysis and mapping.

3. Results

In Scotland, 1088, 1077, and 1076 practices prescribed and dispensed opioids in 2016, 2017, and 2018. Of these, 821 (75.5%), 887 (82.4%), and 879 (81.7) practices could be assigned the number of registrants and potential determinants. Among the 821 practices that prescribed and dispensed opioids in 2016, 798 practices were included in calculating monthly opioid utilisation throughout 2017 and 2018 (Supplementary 1).

3.1. Practice-level population characteristics and annual prescription opioids dispensed in 2018

In 2018, the utilisation of prescription opioids dispensed across the 879 practices ranged from 1498.9 to 79785.8 DDDs/1000 registrants. The annual opioid utilisation significantly increased with a higher proportion of registrants residing in the top 20% of most deprived areas (CE: 358.2; 95%CI: 327.6, 388.8; $p < 0.001$), registrants aged more than 65 years (CE: 606.3; 95%CI: 487.3, 725.3; $p < 0.001$) or diagnosed with depression (CE: 292.6; 95%CI: 136.7, 448.6; $p < 0.001$) (Table 2). Likewise, similar results were found in 2016 and 2017.

However, an additional factor, a higher proportion of registrants coming from the urban area, was found significantly associated with a lower annual opioid utilisation in 2016

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(CE: -25.9; 95%CI: -43.0, -8.8; $p=0.003$) and 2017 (CE: -20.8; 95%CI: -37.7, -3.8; $p=0.016$). The median (interquartile range) proportion of registrants residing in the top 20% most deprived area is 13.8% (0.42%, 36.7%). The marginal annual opioid utilisation for practices with 13.8% of registrants residing in the top 20% most deprived area is 23246.98 (95%CI: 21157.63 to 25336.34) DDDs/1000 registrants. The marginal annual opioid utilisation is to consider the proportions of registrants aged over 65 and diagnosed with depression at their median level of 18.6% and 6.8%, respectively.

There was a visible geographical variation that a greater opioid utilisation was found in the Scottish Lowlands (west-central Scotland) (Figure 1). After considering factors significantly associated with opioid utilisation, the results of the random intercept regression model showed that Health Boards were significantly associated with opioid utilisation in 2018 ($p<0.001$) (Table 2). Practices located at the west-central adjacent Health Boards, NHS Lanarkshire, NHS Ayrshire and Arran and NHS Dumfries and Galloway, and NHS Fife, tended to have greater opioid utilisation when compared to other Health Boards (Figure 2). These results were consistent with the sensitivity analysis when including buprenorphine products indicated for opioid dependence.

3.2. Trajectory of the marginal change in monthly opioid utilisation comparing

2017 and 2018 against 2016

When comparing monthly utilisation in 2017 and 2018 to monthly utilisation in 2016 by calculating monthly marginal opioid utilisation, a first-order trajectory model categorised the 798 practices into four trajectories. Most of them were grouped into the trajectory with stable (29.2%), decreased (29.4%), and largely decreased (10.9%) in the monthly marginal opioid utilisation. However, 240 (30.5%) of the 798 practices showed an additional increase of about 100 DDDs/1000 registrants per month during 2017 and 2018 compared with the corresponding calendar month in 2016 (Figure 3).

3.3. Regional variation of practices in the trajectories of marginal monthly opioid utilisation

A higher proportion of practices located in the Health Boards in the southwest (e.g. Ayrshire and Arran [41.5%], Dumfries and Galloway [34.5%]) and western Scotland (e.g. Greater Glasgow and Clyde [33.3%], Lanarkshire [47.5%]) were categorised into the trajectory with increasing prescription opioids dispensed. A higher proportion of practices in NHS Orkney (50%) and NHS Shetland (44.4%) were also categorised into the trajectory with increasing prescription opioids dispensed. **In addition, a higher proportion of practices located at the Health Boards with greater random effects on opioid prescribing (NHS Ayrshire and Arran (20.8%), NHS Dumfries and Galloway**

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(13.8%) and NHS Lanarkshire (11.1%) were categorised into the trajectory with largely decreased prescription opioids dispensed (Figure 4) (Supplementary 2). In addition to Health Boards, practices with more than 20% of registrants coming from the top 20% of most deprived areas were associated with a higher risk (OR:2.2, 95%CI:1.5, 3.2; $p<0.001$) to be categorised into the trajectory with increasing monthly opioid utilisation (Supplementary 3).

4. Discussion

4.1. Main findings

General practice with a higher proportion of registrants with older age, depression, and deprived SES was associated with higher prescription opioids dispensed in Scotland. However, after considering those factors, there was still a visible geographical variation in opioid prescribing across Health Boards. Notably, there is a wide variation in longitudinal opioid utilisation across practices in Scotland. Compared with the corresponding calendar month in 2016, around 30% of the practices prescribed an additional 100 DDDs/1000 registrants in each month in 2017 and 2018. This equates to additionally prescribed and dispensed 600 tablets of 50 mg tramadol or 1000 tablets of 10 mg morphine each month in 2017 and 2018 for practices with 1000 registrants, even though policies to monitor opioid prescribing have been implemented since 2014.

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Practices with increased prescription opioids dispensed are in the deprived southwest and western Scotland, which implies a variation in the effectiveness and implementation of strategies in monitoring or deprescribing opioids across Health Boards.

4.2. Comparison with existing literature

Advancing on the statistics published by NHS Scotland and indicating a variation in opioid utilisation between Health Boards [39], this study found that practices within Health Boards located in west-central Scotland were deindustrialised since the 1980s tend to have the greatest overall opioid utilisation. Moreover, the different random effects of the Health Board remained in our study after adjusting for demographic characteristics, SES, and prevalence of depression. Similar to studies identifying a significant association between SES and opioid utilisation when applied only data from one Health Board [40], our study also showed a significant association when adopted data from the whole of Scotland. In addition to estimating the association in a cross-sectional method [6,12-14], our study adds to the current knowledge by presenting a significant association between SES and the longitudinal trajectories.

4.3. Implications for research or practice

The variation between Health Boards implied the difference in the implementation of guidance "Quality of Prescribing for Chronic Pain" (2018) by various strategies and care models, such as involving community pharmacies to undertake reviews of analgesic prescribing (NHS Fife), establishing pharmacist-led pain clinics to review opioids and other medications for managing chronic pain (NHS Greater Glasgow and Clyde and NHS Lanarkshire), and training/upskilling prescribers to identify and review patients on high dose opioids (NHS Dumfries and Galloway) [10,41]. Those strategies might attribute to the variation in prescription opioids dispensed between Health Boards and need further evaluation.

This increase in opioid utilisation in practices with a higher proportion of registrants with lower SES alluded that opioid deprescribing strategies are less easy to implement in deprived SES areas. Studies have highlighted the correlation between prevalent chronic pain conditions and deprived SES [42,43]. Previous studies also suggested that policies to control opioid prescribing are less effective in listing persistent users who are more likely to have a deprived SES [44-48]. Besides, lower SES was related to poor healthcare accessibility [33]. The geographical variation in accessibility, availability and quality of multidisciplinary pain management services has been

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indicated in the US and England [11,13]. In 2017/2018, there was a 1.8, and 3-fold variation in the rate of knee replacement and length of stay for patients admitted to the General Psychiatry speciality across Health Boards in Scotland [49,50].

In this study, the significant association between lower annual opioid utilisation and a higher proportion of urban registrants also highlights the imbalance in healthcare accessibility between urban and rural areas. This proposition is also supported by the variation in the waiting time for referring to a pain clinic across each Health Board in Scotland [51]. Further policy or strategies to balance the inequality in pain management services between Health Boards is as important as the strategies to manage opioid prescribing.

4.4. Strengths and limitations

This study applied national data, including all prescribing from general practices in Scotland, and hence the results are highly representative. As the opioid utilisation was quantified at the practice level and smoothly mapped by Spline regression, the variation in prescription opioids dispensed and marginal change within Health Boards could be better visualised. Besides, compared to similar studies in England that apply SES to the neighbourhood area of the practice [12-14], the proportion of registrants

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from different SES in general practice could be accessed in Scotland. Hence, the estimated association is less biased.

There are some limitations to this study. This study applies aggregate level data for hypothesis building, and hence each individual's characteristics concerning the need to take opioids, such as cancer, cannot be considered. In addition, the change in opioid prescribing at the individual-patient level cannot be measured in this study. Hence, it is still unclear if the increasing prescribing is related to more opioid users, increased prescribed dose or prolonged prescribing. **It is possible that the estimated opioid prescribing was consumed by only a few patients with high dose of opioid prescriptions.**

As a cross-sectional design, the causal relationship cannot be easily identified, and the results should be interpreted with caution. Compared to data availability in England [52,53], smoking status and registrants with obesity at the practice level cannot be accessed in Scotland.

Moreover, pain conditions and opioid dependence were not included in QOF indicators and TQA measures. **Also, this study focused on practices with patients registered because practice-level factors (geographic location, deprivation index and demographic characteristics) were retrievable in those practices. The prescriptions**

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issued by Out of Hours Services were not included, and the characteristics of patients using these services were unknown. Further studies are needed to apply individual patient data to evaluate the effects of policies or strategies to optimise pain management or opioid prescribing.

5. Conclusion

Implementing opioid monitoring strategies across Health Boards has effectively sustained the total amount of opioid utilisation in Scotland. However, the variation of opioid utilisation is associated with Health Boards, deprived SES, and other population characteristics. Deprived SES is associated with the increasing number of prescription opioids dispensed and the ineffectiveness of opioid optimisation strategies. Although the causation between SES and prescription opioids dispensed is complex and has not been thoroughly studied, deprived SES may be associated with the prevalence of chronic pain and inequality in pain management services in primary care between regions.

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Tables

Table 1. Publicly available aggregate-level data retrieved from the National Health Services National Services Scotland

Dataset	Time	Information retrieved from datasets	Outcome measure used in this study
Monthly practice-level dispensing data ^[18]	January 2016 to December 2018	Monthly quantity of dispensed opioid preparations for each practice	<ul style="list-style-type: none"> • Annual DDD/1000 registrants at practices • Monthly DDD/1000 registrants at practices
Practice list sizes by gender and age group ^[19,22]	2016 to 2018	For each practice: <ul style="list-style-type: none"> • Number of registrants • Number of females • Number of patients aged more than 65 years 	<ul style="list-style-type: none"> • Annual DDD/1000 registrants at practices • Monthly DDD/1000 registrants at practices • Proportion of female gender • Proportion of registrants aged more than 65 years
Quality and Outcomes Framework 2015-16 ^[24]	2016	Proportion of registrants with cancer, depression and mental health disease in each practice	Proportion of registrants with specific characteristics
Transitional Quality Arrangements 2016-18	2017 and 2018	Proportion of registrants with cancer, depression and mental health disease in each practice	Proportion of registrants with specific characteristics
Practice populations by deprivation status ^[20,25]	2016 to 2018	Number of registrants by deprivation quintile	Proportion of registrants from the most deprived quintile
Practice populations by urban/rural classification ^[21,23]	2016 to 2018	Number of registrants by urban/rural classification	Proportion of registrants from settlements with a population of more than 10000 residents

(Note) DDD: Defined Daily Dose

Table 2. Association between opioid utilisation and determinants among the 879 practices in 2018 from the random effect regression model

	Univariate analysis	Multivariate analysis	Parsimonious model ^b
<i>Demographic characteristics</i>			
Proportion of females	28.2 (-317.8, 374.2)	269.0 (-9.7, 547.8)	-
Proportion of registrants aged over 65 years	131.7 (-15.1, 278.5)	605.0 (439.5, 770.4) *	606.3 (487.3, 725.3) *
<i>Socioeconomic status</i>			
Proportion registrants residing in the top 20% most deprive areas	321.4 (291.5, 351.3) *	360.3 (327.1, 393.5) *	358.2 (327.6, 388.8) *
<i>Rural/urban classification</i>			
Proportion of registrants from a settlement with population more than 10000 residents	17.3 (-2.1, 36.7)	-15.5 (-32.6, 1.6)	-
<i>Quality of Outcomes Framework indicators</i>			
Proportion of registrants with cancer	412.9 (-466.3, 1292.2)	-611.6 (-1576.1, 352.8)	-
Proportion of registrants with depression	719.3 (528.0, 910.6) *	309.0 (140.9, 477.2) *	292.6 (136.7, 448.8) *
Proportion of registrants with mental health diseases	7915.4 (5954.2, 9876.5) *	692.0 (-1025.1, 2409.2)	-
<i>Random intercept at the Health Board level</i>			
Standard deviation estimate (SE) ^a	NA	3751.8 (808.7) *	3658.6 (783.5) *

(Note) * p<0.05, all statistics are presented in coefficient and 95% confidence interval, ^a presented in the estimate and standard error. ^b after elimination of non-significant terms from multivariate analysis model, NA: not applicable

Figures

Figure 1. Opioid utilisation among 879 practices in 2018 in Scotland

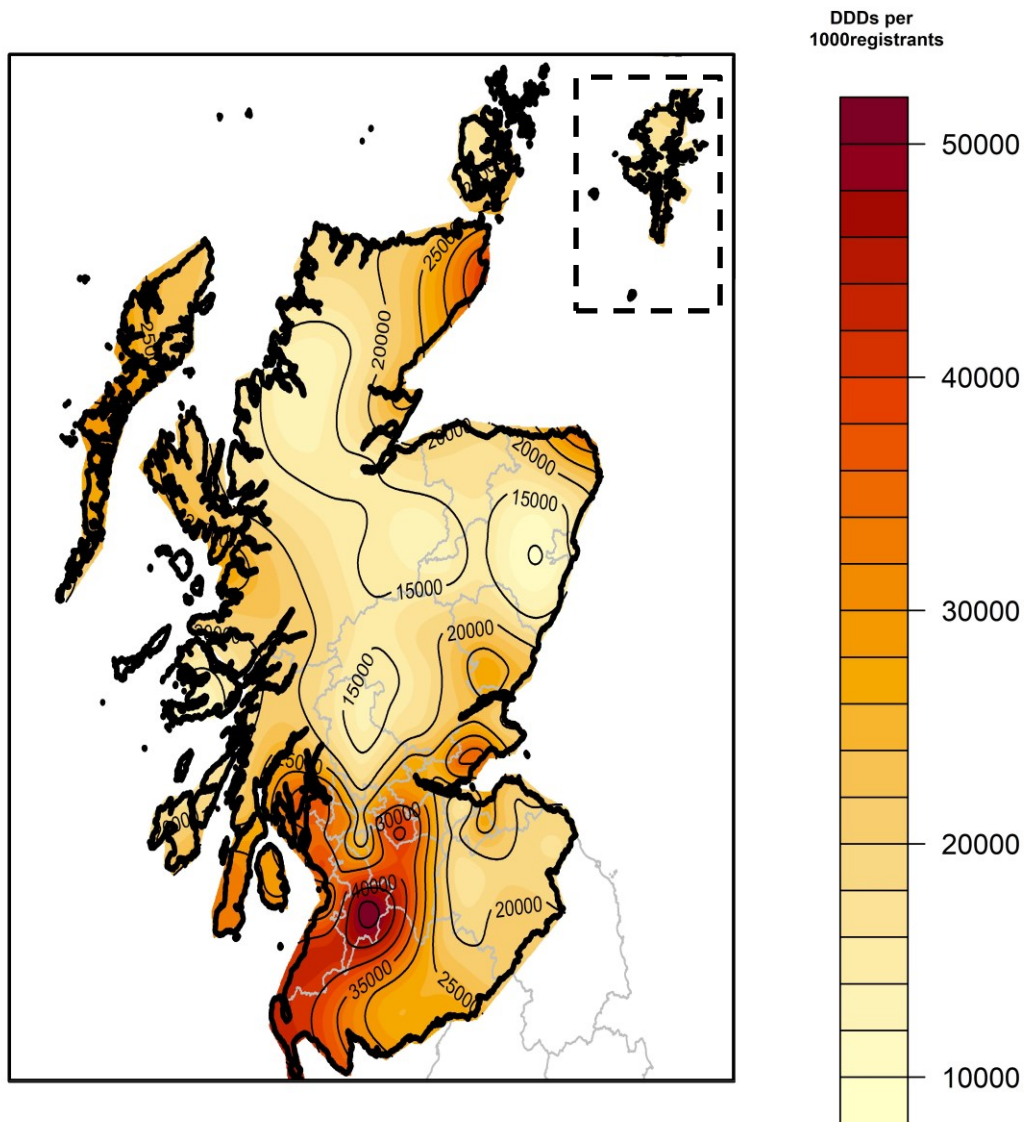
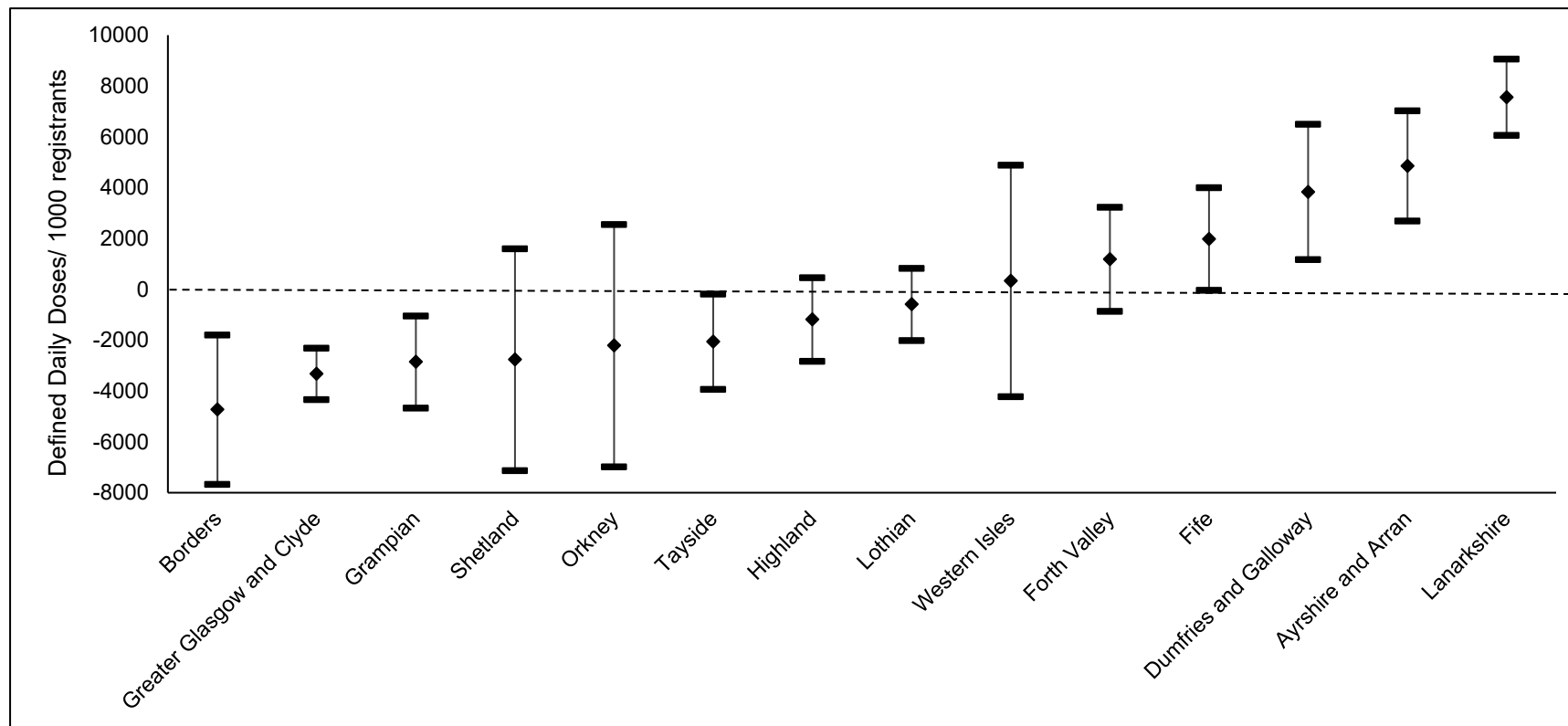


Figure 2. The estimated Health Boards effect on opioid utilisation after adjusting factors associated with opioid utilisation in the random intercept model



(Note) The data was presented in mean± two standard deviations.

Figure 3. Trajectory of marginal change from 2016 in monthly opioid utilisation across 798 general practices

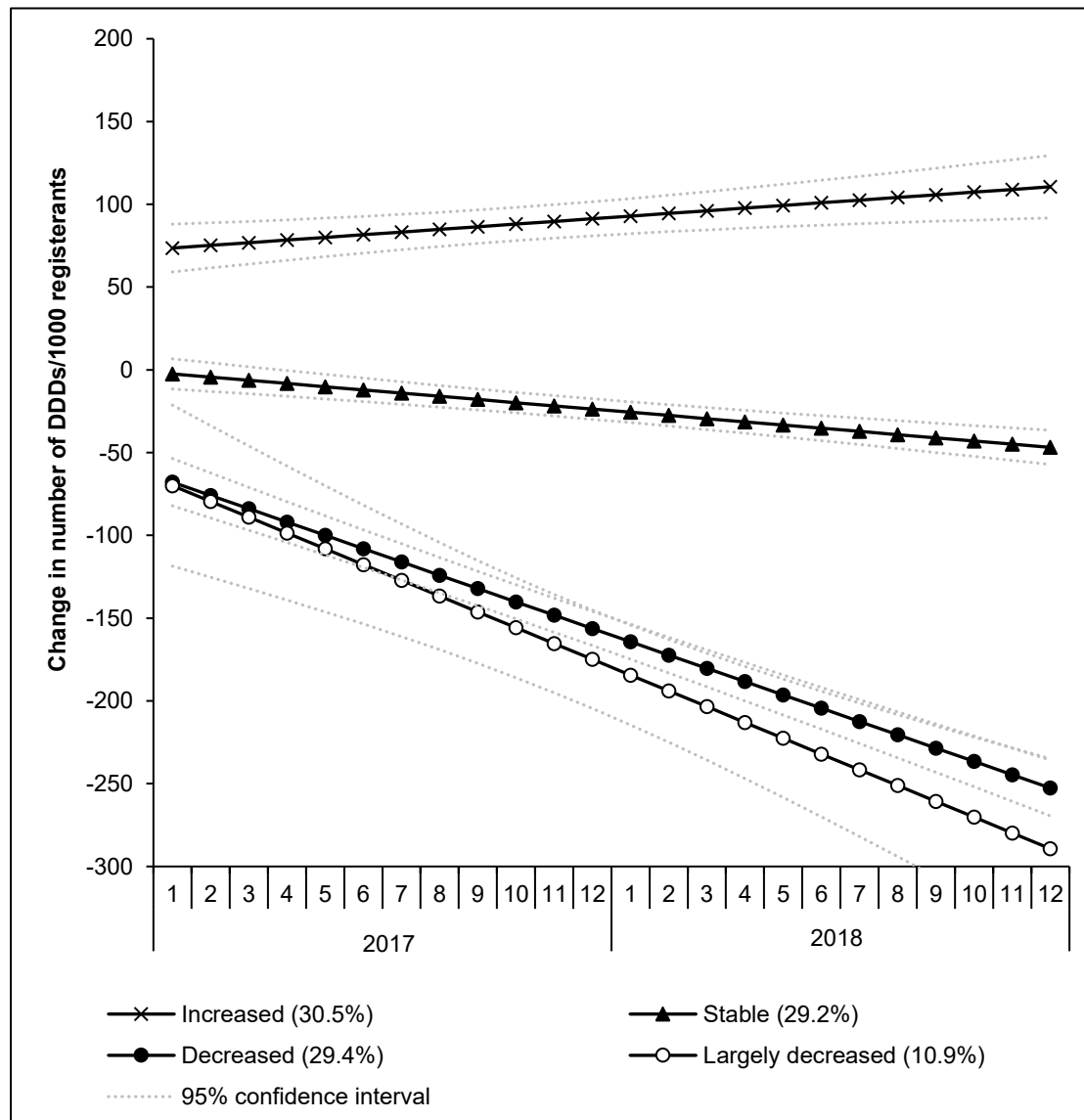
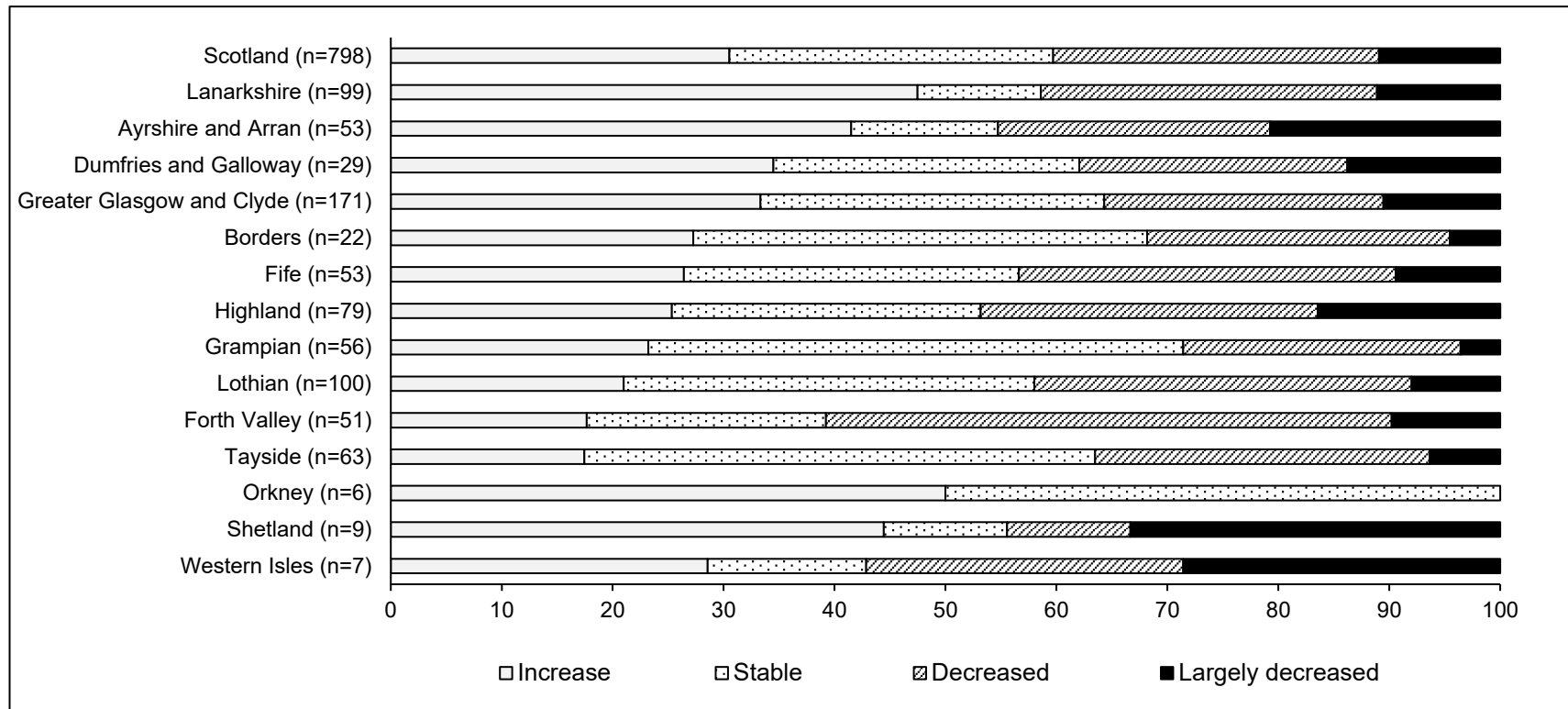


Figure 4. Proportion of general practices categorised into different trajectories of a marginal change in monthly opioid utilisation by Health Boards



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Disclosure

Data availability statement

This study used publicly available data from the NHS National Services Scotland.

Funding details

This study used publicly available data from the NHS National Services Scotland. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

TCC proposed the concept and study design, accessed, analysed the research data, and drafted the manuscript. TLS performed the geographical analysis and contributed to the manuscript review. AK contributed to the study design, interpretation of results and manuscript revision. LCC led the research project, study design, interpretation of results and manuscript revision.

Financial and competing interests disclosure

The authors declare that they have no known competing financial interests or personal

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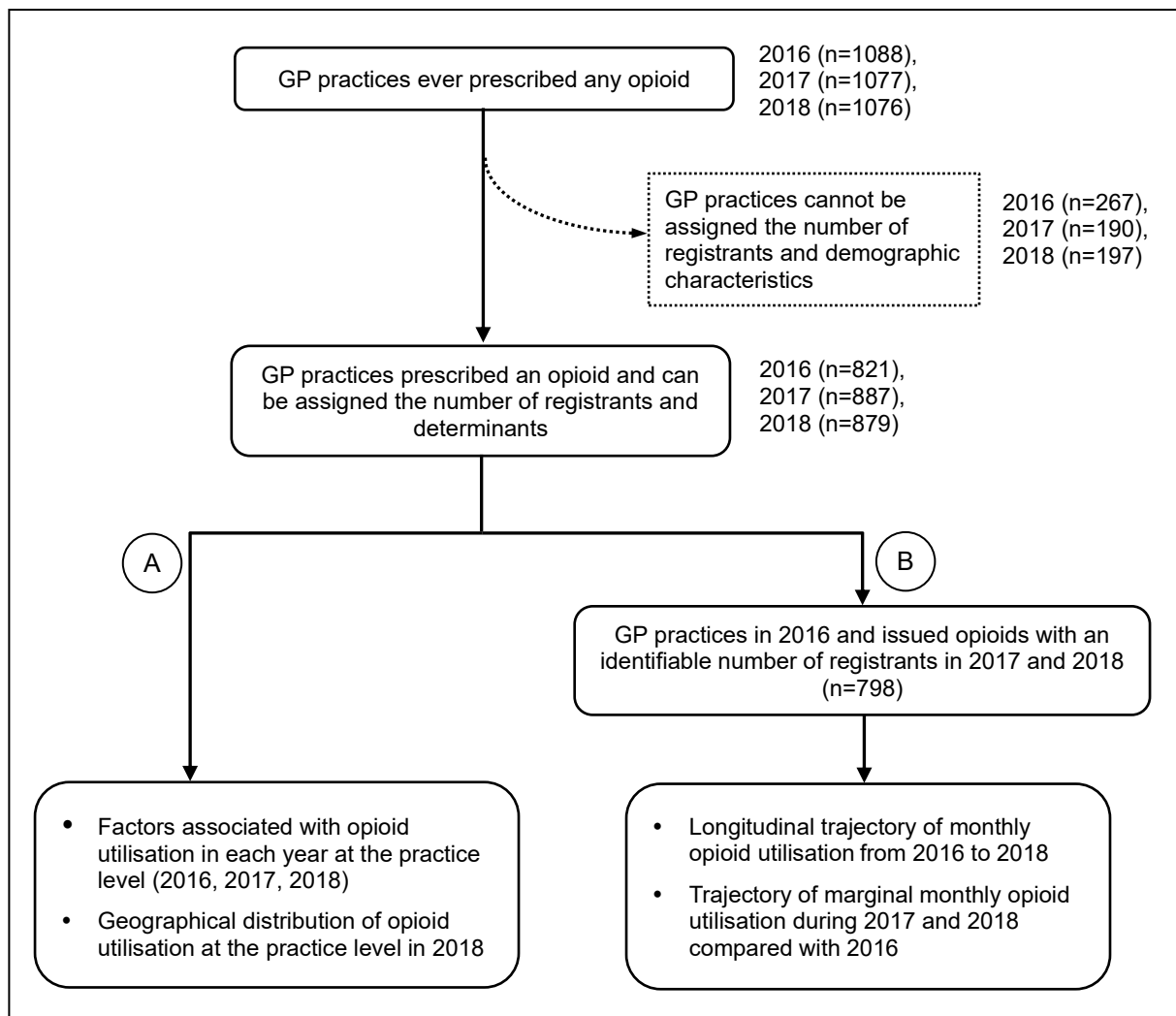
relationships that could have influenced the work reported in this paper.

Ethics approval statement

This study used aggregate-level data that are publicly available and do not require ethical approval.

Supplementary materials

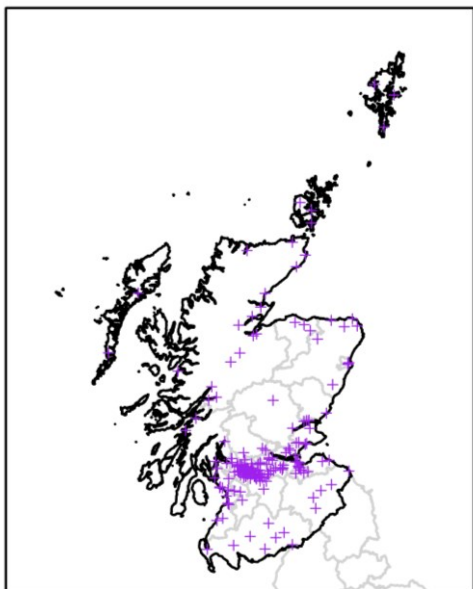
Supplementary 1. Research framework illustrating study subject selection and outcome identification



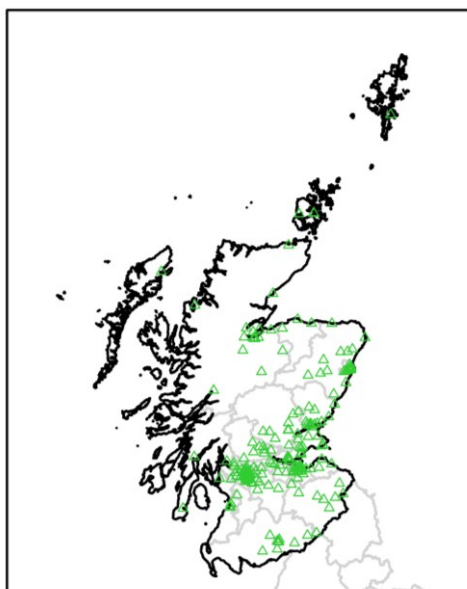
Supplementary 2. Regional variation of 798 practices in the four trajectories identified

from the marginal change in monthly opioid utilisation

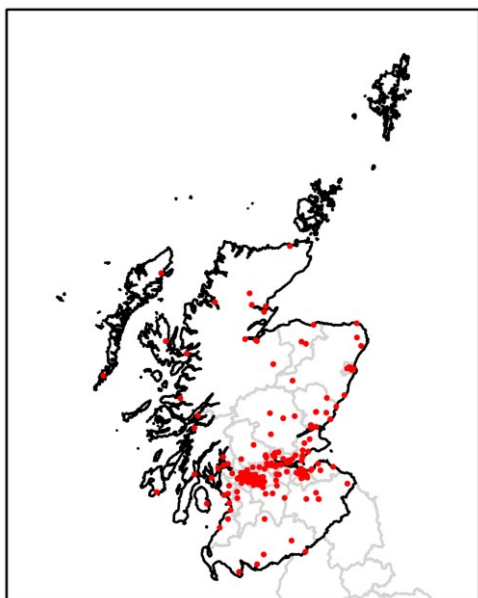
Increased (30.5% of practices)



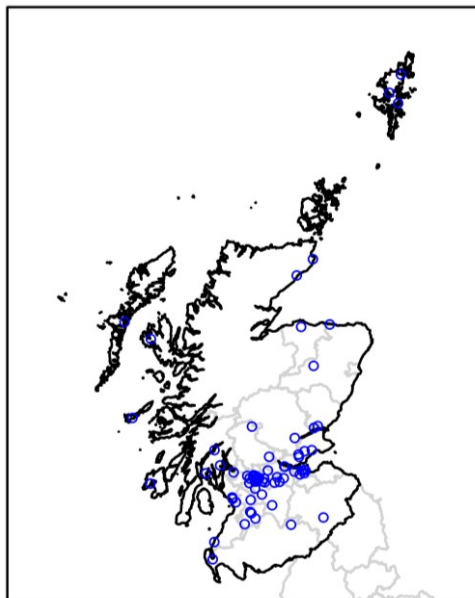
Stable (29.2% of practices)



Decreased (29.4% of practices)



Largely decreased (10.9% of practices)



(Note) The four trajectories from the monthly marginal opioid utilisation as presented in Figure 33.

Supplementary 3. Association between the trajectory of increased marginal monthly opioid utilisation and determinants among the 798 practices in 2016 from the conditional logistic regression

	Univariate analysis OR (95%CI)
<i>Demographic characteristics</i>	
Proportion of females	0.95 (0.87, 1.0)
Proportion of registrants aged over 65 years	1.0 (0.97, 1.04)
<i>Socioeconomic status</i>	
Proportion registrants residing in the top 20% of most deprived areas	1.02 (1.01, 1.03) *
More than 20% of registrants residing in the top 20% of most deprived areas ⁺	2.2 (1.5, 3.2) *
<i>Rural/urban classification</i>	
Proportion of registrants from a settlement with population more than 10000 residents	1.0 (0.99, 1.01)
<i>Quality of Outcomes Framework indicators</i>	
Proportion of registrants with cancer	1.0 (0.8, 1.3)
Proportion of registrants with depression	1.3 (0.79, 2.1)
Proportion of registrants with mental health diseases	1.04 (0.99, 1.09)
(Note) * p<0.05, all statistics are presented in odds ratio and 95% confidence interval (95%CI). ⁺ As the proportion of registrants residing in the top 20% of most deprived areas was the only significant factor, we grouped the original continuous variable into a categorical variable for presentation purposes.	