BMJ Open

Prescribing patterns for medical treatment of suspected prostatic obstruction: A spatiotemporal statistical analysis of Scottish open access data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042606
Article Type:	Original research
Date Submitted by the Author:	09-Jul-2020
Complete List of Authors:	Andreis, Federico; University of Stirling, Health Sciences Bryant, Richard; University of Oxford Nuffield Department of Surgical Sciences; Churchill Hospital, Urology Giorgi, Emanuele; Lancaster University Lancaster Medical School, Williamson, Andrea; University of Glasgow, GPPC, School of Medicine, Dentistry and Nursing, MVLS Ward, Ashleigh; University of Stirling, Health Sciences
Keywords:	STATISTICS & RESEARCH METHODS, Prostate disease < UROLOGY, Bladder disorders < UROLOGY, PUBLIC HEALTH
Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
bmjopen_supplement_2.R	

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Prescribing patterns for medical treatment of suspected prostatic obstruction: A spatiotemporal statistical analysis of Scottish open access data

Authors

Federico Andreis, PhD [Faculty of Health Sciences and Sport, University of Stirling]

Richard Bryant, BMedSci MBChB FRCSEd(Urol) PHD [Nuffield Department of Surgical Sciences, University of Oxford, Oxford Cancer Research Centre, Oxford] & [Department of Urology, Churchill Hospital , Oxford University Hospitals NHS Foundation Trust]

Emanuele Giorgi, PhD [Lancaster Medical School, University of Lancaster]

Andrea Williamson, MBChB MPH PhD FRCGP FHEA DTM&H [General Practice and Primary Care, School of Medicine, Dentistry and Nursing, MVLS, University of Glasgow] & [General Practitioner Homelessness Health, Medical Officer Addictions, NHS Glasgow and Clyde, Homeless Health and Resource Services]

Ashleigh Ward, PhD [Faculty of Health Sciences and Sport, University of Stirling]

Corresponding author

Federico Andreis, PhD

Faculty of Health Sciences and Sport, Pathfoot Building, University of Stirling, FK9 4LA, Stirling

email: federico.andreis@stir.ac.uk

tel: +44(0)1786466252

Word count 3714 (abstract: 252 / text: 3463, excl. figures, tables, equations and captions)

Abstract

Background Healthcare services treating men with prostate conditions are increasingly burdened worldwide. One of the competing factors in this demand is increasing diagnosis and treatment of lower urinary tract symptoms in men, much of which is suspected bladder outflow obstruction secondary to benign prostate hyperplasia/enlargement. However, the impact of increases on services is largely hidden, and there is limited knowledge of potential differences in management based on geography.

Objective To investigate potential variation in the prescribing of drugs for suspected bladder outflow obstruction in Scotland based on analysis of publicly available data, and identify trends that may help to inform future prescribing behaviour.

Design, setting, and participants We linked the relevant publicly available prescribing and patient data to all general practices in Scotland between October 2015 and November 2019.

Outcome measurements and statistical analysis We analysed the numbers of daily doses of drugs for suspected bladder outflow obstruction prescribed per month using a Bayesian Poisson regression analysis, incorporating random effects to account for spatial and temporal elements in prescribing.

Results: Prescriptions for drugs to treat suspected bladder outflow obstruction increased during the observation period in Scotland, consistent with an ageing population and increased diagnosis. Whilst some determinants of health inequality regarding prescribing practices across health boards are consistent with those known from the literature, other inequalities remain unexplained after accounting for practice- and patient-specific characteristics such as deprivation and rurality.

Conclusions Variations in spatiotemporal prescribing for suspected bladder outflow obstruction exist in Scotland, some of which are unexplained and require further investigation.

Keywords

Suspected bladder outflow obstruction, benign prostate hyperplasia, benign prostate enlargement, lower urinary tract symptoms, drug prescription, open access data, spatiotemporal modelling, medical practice

Summary section

Strengths and limitations of this study

- This is the first study to investigate spatial and temporal variations in drug-prescribing patterns for bladder outflow obstruction using geostatistical models
- The statistical framework described in this paper is very general, and can be readily extended to other settings and conditions
- Data on drug-prescribing in Scotland only exists in the public domain at an aggregate (i.e. individual GP practice or patient list) level, which limits the granularity of the analysis
- The use of summary data regarding levels of socio-economic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome, with these factors likely to be important in terms of access to healthcare and prescribing.

Contributors

FA and AW2 initiated the study. FA and EG developed the statistical model. FA had full access to all the data in the study, carried out the statistical analysis and took responsibility its accuracy and for the integrity of the data. FA drafted the manuscript, and all authors (FA, RB, EG, AW1, AW2) contributed to the critical revision for important intellectual content, and to the interpretation of the data analysis results. RB and AW1 provided expert advice on the more clinical aspects.

Non-author contributors: the authors would like to acknowledge support and encouragement received by Prof Alan McNeill (NHS Scotland) and Prostate Scotland at the initial conception of this project.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared. None of the contributing authors have any conflict of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

Patient and public involvement

No patients or public was involved for this study.

Patient consent for publication

Not required.

Ethics approval

Not required. This study is an analysis of publicly available electronic health records.

Data availability statement

A technical supplement, the statistical code (in R), and the final processed dataset used for the study available from medRxiv: https://www.medrxiv.org/content/10.1101/2020.06.19.20135459v1. The original, unprocessed data is publicly available online from the sources indicated in the manuscript in the Material and Methods section.

Licence statement

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a

non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in BMJ Open and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Introduction

The incidence of bothersome lower urinary tract symptoms (LUTS) in men, which are predominantly attributable to benign prostate hyperplasia (BPH) and/or benign prostatic enlargement (BPE) causing proven or suspected bladder outflow obstruction (BOO), is increasing globally [1] resulting in a reduced quality of life and increased healthcare expenditures [1, 2]. In Scotland as elsewhere in the United Kingdom and globally, some men may be managed conservatively or medically using drugs in the primary care setting for suspected or proven BOO, whilst other men may have received investigation in a tertiary care setting, before being recommended to receive medication in primary care. In Scotland healthcare services treating men with prostate conditions face an increasing burden from combinations of an ageing population, increased prostate cancer investigation and incidence [3, 4], and increased awareness of male health issues. As a result of these combined factors, the impact of bothersome LUTS arising from BOO on service demand is largely hidden, and studies reporting their incidence and prevalence are predominantly cross-sectional in nature, with widely varying results [5].

Data regarding the prescription of drugs for the medical management of BOO as a cause for male bothersome LUTS has been used internationally in recent years to increase the understanding of patterns of prescribing within specific populations. This approach can be useful in order to identify potential demographic inequalities in patients access to this aspect of healthcare, and to understand the patient experience, predominantly using longitudinal datasets [6, 7, 8]. However, to date there is limited understanding of how the prescribing patterns for drugs used to medically treat BOO may differ both spatially and temporally. The increasing availability of high quality open access healthcare data in Scotland has created the

opportunity for a more refined and broader-based analysis of prescribing patterns for BOO. Moreover, Scotland's diverse geography provides an ideal landscape to understand how factors that may impact on prescribing patterns differ spatially in terms of geography, as well as longitudinally [9]. We describe a statistical framework that allows the study of variations in the patterns of drug prescribing in both space and time, while accounting for numerous relevant socioeconomic and health-related factors. We have used this approach in order to statistically analyse publicly available data regarding the prescription of the two main classes of medications used to treat bothersome LUTS secondary to BOO in Scotland. Using this approach we describe spatiotemporal trends that may help inform future urological practice for this common and ubiquitous condition.

Material and Methods

Data sources

Data was acquired and linked from numerous independent and publicly accessible sources. The dataset comprised information at the level of individual General Practices (GPs) and was been created from the following four sources:

1. NHS Scotland OpenData: drug prescriptions monthly data (https://www.opendata.nhs.scot/dataset/prescriptions-in-the-community)
2. Information Services Division Scotland (ISD): practice details, deprivation, rurality (https://www.isdscotland.org/Health-Topics/General-Practice/)
3. National Institute for Health and Care Excellence (NICE): daily dosages (https://www.nice.org.uk)
4. National Records of Scotland (NRS): postcodes, health boards (https://www.nrscotland.gov.uk/statistics-and-data/geography/our-products/scottish-postcode-directory/2018-2)

The keys used to link the sources were the unique GP code and date. The ISD and NRS portals provided information regarding both the medical practice (i.e. GP) and their patient population. Table 1 contains a list of the variables extracted from these sources. We used both deprivation and rurality to account for socio-demographic status. In particular, we used the 2016 Scottish Index of Multiple Deprivation (SIMD) [10] and a recoded version of the 2018 Scottish Government Urban Rural Classification [11]. Additionally, the ISD and NRS sources provided GP-level information regarding the size of the individual practice patient list, the gender and age distribution, and the location of the practice (based on postcode and name of relevant Health Board). All GP practices open for the whole study period (October

2015 to November 2019) were included in the dataset (903 of 944, 95.7%, practices in Scotland open as of 1st January 2019). The Scottish Open Data portal provided the prescribed amounts of the drugs of interest per month.

Table 1. Variables extracted from the four data sources and used as covariates in the statistical model.

Variable	Type	Short description
Drug group	Categorical	α-1 blocker or 5-α reductase inhibitor
GP patient list size	Numerical, time-varying	Number of registered patients per GP practice
GP practice run	Categorical, baseline	Is the practice run by GPs (contract type 17J and 17C), rather than by the NHS (contract type 2C)? Yes/No
Dispensing GP practice	Categorical, baseline	Does the GP practice have a license to dispense medicines? Yes/No
Males 45p	Numerical, time-varying	Proportion of patients that are males aged ≥45 years
Deprived 15	Numerical, time-varying	Proportion of patients under the 15th national percentile of deprivation (SIMD)
Remote	Categorical, time-varying	Modal rurality index among the patients (Scottish Government 8-fold Urban Rural Classification) recoded as remote (4, 5, 7, 8) or non-remote (1, 2, 3, 6). Yes/No
Postcode	Categorical, baseline	GP practice postcode as of 2019
Health board	Categorical, baseline	Name of Scottish Health Board where the GP practice is situated.

BOO medications analysed

We specifically focussed on the prescribing of α-1 blocking drugs and 5-α reductase inhibitors as these are the only specific medications used for BOO. α-1 blockers are the first-line and most commonly used drugs prescribed for LUTS secondary to BOO [1, 12], whilst 5-α reductase inhibitors are generally recommended where men are considered at high risk of BPH progression due to a significantly enlarged prostate, either as monotherapy or in combination with α-1 blockers [1, 12, 13]. The α-1 blockers alfuzosin and tamsulosin hydrochloride were included in the study, however doxazosin and terazosin were not included as the amounts of these drugs prescribed were negligible, whilst doxazosin may be prescribed for hypertension. The 5-α reductase inhibitors dutasteride and finasteride were both included in this study. When combined with the suggested daily dosages from the NICE website (see Table

2), a proxy for the number of daily doses was constructed by rounding to the nearest integer the following expression:

$$n_{dti} = \frac{\#\text{tablets of drug } d \text{ prescribed during month } t \text{ at practice } i}{\text{daily suggested dosage for drug } j} \#(1)$$

where *i*, *d*, and *t* represent the GP practice, drug, and month respectively. In our dataset, we have observations for $i = 1,\ldots,903$ GP practices over $t = 1,\ldots,50$ months; *d* indexes the drugs reported in Table 2. The number of daily doses for each of the drug groups was then constructed by summation of the respective drugs' monthly amounts of daily doses. We denote with n_{jti} the number of daily doses of drugs belonging to group $j \in \{\alpha 1 - \text{blocker}, 5 - \alpha \text{ reductase inhibitor}\}$, prescribed during month *t*, at each GP practice *i*.

Table 2. Suggested daily dosages of the study α-1 blockers and 5-α reductase inhibitors according to NICE guidelines.

Drug	Drug group	Suggested daily dosage (NICE)
Alfuzosin	α-1 blocker	2.5 mg 3 times a day
Tamsulosin cap/tab	α-1 blocker	10 mg once daily 400mcg once daily
Dutasteride	5-α reductase inhibitor	500mcg once daily
Finasteride	5-α reductase inhibitor	5mg once daily

We then used a Poisson model in order to describe the average number of daily doses of BOO medication prescribed each month, accounting for each of the covariates presented in Table 1, with additional spatial and temporal random effects. Possible interactions between individual GP prescribing pattern, or GP geographical location, with the prescribed drug type were also investigated.

Equation 1 describes the model's functional form, while Table 3 summarises our choices in terms of spatial and temporal structure. Further details of the statistical analysis are provided as supplementary material.

$$n_{jti} \sim \text{Poisson}(\lambda_{jti})$$

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ti}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males 45p}_{ti} + \beta_6 \text{deprived 15}_{ti} + \beta_7 \text{remote}_{ti} \quad \#(2)$$

where *j* (drug group), *t* (month), and *i* (each GP practice) are as described, and $\alpha_{[i]}$, $\alpha_{[ji]}$,$\alpha_{[tji]}$ denote the random effects, summarised in Table 3. A detailed discussion of the choice of the random components of the model is available in the technical supplement.

Table 3. Spatial and temporal random effects.

Parameter	Type	Short description
$\alpha_{[i]}$	Spatial	intrinsic Conditional Auto Regressive (iCAR)
$\alpha_{[ji]}$	Unstructured	Unstructured interaction between GP and drug type
$\alpha_{[tji]}$	Temporal	First-order Auto Regressive (AR1), grouped by health board and drug type

Computational analysis

All computational analyses were carried out in R 3.6.1 [14]. We estimated the model parameters within the Integrated Nested Laplace Approximation framework using the inla package [15].

Results:

We investigated the effects of each the available covariates (including GP patient list size; BOO drug group; whether the practice was GP run; whether the GP practice dispensed medication; proportion of males aged 45 years; higher proportion of socio-economic deprivation; and remote/rural location) on the study outcome. Table 4 summarises the output of the Poisson regression estimates of each of the associated parameters. In a further analysis, we interpreted each of these parameters in terms of relative differences from the model average (with the exception of GP practice list size).

Table 4. Summary of estimated posterior distributions for fixed effects. This summarises the model estimates of the fixed effect, and the uncertainty surrounding the estimates.

	Mean	SD	2.5%	50%	97.5%	Mode
α – Intercept	-1.570	0.040	-1.648	-1.570	-1.492	-1.570
β_1 – log(GP patient list size)	0.915	0.002	0.911	0.915	0.919	0.915
β_2 – Drug group (5-α reductase inhibitors)	-0.625	0.017	-0.658	-0.625	-0.591	-0.625
β_3 – GP run practices	0.238	0.033	0.174	0.238	0.302	0.238
β_4 – Dispensing GP practice	-0.086	0.026	-0.138	-0.086	-0.035	-0.086
β_5 – Males aged ≥45 years	4.816	0.032	4.754	4.816	4.879	4.816
β_6 – Socially deprived area	0.017	0.007	0.003	0.017	0.030	0.017
β_7 – Remote/rural GP practice	0.002	>0.001	0.002	0.002	0.003	0.002

The GP practice patient list size was observed to have an effect consistent with an estimated increase of slightly less than one daily dose per month per additional patient (point estimate 0.915). As expected, the prescribed doses of the $5-\alpha$ reductase inhibitor drug group were observed to be on average less than the

prescribed doses of the $\alpha - 1$ blocker drug group. The estimated relative difference was calculated to be on average 45-48% fewer $5 - \alpha$ reductase inhibitor drug prescriptions than $\alpha - 1$ blocker drug prescriptions per month (point estimate 46%).

We observed that the nature of how the GP practices are individually run are associated with BOO drug prescribing practice, with GP-run practices (rather than by direct NHS-run practices) having larger volumes of these prescriptions. The model results are consistent with a 19-35% (point estimate 27%) increased number of monthly prescriptions for GP-run practices compared with NHS-run practices, all else being equal. This is an interesting result, and to the best of our knowledge no rigorous research has been undertaken to investigate the role that how a GP practice is managed plays on the stability of GP provision of care and, in turn, on help seeking behaviours and clinical outcomes. Conversely, we observed that GP-dispensing practices are associated with 3-13% (point estimate 8%) lower volumes of BOO drug prescriptions, compared to GP practices without a pharmacy, keeping all other variables constant. Practices that dispense usually tend to do so because there is no local community pharmacy, and they need one to fit a need; one way of thinking about this is that having a dispensing licence may reflect an aspect of remoteness that is not captured by the rurality measure we employ. We found the proportion of males aged ≥45 years in the GP practice patient list to be positively associated with the volume of BOO prescriptions, with an estimated average increase of 4.9% monthly prescriptions per percentage point. In contrast, the levels of deprivation, and a remote/rural geographical location of each GP practice, were found to have a negligible association with prescribing practice.

Next, we investigated the statistical model's interpolations according to Health Board and drug group (α-1 blocking drugs and 5-α reductase inhibitors) (**Figure 1**). This

analysis highlighted a general increase in the volumes of prescriptions for these medications over the 4-year study period**.** Trends in prescribing were observed to be broadly similar across most Health Boards, with a less prominent increase in less populated areas, which may potentially be attributable to a more stable population structure over the 4-year period of observation, as well as unaccounted for differences in help seeking behaviours. Within most Health Boards the growth in prescriptions for each drug group were almost parallel during the four-year observation period, suggesting consistency in terms of increased BOO drug prescribing. Additional observations included a marked shift in volumes of α-1 blocking drug prescriptions in Lanarkshire between November 2016 and February 2017, however no further specific information regarding this phenomenon was available within the publicly available dataset. In the absence of a reasonable explanation for this singular observation in this one Health Board, this has been treated as an artefact due to a change in data-recording criteria.

Next, we investigated how the statistical model residuals may provide insight into how BOO drug prescribing behaviour differed across Scotland during the 4-year study period. **Figure 2** illustrates histograms of exponentiated residuals for each individual Health Board across Scotland, where a reference value of $1 = e^0$ represents a null residual (i.e. there is no deviation from the model's predicted average). Each residual is specific to one individual anonymous GP practice. On an exponential scale, a value of 1 indicates a prescribing behaviour in line with the average as described by the statistical model across Scotland during the study period. A value below 1 indicates prescribing volumes higher than expected based on the model, whilst a value larger than 1 indicates prescribing volumes lower than expected. Asymmetry around the reference value of 1, and/or multiple modes of

distribution, suggests a different behaviour of individual GP practices within a Health Board compared against the national average across Scotland.

Using this statistical approach, we generally observed consistency in the prescription of drugs for BOO across Health Boards in Scotland, with most distributions appearing to be approximately unimodal and symmetric around the null residual (i.e. the reference value of $1 = e^0$). However, some interesting patterns of prescribing can be observed, such as the reduced level of BOO drug prescribing in some individual Health Boards (most notably Borders, Forth Valley, Tayside, Orkney and Shetland) compared to the average prescribing rate across Scotland. The reasons for these differences in prescribing pattern in these individual Health Boards are unclear and require further investigation.

Next, we examined the BOO drug prescribing patterns of GP practices with the aim of assessing and visualising possible spatial patterns. Once again using the model residuals, it was possible to identify individual anonymous practices at the extremes of the BOO prescribing distribution, and show their Health Board location on a map. This approach can be useful in order to detect geographic clusters of similar prescribing patterns, while accounting for temporal trends and other potential confounding factors that are already included in the model. For example, the policymaker might be interested in identifying clusters of GP practices where the rates of prescribing are either very low or very high with respect to the national average. We present the results of such analysis in **Figure 3** where, to preserve anonymity of the individual practices, we have aggregated the information at the Health Board level. We denote those GP practices with a model residual below the 2.5% percentile of the overall distribution of residuals as “high-volumes prescribers”, and those above the 97.5% percentile as “low-volumes prescribers”. We stress that

high- and low- are with respect to the national average as described by the model. Moreover, the quantile thresholds are arbitrary and can be adjusted according to the analytical need.

We observed that Highland is the Health Board with the largest percentage (~9.5%) of GP practices that were identified as being in the upper tail of prescribing volumes (identified by model residuals <2.5% percentile), followed by Lothian (~5.3%), Dumfries and Galloway (~3.2%), Grampian (~2.9%), Forth Valley (~2%) and Greater Glasgow and Clyde (~1.7%). No over-prescribing GP practices were found within the remaining Health Boards. On the other hand, Tayside was identified as the Health Board with the largest percentage (~19%) of under-prescribers (identified by model residuals >97.5% percentile). Shetland (10%), Borders (~8.7%), Grampian (~5.7%), Highland (~1.1%), Lothian (~1%), and Greater Glasgow and Clyde (~0.9%) also contained GP practices that prescribed far below the national average. The remaining Health Boards did not contain any under-prescribing practices. The underlying reasons for these observations are currently unclear and require further investigation.

Discussion

This study has investigated patterns of medical prescribing for the two most common classes of drug (i.e. $\alpha - 1$ blockers and $5 - \alpha$ reductase inhibitors) used to treat BOO in Scotland over a recent 4-year period (October 2015 - November 2019) using publicly available data from individual GP practices across all Health Boards. Using this approach, we generated a study dataset by linking prescribing data to GP practice-specific information (such as their type of contract with NHS, and their licence to dispense) and summary characteristics of their patient populations (such as patient age, and GP practice-associated levels of deprivation and rurality). This has enabled us to develop an improved understanding of patterns of prescribing of these medications across Scotland, and identify where prescription volumes may vary, having accounted for these variables.

A trend of increased BOO drug prescribing practice was observed throughout the 4-year observation window consistent with an ageing Scottish population, and perhaps also due to an increased awareness of male health issues amongst both patients and general practice teams, and increased referral of men to secondary care due to a raised PSA, which may indicate BPH as well as possible prostate cancer [16, 17]. However, it would be interesting to understand more fully the reasons behind the observed increase in prescribing across all Scottish Health Boards and the role that increased awareness and help seeking behaviour may have. It may also be interesting to identify the relative contribution (or otherwise) made by increased referral to secondary care with suspected prostate cancer (as identified by a raised PSA), which might result in increased BOO/BPH prescribing as a secondary consequence of a raised PSA referral. A further possibility may be that an increased focus on cancer management, rather than BPH surgery, may lead to an increase in

medical drug use for BOO, rather than definitive intervention – this is speculative, but would be very interesting to investigate in future studies, particularly in order to investigate how this may vary geographically. Although it has been acknowledged that aspects regarding individual GP medical practices may potentially contribute to prostate health inequalities [18, 19], to our knowledge this is the first time that the particular characteristics of a GP practice (such as patient ages, GP-run practices, dispensing ability, deprivation levels, and rurality) have been identified as being potential factors influencing BOO drug prescribing patterns. It was interesting to observe that whether a practice was NHS or GP-run, and whether a dispensing pharmacy was present within the GP practice, was associated with higher and lower prescribing volumes respectively. While the individual characteristics of GP medical practices are known to differ by region [20], research accounting for these factors is relatively sparse; hence it is unclear why this difference exists.

This study has several limitations. Firstly, the available data only exists in the public domain at an aggregate (i.e. individual GP practice or patient list) level, and further information would be helpful in order to identify the reasons why prescribing practices vary at a more granular level (perhaps by associating the prescribing practice with the presence or absence of a GP with a particular interest in men's health issues, as an example). Secondly, the use of summary data regarding levels of socio-economic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome, with these factors likely to be important in terms of access to healthcare and prescribing. Similarly, not having information about specific GP practice catchment areas made it necessary to use an adjacency matrix based on postcodes, rather than actual distances, resulting in a sub-optimal method of accounting for underlying spatial

processes. Finally, it would be useful to analyse potential relationships between BOO drug prescribing patterns and longer-term outcomes from BOO in terms of clinical progression of this condition, such as need for future surgical intervention or treatment for BOO complications such as acute urinary retention. Such an analysis requires additional hospital data, which at present is unavailable and will require additional work in due course, which could be most insightful.

Nevertheless, despite these caveats and limitations, the analyses presented herein have identified interesting BOO medical prescribing trends across Scotland that require further investigation in future studies. For example, it would be very interesting to understand how the prescribing patterns relate to access to surgical intervention for BPH and BOO, and how they may relate to investigation for suspected prostate cancer based on PSA testing. It would also be interesting to understand the relative contribution of patient ageing to the rate of rise in BOO drugs prescription, and the degree to which other factors such as help seeking behaviour and clinician awareness might be contributing to this rate of rise in prescription volumes. These possibilities require further investigation.

In addition to identifying influences from spatial, temporal, and socioeconomic factors in regards to volumes of prescription of BOO medications, our analysis suggests that other sources of variability might account for inequalities in prescribing practice. In recent decades a considerable amount of research has been undertaken in order to better understand the so-called ‘Glasgow effect’ which describes health behaviours that transcend sociodemographic factors, and can best be described by a unique regional culture or a strong ‘social patterning’ [21, 22]. Although at this stage it is unclear what the remaining hidden determinants of the variations in BOO drug prescribing patterns may be, Scotland’s cultural diversity as described in the wider

literature may constitute a potential explanation, and it is unlikely that such effects are unique to Glasgow [9]. This warrants further investigation in future research.

It would be interesting for future research to investigate trends and potential inequalities regarding all prostate-related conditions (both benign and malignant) over space and time in other settings and geographical locations. In particular, it would be interesting to investigate whether the trends observed in Scotland may similarly exist in other regions of Great Britain and Ireland, and if so, are variations attributable to common factors such as remoteness/rurality and socioeconomic status. Further research to investigate medical practice phenomena as complex as prescribing patterns using publicly available data may identify key limitations in practice, and may inform data collection and data sharing in the future. In addition, the general nature of the statistical modelling framework we have proposed in this study may be extended to investigate other kinds of models, covariates, and medical conditions in a range of future studies.

Conclusions

The volume of prescriptions of drugs for LUTS secondary to BOO has steadily increased across Scotland during a recent 4-year observation period, which may, at least in part, be attributable to an ageing population and increased diagnosis. Prescription volume for these medications is associated with various characteristics of the GP practice (such as type of contract and presence of a licence to dispense). However, some inequalities in prescribing across Health Boards in Scotland remain unexplained after accounting for GP practice- and patient-specific characteristics such as socioeconomic deprivation and rurality, suggesting there may be other hitherto unknown determinants of BOO drug prescribing practice. Further research is warranted to understand these differences more fully.

Figure Legends

Figure 1:

Statistical model average number of daily doses of each BOO drug type prescribed per month, by individual Scottish Health Board and adjusted for GP practice patient roll size.

Figure 2:

Frequency histograms of the statistical model's exponentiated residuals for each Scottish Health Board. The vertical dashed line represents the null residual (value=1 on the exponentiated scale), and each small black square represents the average number of daily prescriptions of BOO drugs (combined $\alpha - 1$ blockers and $5 - \alpha$ reductase inhibitors) per month per individual anonymous GP practice within each Health Board. The boxplot below each histogram illustrates the same data distribution (the white point marks the median, the thick line represents the usual box, and the thin line represents the whiskers). Ideally the exponentiated residuals for each GP practice would lie around the null residual (i.e. value=1), however the heterogeneity in prescribing practice is illustrated by increased spread to the left and right of the null residual. A shift of GP practice distributions to the right of the null residual, as seen in Health Boards such as Borders, Fife, Orkney, Shetland and Tayside, illustrates less prescribing of these medications than would be expected.

Figure 3:

Maps of Scotland highlighting the Health Board locations of anonymous GP practices at the extremes of the distribution of BOO drug prescribing. The left panel shows the percentage of GP practices within each Health Board that have been identified (via model residuals) as being high in prescribing volumes with respect to

the national average (i.e. model residuals <2.5% percentile). Similarly, the right panel shows the percentage of GP practices low in prescribing volumes with respect to the national average (i.e. model residuals >97.5% percentile).

References

[1] European Association of Urology. EAU guidelines on non-neurogenic male LUTS. 2019.

[2] Patel ND, Parsons JK. Epidemiology and etiology of benign prostatic hyperplasia and bladder outlet obstruction. Indian J Urol 2014;30:170—6.

[3] Allemani C, Matsuda T, Di Carlo V et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): Analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018; 391:1023–75.

[4] NHS National Services Scotland. Cancer waiting times. NHS National Services Scotland. 2019.

[5] Lee SWH, Chan EMC, Lai YK. The global burden of lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a systematic review and meta-analysis. Sci Rep. 2017;7(1):7984. doi: 10.1038/s41598-017-06628-8.

[6] Bajic P, Montgomery J, Nelson M et al. (2020). 133 comparisons fo BPH medication prescribing among sexagenarians with Medicare an private insurance. J Sex Med. 2020; 17(1):37—38.

[7] Fu Y, Han S, Wang L, Geo W, Cao X, Wang J. Comparison of characteristics of benign prostatic hyperplasia (BPH) patients treated with finasteride and alpha blocker combination therapy verses alpha blocker monotherapy in China: An analysis of electronic medical record data. Adv. Ther. 2018; 35:1191—1198.

[8] Moon HW, Yang JH, Choi JB, Bae WJ. Prescription pattern of alpha-blockers for management of lower urinary tract symptoms/benign prostatic hyperplasia. Sci Rep. 2018; 8.

[9] Taulbut M, Walsh D, McCartney G et al. Spatial inequalities in life expectancy within post-industrial regions of Europe: A cross-sectional observational study. BMJ Open. 2014; 4.

[10] Scottish Government. Scottish Index Of Multiple Deprivation. [online] available at: http://www.gov.scot/Topics/Statistics/SIMD [accessed 9 Mar 2020].

[11] Scottish Government. Scottish Government Urban Rural Classification. [online] available at: https://www2.gov.scot/Topics/Statistics/About/Methodology/UrbanRuralClassification [accessed 9 Mar 2020]

[12] National Institute for Health and Care Excellence. LUTS in men. National Institute for Health and Care Excellence. 2019.

[13] McConnell JD, Roehrborn CG, Bautista OM et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. Clinical Trial N Engl J Med. 2003 Dec 8;349(25):2387-98. doi: 10.1056/NEJMoa030656.

[14] R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria 2019. URL https://www.R-project.org/.

[15] H. Rue, S. Martino, and N. Chopin. Approximate Bayesian inference for latent Gaussian models using integrated nested Laplace approximations (with discussion). Journal of the Royal Statistical Society, Series B. 2009; 71(2):319--392.

[16] National Records of Scotland. Mid-year population estimates Scotland, Mid-2018. 2019.

[17] European Association of Urology. EAU guidelines on prostate cancer. 2019.

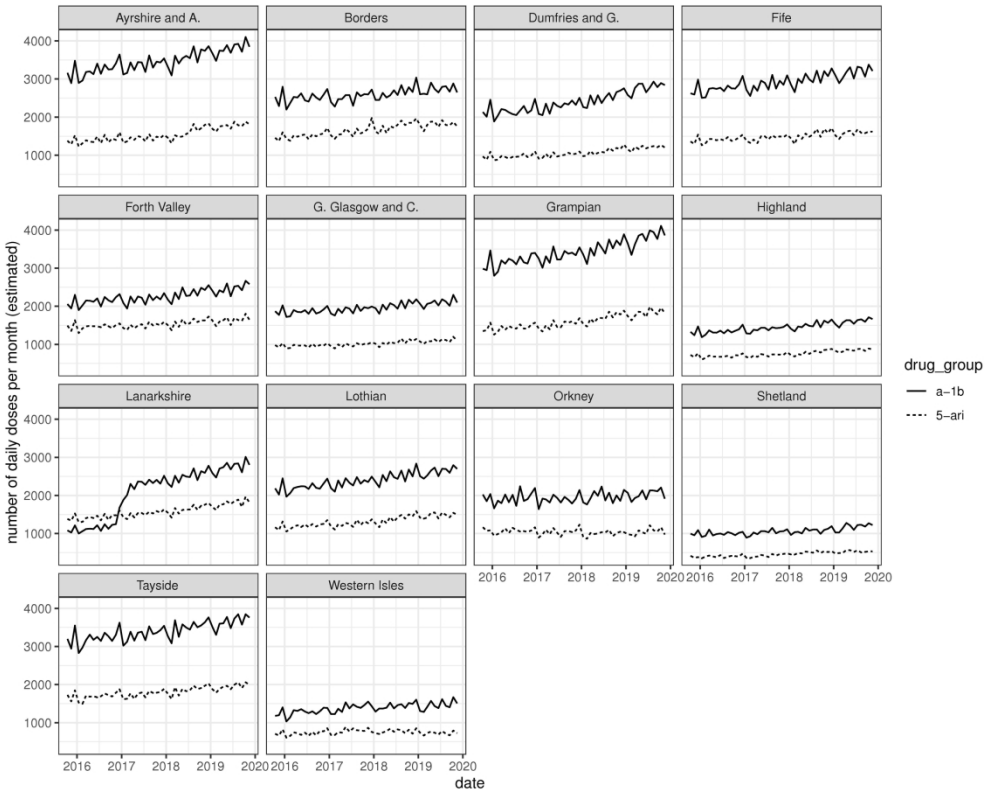
[18] Public Health England. Prostate cancer risk management programme: overview. 2016.

[19] Clements A, Bukach C, Rai T, Shine B, Austoker J, Watson E. What influences men's decision to have a prostate-specific antigen test? A qualitative study. Family Practice. 2007; 24.

[20] Burgess L. Primary Care in Scotland. The Scottish Parliament. 2018.

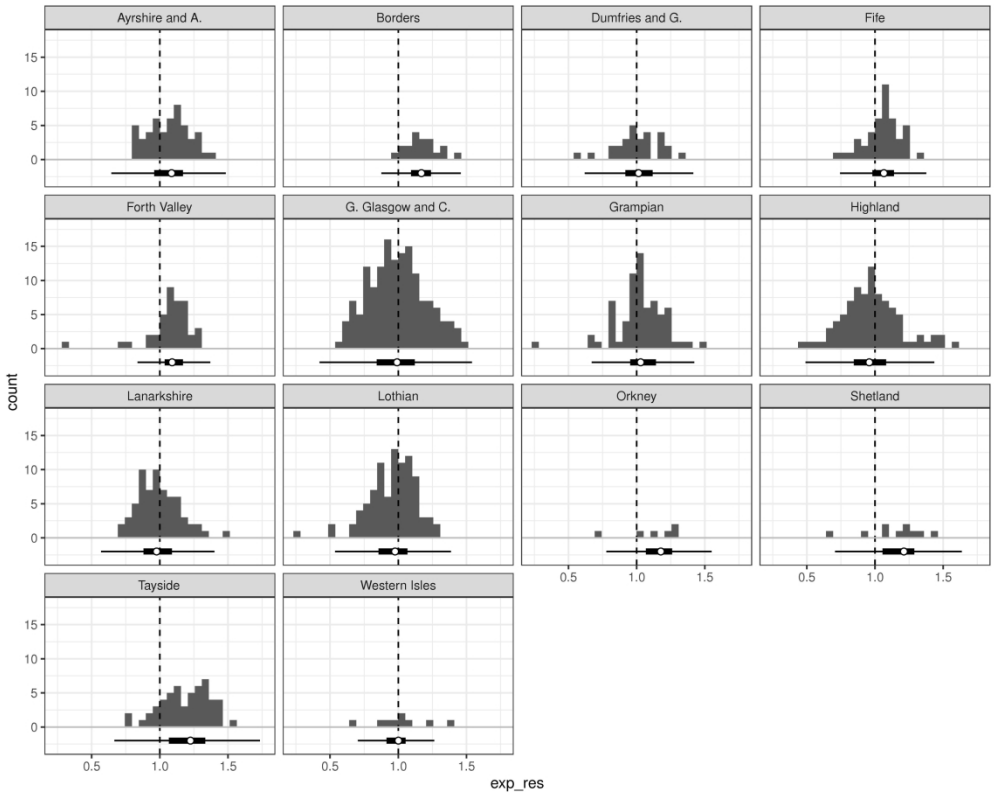
[21] Walsh D, McCartney G, Collins C, Taulbut M, Batty GD. History, politics and vulnerability: explaining excess mortality in Scotland and Glasgow. Public Health. 2017; 151:1—12.

[22] Cowley J, Kiely J, Collins D. Unravelling the Glasgow effect: The relationship between accumulative bio-psychosocial stress, stress reactivity and Scotland's health problems. Prev. Med. Rep. 2016; 4:370-375.



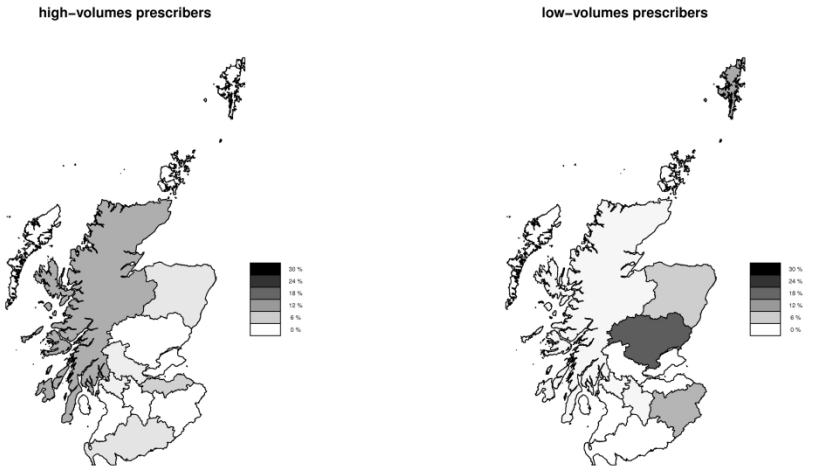
Statistical model average number of daily doses of each BOO drug type prescribed per month, by individual Scottish Health Board and adjusted for GP practice patient roll size.

254x203mm (300 x 300 DPI)



Frequency histograms of the statistical model's exponentiated residuals for each Scottish Health Board. The vertical dashed line represents the null residual (value=1 on the exponentiated scale), and each small black square represents the average number of daily prescriptions of BOO drugs (combined α-1 blockers and 5-α reductase inhibitors) per month per individual anonymous GP practice within each Health Board. The boxplot below each histogram illustrates the same data distribution (the white point marks the median, the thick line represents the usual box, and the thin line represents the whiskers). Ideally the exponentiated residuals for each GP practice would lie around the null residual (i.e. value=1), however the heterogeneity in prescribing practice is illustrated by increased spread to the left and right of the null residual. A shift of GP practice distributions to the right of the null residual, as seen in Health Boards such as Borders, Fife, Orkney, Shetland and Tayside, illustrates less prescribing of these medications than would be expected.

254x203mm (300 x 300 DPI)



Maps of Scotland highlighting the Health Board locations of anonymous GP practices at the extremes of the distribution of BOO drug prescribing. The left panel shows the percentage of GP practices within each Health Board that have been identified (via model residuals) as being high in prescribing volumes with respect to the national average (i.e. model residuals <2.5% percentile). Similarly, the right panel shows the percentage of GP practices low in prescribing volumes with respect to the national average (i.e. model residuals >97.5% percentile).

355x203mm (300 x 300 DPI)

Technical supplement for the paper "Prescribing patterns for medical treatment of suspected prostatic obstruction: A spatiotemporal statistical analysis of Scottish open access data"

Authors: Federico Andreis, Richard Bryant, Emanuele Giorgi, Andrea Williamson, Ashleigh Ward

We employ a Bayesian hierarchical Poisson model that estimates spatial and temporal structured patterns. The outcome of interest is the number of daily doses prescribed in a month at a general practice in Scotland, between October 2015 and November 2019. Let n_{jti} denote the number of prescriptions of drugs belonging to group $j \in \{\alpha - 1\text{b}, 5 - \alpha\text{ri}\}$, for practice $i = 1,...,903$, in month $t = 1,...,50$.

Conditionally on a set of random effects $\alpha_{[i]}$, $\alpha_{[ji]}$ and $\alpha_{[t]}$, let n_{jti} follow a Poisson distribution with parameter λ_{jti}, modelled with an additive linear predictor on a natural logarithm scale:

$$n_{jti} \sim \text{Poisson}(\lambda_{jti})$$

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ti}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males 45p}_{ti} + \beta_6 \text{deprived 15}_{ti} + \beta_7 \text{remote}_{ti}$$

The random effects, as described in Table 3 in the paper, relate to:

- A structured component accounting for spatial correlation ($\alpha_{[i]}$)
- An unstructured component accounting for potential interactions between individual practice and type of drug ($\alpha_{[ji]}$)
- A component accounting for temporal correlation, grouped by health board and type of drug ($\alpha_{[t]}$).

To model the spatial component $\alpha_{[i]}$, we employ an intrinsic Conditional Auto Regressive (iCAR [1,2,3]) structure that exploits an adjacency matrix based on location of the practices. The postcodes are linked to Easting/Northing coordinates and Voronoi tessellation is used to find nearest neighbours and their distances (this was done using the caramellar package, available from github via devtools::install_github("barryrowlingson/caramellar")). In this way, the model allows the borrowing of strength of information across neighbouring regions.

The component accounting for potential interactions between the individual medical practice and the type of drug prescribed $\alpha_{[ji]}$ is modelled in an unstructured way, using *iid* gaussian terms with common precision parameter [3].

The temporal component $\alpha_{[t]}$ is modelled using a first-order autoregressive process [1], allowing grouping by health board and drug type. This approach allows the estimation of a common temporal autocorrelation structure for practices in the same health board and with respect to the same drug group type.

An Integrated Nested Laplace Approximation [4] approach is used to approximate the posterior distribution and obtain the estimates, using the inla package in R; default prior distributions are used for all parameters. To make estimation computationally easier, a cheap Gaussian approximation is first used and the resulting estimates employed as reasonable starting values for the actual model fitting procedure (details in the R code in Supplement 2). Kullback-Leibler divergence statistics [3] indicate a satisfactory approximation to all marginal posterior densities.

Figure 1 contains the summary of the model fit, while Table 1 contains a summary of estimated posterior distributions for the random effects in terms of standard deviations, rather than precision parameters (as in Figure 1). Estimation took

approximately 7 hours on an AMD Ryzen 7 2700x processor with 32GB DDR4 RAM, under Windows 10.

Figure 1. Summary of model fit

```
Call:
   c("inla(formula = formula_mod_IV, family = \"poisson\", data = df_joint, ", " verbose = TRUE,
   control.compute = control$compute, control.predictor = control$predictor, ", " control.inla =
   list(diagonal = 10), control.results = control$results, ", " control.fixed = list(prec.intercept =
   0.1), control.mode = list(result = mod_inla_approx_IV, ", " restart = TRUE))")
Time used:
    Pre = 0.612, Running = 24085, Post = 4.97, Total = 24091
Fixed effects:
                  mean    sd 0.025quant 0.5quant 0.975quant   mode kld
(Intercept)     -1.570 0.040     -1.648   -1.570     -1.492 -1.570   0
drug_group5-ari -0.625 0.017     -0.658   -0.625     -0.591 -0.625   0
gp_runY          0.238 0.033      0.174    0.238      0.302  0.238   0
dispensingY     -0.086 0.026     -0.138   -0.086     -0.035 -0.086   0
log(list_size)   0.915 0.002      0.911    0.915      0.919  0.915   0
prop_m_45p       4.816 0.032      4.754    4.816      4.879  4.816   0
p_15             0.017 0.007      0.003    0.017      0.030  0.017   0
ur_codeRemote    0.002 0.000      0.002    0.002      0.003  0.002   0

Random effects:
  Name    Model
    postcode_n Besags ICAR model
   time_n AR1 model
   gp_drug IID model

Model hyperparameters:
                           mean    sd 0.025quant 0.5quant 0.975quant   mode
Precision for postcode_n  4.353 0.328      3.753    4.337      5.039  4.302
Precision for time_n     29.235 5.693     18.647   29.144     40.766 29.217
Rho for time_n            0.899 0.013      0.871    0.900      0.923  0.901
GroupRho for time_n       0.685 0.043      0.604    0.683      0.771  0.676
Precision for gp_drug    20.286 0.802     18.736   20.277     21.895 20.269

Expected number of effective parameters(stdev): 4095.95(1.50)
Number of equivalent replicates : 22.01

Deviance Information Criterion (DIC) ...............: 4371157.00
Deviance Information Criterion (DIC, saturated) ....: 3605454.27
Effective number of parameters .....................: 4097.92

Watanabe-Akaike information criterion (WAIC) ...: 4488316.21
Effective number of parameters .................: 159926.14

Marginal log-Likelihood:  -2217597.61
CPO and PIT are computed

Posterior marginals for the linear predictor and
 the fitted values are computed
```

Table 1. Summary of estimated posterior distributions for random effects. SD denotes the standard deviation.

	mean	Sd	2.5%	50%	97.5%	mode
SD of $\alpha_{[i]}$ (spatial)	0.480	0.018	0.446	0.480	0.516	0.480
SD of $\alpha_{[ji]}$ (unstructured)	0.222	0.004	0.214	0.222	0.231	0.222
SD of $\alpha_{[tji]}$ (temporal)	0.188	0.019	0.157	0.185	0.231	0.178
ρ_1 of $\alpha_{[tji]}$ (autocorrelation)	0.899	0.013	0.871	0.900	0.923	0.901
ρ_2 of $\alpha_{[tji]}$ (group correlation)	0.685	0.043	0.604	0.683	0.771	0.676

References

[1] Banerjee S, Carlin BP, Gelfand AE. Hierarchical Modeling and Analysis for Spatial Data. 2nd ed. Boca Raton: Chapman & Hall. 2015.

[2] Paciorek CJ. Understanding Intrinsic Gaussian Markov Random Field Spatial Models, Including Intrinsic Conditional Autoregressive Models. University of California, Berkeley. 2009. http://www.stat.berkeley.edu/~paciorek/research/techVignettes/techVignette5.pdf.

[3] Rue H, Held L. Gaussian Markov Random Fields: Theory and Applications. Boca Raton: Chapman & Hall. 2005.

[4] H. Rue, S. Martino, and N. Chopin. Approximate Bayesian inference for latent Gaussian models using integrated nested Laplace approximations (with discussion). Journal of the Royal Statistical Society, Series B. 2009; 71(2):319--392.

BMJ Open

Prescribing patterns for medical treatment of suspected prostatic obstruction: a longitudinal register-based study the Scottish Health and Social Care Open Data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042606.R1
Article Type:	Original research
Date Submitted by the Author:	26-Dec-2020
Complete List of Authors:	Andreis, Federico; University of Stirling, Health Sciences Bryant, Richard; University of Oxford Nuffield Department of Surgical Sciences; Churchill Hospital, Urology Giorgi, Emanuele; Lancaster University Lancaster Medical School, Williamson, Andrea; University of Glasgow, GPPC, School of Medicine, Dentistry and Nursing, MVLS Ward, Ashleigh; Dundee City Council, School of Health Sciences
Primary Subject Heading:	Urology
Secondary Subject Heading:	Public health
Keywords:	STATISTICS & RESEARCH METHODS, Prostate disease < UROLOGY, Bladder disorders < UROLOGY, PUBLIC HEALTH
Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
bmjopen_supplement_2.R	

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Prescribing patterns for medical treatment of suspected prostatic obstruction: a longitudinal register-based study the Scottish Health and Social Care Open Data

Authors

Federico Andreis, PhD [Faculty of Health Sciences and Sport, University of Stirling]

Richard J Bryant, BMedSci MBChB FRCSEd(Urol) PhD [Nuffield Department of Surgical Sciences, University of Oxford, Oxford Cancer Research Centre, Oxford] & [Department of Urology, Churchill Hospital , Oxford University Hospitals NHS Foundation Trust]

Emanuele Giorgi, PhD [Lancaster Medical School, University of Lancaster]

Andrea Williamson, MBChB MPH PhD FRCGP FHEA DTM&H [General Practice and Primary Care, School of Medicine, Dentistry and Nursing, MVLS, University of Glasgow] & [General Practitioner Homelessness Health, Medical Officer Addictions, NHS Glasgow and Clyde, Homeless Health and Resource Services]

Ashleigh Ward, PhD RN FHEA MRSB [School of Health Sciences, University of Dundee]

Corresponding author

Federico Andreis, PhD

Faculty of Health Sciences and Sport, Pathfoot Building, University of Stirling, FK9 4LA, Stirling

email: federico.andreis@stir.ac.uk

tel: +44(0)1786466252

Word count 3659 (abstract: 247 / text: 3412, excl. figures, tables, equations and captions)

Abstract

Background The diagnosis of lower urinary tract symptoms related to suspected bladder outflow obstruction from benign prostate hyperplasia/enlargement in men is increasing. This is leading to high demand on healthcare services. However, there is limited knowledge of differences in pharmacotherapy prescribing for this condition based on geography.

Objective To investigate potential variation in drug prescribing for suspected bladder outflow obstruction in Scotland, based on analysis of publicly available data, to identify trends and inform future prescribing.

Study design A longitudinal register-based data study of prescribing and patient data publicly available from Scottish registries. All information is available as monthly aggregates at the level of single general practices.

Setting and participants 903 (97%) general practices in Scotland, over a 50-month period (October 2015 to November 2019).

Outcome measurements and statistical analysis We analysed numbers of daily doses of drugs for suspected bladder outflow obstruction prescribed per month using a Bayesian Poisson regression analysis, incorporating random effects to account for spatial and temporal elements.

Results: Prescriptions for suspected bladder outflow obstruction medications increased during the observation period (overall average rate of change 1.24 ± 0.28, ranging from 0.893 in Orkney to 1.95 in Lanarkshire). Whilst some determinants of

health inequality regarding prescribing practices across health boards are consistent with those known from the literature, other inequalities remain unexplained after accounting for practice- and patient-specific characteristics such as deprivation and rurality.

Conclusions Variations in spatiotemporal prescribing for suspected bladder outflow obstruction medications exist in Scotland, some of which remain unexplained.

Keywords

Suspected bladder outflow obstruction, benign prostate hyperplasia, benign prostate enlargement, lower urinary tract symptoms, drug prescription, open access data, spatiotemporal modelling, medical practice

Summary section

Strengths and limitations of this study

- This is the first study to investigate spatial and temporal variations in drug-prescribing patterns for bladder outflow obstruction using geostatistical models
- As such, this data provides a new perspective to inform clinical practice
- The statistical framework described in this paper is very general, and can be readily extended to other settings and conditions
- Data on drug-prescribing in Scotland only exists in the public domain at an aggregate (i.e. individual GP practice or patient list) level, which limits the granularity of the analysis
- The use of summary data regarding levels of socio-economic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome. These factors are likely to be important in terms of access to healthcare and prescribing.

Contributors

FA and AW2 initiated the study. FA and EG developed the statistical model. FA had full access to all the data in the study, carried out the statistical analysis and took responsibility its accuracy and for the integrity of the data. FA drafted the manuscript, and all authors (FA, RB, EG, AW1, AW2) contributed to the critical revision for important intellectual content, and to the interpretation of the data analysis results. RB and AW1 provided advice on clinical aspects of the results.

Non-author contributors: the authors would like to acknowledge support and encouragement received by Prof Alan McNeill (NHS Scotland) and Prostate Scotland at the initial conception of this project.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared. None of the contributing authors have any conflict of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

Patient and public involvement

No patients or public was involved for this study.

Patient consent for publication

Not required.

Ethics approval

Not required. This study is an analysis of publicly available electronic health records.

Data availability statement

A technical supplement, the statistical code (in R), and the final processed dataset used for the study available from medRxiv: https://www.medrxiv.org/content/10.1101/2020.06.19.20135459v1. The original, unprocessed data is publicly available online from the sources indicated in the manuscript in the Material and Methods section.

Licence statement

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in BMJ Open and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Introduction

The incidence of bothersome lower urinary tract symptoms (LUTS) in men, which are predominantly attributable to benign prostate hyperplasia (BPH) and/or benign prostatic enlargement (BPE) causing proven or suspected bladder outflow obstruction (BOO), is increasing globally [1]. This results in a reduced quality of life and increased healthcare expenditure [1, 2]. In Scotland, men with suspected or proven BOO are generally managed in primary care with medication prescribed by general practitioners (GPs) and/or specialist practitioners, with such medication either prescribed by GPs alone, or as part of shared care with specialists such as urologists [1]. In Scotland healthcare services treating men with prostate conditions face increased demand resulting from an ageing population, increased prostate cancer (PCa) investigation [3, 4], and increased awareness of men's health issues. As a result of these combined factors, the increasing burden of bothersome LUTS arising from BOO is likely to impact upon drug prescription patterns. Studies reporting the incidence and prevalence of LUTS in men are predominantly cross-sectional in nature, with widely varying results [5].

Scotland's diverse geography provides an ideal landscape to understand how factors that may impact upon prescribing patterns may differ spatially in terms of geography, and longitudinally [6]. Prescribing trends in Scotland vary geographically by urban/rural and sociodemographic classifications [6], and by unique regional cultures or as a result of strong 'social patterning', one example being the so-called 'Glasgow effect' [7, 8]. Furthermore, it has been acknowledged that aspects regarding individual GP medical practices may contribute to prostate health inequalities across the UK [9, 10].

Data regarding the prescription of drugs for the medical management of BOO as a cause for male bothersome LUTS has been used internationally in recent years to increase the understanding of patterns of prescribing within specific populations. This approach can be useful to identify potential demographic inequalities in patient access to healthcare for this condition, and to understand the patient experience, predominantly using longitudinal datasets [11, 12, 13]. However, to date there is limited knowledge of how the prescribing patterns for drugs used to treat BOO may differ both spatially and temporally. The increasing availability of high quality open access healthcare data in Scotland has created the opportunity for a more refined and broader-based analysis of prescribing patterns for BOO.

We investigated the possibility that differences may exist in Scotland in the prescribing patterns of the two main classes of medications used to treat bothersome LUTS secondary to BOO. We performed an analysis of publicly available data in order to identify possible variations in prescribing trends that may help inform future prescribing practice.

Material and Methods

Data sources

Data was acquired and linked from numerous independent and publicly accessible sources. The dataset comprised information at the level of individual General Practices (GPs) and was been created from the following four sources:

1. NHS Scotland OpenData: drug prescriptions monthly data (https://www.opendata.nhs.scot/dataset/prescriptions-in-the-community)
2. Information Services Division Scotland (ISD): practice details, deprivation, rurality (https://www.isdscotland.org/Health-Topics/General-Practice/)
3. National Institute for Health and Care Excellence (NICE): daily dosages (https://www.nice.org.uk)
4. National Records of Scotland (NRS): postcodes, health boards (https://www.nrscotland.gov.uk/statistics-and-data/geography/our-products/scottish-postcode-directory/2018-2)

The keys used to link the sources were the unique GP code and date. The ISD and NRS portals provided information regarding both the medical practice (i.e. GP) and their patient population. Table 1 contains a list of the variables extracted from these sources. We used both deprivation and rurality to account for socio-demographic status. In particular, we used the 2016 Scottish Index of Multiple Deprivation (SIMD) [14] and a recoded version of the 2018 Scottish Government Urban Rural Classification [15]. Additionally, the ISD and NRS sources provided GP-level information regarding the size of the individual practice patient list, the gender and age distribution, and the location of the practice (based on postcode and name of relevant Health Board). All GP practices open for the whole study period (October

2015 to November 2019) were included in the dataset (903 of 944, 95.7%, practices in Scotland open as of 1st January 2019). The Scottish Open Data portal provided the prescribed amounts of the drugs of interest per month.

Table 1. Variables extracted from the four data sources and used as covariates in the statistical model.

Variable	Type	Short description
Drug group	Categorical	α-1 blocker or 5-α reductase inhibitor
GP patient list size	Numerical, time-varying	Number of registered patients per GP practice
GP practice run	Categorical, baseline	Is the practice run by GPs (contract type 17J and 17C), rather than by the NHS (contract type 2C)? Yes/No
Dispensing GP practice	Categorical, baseline	Does the GP practice have a license to dispense medicines? Yes/No
Males 45p	Numerical, time-varying	Proportion of patients that are males aged ≥45 years
Deprived 15	Numerical, time-varying	Proportion of patients under the 15th national percentile of deprivation (SIMD)
Remote	Categorical, time-varying	Modal rurality index among the patients (Scottish Government 8-fold Urban Rural Classification) recoded as remote (4, 5, 7, 8) or non-remote (1, 2, 3, 6). Yes/No
Postcode	Categorical, baseline	GP practice postcode as of 2019
Health board	Categorical, baseline	Name of Scottish Health Board where the GP practice is situated.

BOO medications analysed

We specifically focussed on the prescribing of α-1 blocking drugs and 5-α reductase inhibitors as these are the only specific medications used for BOO. α-1 blockers are the first-line and most commonly used drugs prescribed for LUTS secondary to BOO [1, 16], whilst 5-α reductase inhibitors are generally recommended where men are considered at high risk of BPH progression due to a significantly enlarged prostate, either as monotherapy or in combination with α-1 blockers [1, 16, 17]. The α-1 blockers alfuzosin and tamsulosin hydrochloride were included in the study, however doxazosin and terazosin were not included as the amounts of these drugs prescribed were negligible, whilst doxazosin may be prescribed for hypertension. The 5-α reductase inhibitors dutasteride and finasteride were both included in this study. When combined with the suggested daily dosages from the NICE website (see Table

2), a proxy for the number of daily doses was constructed by rounding to the nearest integer the following expression:

$$n_{dti} = \frac{\#\text{tablets of drug } d \text{ prescribed during month } t \text{ at practice } i}{\text{daily suggested dosage for drug } j} \#(1)$$

where *i*, *d*, and *t* represent the GP practice, drug, and month respectively. In our dataset, we have observations for $i = 1,\ldots,903$ GP practices over $t = 1,\ldots,50$ months; *d* indexes the drugs reported in Table 2. The number of daily doses for each of the drug groups was then constructed by summation of the respective drugs' monthly amounts of daily doses. We denote with n_{jti} the number of daily doses of drugs belonging to group $j \in \{\alpha 1 - \text{blocker}, 5 - \alpha \text{ reductase inhibitor}\}$, prescribed during month *t*, at each GP practice *i*.

Table 2. Suggested daily dosages of the study α-1 blockers and 5-α reductase inhibitors according to NICE guidelines.

Drug	Drug group	Suggested daily dosage (NICE)
Alfuzosin	α-1 blocker	2.5 mg 3 times a day
Tamsulosin cap/tab	α-1 blocker	10 mg once daily
Dutasteride	5-α reductase inhibitor	400mcg once daily
Finasteride	5-α reductase inhibitor	500mcg once daily 5mg once daily

We then used a Poisson model in order to describe the average number of daily doses of BOO medication prescribed each month, accounting for each of the covariates presented in Table 1, with additional spatial and temporal random effects. Possible interactions between individual GP prescribing pattern, or GP geographical location, with the prescribed drug type were also investigated.

Equation 1 describes the model's functional form, while Table 3 summarises our choices in terms of spatial and temporal structure. Further details of the statistical analysis are provided as supplementary material.

$$n_{jti} \sim \text{Poisson}(\lambda_{jti})$$

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ti}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males 45p}_{ti} + \beta_6 \text{deprived 15}_{ti} + \beta_7 \text{remote}_{ti} \#(2)$$

where *j* (drug group), *t* (month), and *i* (each GP practice) are as described, and $\alpha_{[i]}$, $\alpha_{[ji]}$,$\alpha_{[tji]}$ denote the random effects, summarised in Table 3. A detailed discussion of the choice of the random components of the model is available in Supplementary file 1.

Table 3. Spatial and temporal random effects.

Parameter	Type	Short description
$\alpha_{[i]}$	Spatial	intrinsic Conditional Auto Regressive (iCAR)
$\alpha_{[ji]}$	Unstructured	Unstructured interaction between GP and drug type
$\alpha_{[tji]}$	Temporal	First-order Auto Regressive (AR1), grouped by health board and drug type

Computational analysis

All computational analyses were carried out in R 3.6.1 [18]. We estimated the model parameters within the Integrated Nested Laplace Approximation framework using the inla package [19]. The code is available as supplementary file 2, while data and shapefiles from an external repository [20].

Results

We investigated the effects of each the available covariates (including GP patient list size; BOO drug group; whether the practice was GP run; whether the GP practice dispensed medication; proportion of males aged 45 years; higher proportion of socio-economic deprivation; and remote/rural location) on the study outcome. Table 4 contains summary statistics on the sample.

Table 4. Summary statistics of the sample, stratified by health board. Number of practices, median and (interquartile range) for continuous variable, proportions for categorical variables. Counts are rounded to the nearest integer, proportions to the second decimal place.

Health Board	Number of practices	Daily doses prescribed/month		Patients list size	Run by GP	Dispensing practices	Males 45+	Highly deprived	Remote practices
		α-1b	5-αri						
Ayrshire and Arran	53	3091 (2563)	1320 (1192)	6625 (4831)	1.00	0.06	0.25 (0.03)	0.20 (0.24)	0.18
Borders	23	2054 (1838)	1374 (983)	4862 (3343)	1.00	0.17	0.26 (0.01)	0.00 (0.09)	0.13
Dumfries and G.	31	2231 (1449)	966 (782)	3976 (3492)	1.00	0.39	0.27 (0.04)	0.00 (0.08)	0.20
Fife	53	2699 (1805)	1372 (820)	6367 (4313)	0.96	0.02	0.23 (0.03)	0.13 (0.23)	0.04
Forth Valley	51	2144 (1767)	1515 (1260)	5844 (4606)	0.94	0.02	0.23 (0.02)	0.06 (0.16)	0.13
G. Glasgow and Clyde	230	1658 (1692)	826 (924)	4863 (3620)	1.00	0.01	0.21 (0.04)	0.33 (0.43)	0.04
Grampian	70	3204 (2595)	1462 (1228)	7980 (4875)	0.94	0.17	0.24 (0.04)	0.00 (0.02)	0.28
Highland	95	1002 (1486)	504 (810)	2358 (4467)	0.85	0.39	0.27 (0.05)	0.00 (0.05)	0.56
Lanarkshire	97	1665 (2161)	1428 (1406)	6048 (4570)	0.99	0.02	0.22 (0.02)	0.23 (0.22)	0.10
Lothian	112	2205 (1700)	1176 (1008)	7814 (4229)	0.95	0.00	0.21 (0.04)	0.02 (0.12)	0.03
Orkney	6	1675 (1217)	1008 (929)	2908 (2379)	0.83	0.33	0.28 (0.03)	0.00 (-)	0.70

Shetland	10	690 (1107)	253 (560)	1143 (1913)	0.20	0.70	0.24 (0.04)	0.00 (-)	0.92
Tayside	63	3103 (2140)	1645 (1166)	6685 (4676)	0.94	0.02	0.23 (0.05)	0.05 (0.24)	0.12
Western I.	9	892 (1891)	588 (665)	1389 (4046)	1.00	0.89	0.30 (0.06)	0.00 (-)	0.76

Table 5 summarises the output of the Poisson regression estimates of each of the associated parameters. In a further analysis, we interpreted each of these parameters in terms of relative differences from the model average (with the exception of GP practice list size).

Table 5. Summary of estimated posterior distributions for the fixed effects, containing the model estimates with associated uncertainty, on the rate ratio scale. The posterior distribution associated to the patient list size effect estimate β_1 was not transformed and should be read on the outcome scale, as explained in-text.

	Mean	SD	2.5%	50%	97.5%	Mode
α – Intercept	0.208	0.008	0.192	0.208	0.225	0.208
β_1 – log(GP patient list size)	0.915	0.002	0.911	0.915	0.919	0.915
β_2 – Drug group (5-α reductase inhibitors)	0.536	0.009	0.518	0.535	0.554	0.536
β_3 – GP run practices	1.269	0.042	1.190	1.268	1.352	1.269
β_4 – Dispensing GP practice	0.918	0.024	0.871	0.917	0.966	0.918
β_5 – Males aged ≥45 years	1.049	<0.001	1.049	1.049	1.050	1.049
β_6 – Socially deprived area	1.017	0.007	1.003	1.017	1.031	1.017
β_7 – Remote/rural GP practice	1.002	<0.001	1.002	1.002	1.003	1.002

The GP practice patient list size was observed to have an effect consistent with an estimated increase of slightly less than one daily dose per month per additional patient (point estimate 0.915). As expected, the prescribed doses of the $5-$

α reductase inhibitor drug group were observed to be on average less than the prescribed doses of the $\alpha - 1$ blocker drug group. The estimated relative difference was calculated to be on average 45-48% fewer $5 - \alpha$ reductase inhibitor drug prescriptions than $\alpha - 1$ blocker drug prescriptions per month (point estimate 46%).

We observed that the nature of how the GP practices are individually run are associated with BOO drug prescribing practice, with GP-run practices (rather than by direct NHS-run practices) having larger volumes of these prescriptions. The model results are consistent with a 19-35% (point estimate 27%) increased number of monthly prescriptions for GP-run practices compared with NHS-run practices, all else being equal. This is an interesting result, and to the best of our knowledge no rigorous research has been undertaken to investigate the role that how a GP practice is managed plays on the stability of GP provision of care and, in turn, on help seeking behaviours and clinical outcomes. Conversely, we observed that GP-dispensing practices are associated with 3-13% (point estimate 8%) lower volumes of BOO drug prescriptions, compared to GP practices without a pharmacy, keeping all other variables constant. Practices that dispense usually tend to do so because there is no local community pharmacy, and they need one to fit a need; one way of thinking about this is that having a dispensing licence may reflect an aspect of remoteness that is not captured by the rurality measure we employ. We found the proportion of males aged ≥45 years in the GP practice patient list to be positively associated with the volume of BOO prescriptions, with an estimated average increase in the monthly rate of prescription of 4.9% per percentage point. In contrast, the levels of deprivation, and a remote/rural geographical location of each GP practice, were found to have a negligible association with prescribing practice.

Next, we investigated the statistical model's interpolations according to Health Board and drug group (α-1 blocking drugs and 5-α reductase inhibitors) (**Figure 1**). This analysis highlighted a general increase in the volumes of prescriptions for these medications over the 4-year study period**.** Trends in prescribing were observed to be broadly similar across most Health Boards, with a less prominent increase in less populated areas, which may potentially be attributable to a more stable population structure over the 4-year period of observation, as well as unaccounted for differences in help seeking behaviours. Within most Health Boards the growth in prescriptions for each drug group were almost parallel during the four-year observation period, suggesting consistency in terms of increased BOO drug prescribing. Additional observations included a marked shift in volumes of α-1 blocking drug prescriptions in Lanarkshire between November 2016 and February 2017, however no further specific information regarding this phenomenon was available within the publicly available dataset. In the absence of a reasonable explanation for this singular observation in this one Health Board, this has been treated as an artefact due to a change in data-recording criteria.

Next, we investigated how the statistical model residuals may provide insight into how BOO drug prescribing behaviour differed across Scotland during the 4-year study period. **Figure 2** illustrates histograms of exponentiated residuals for each individual Health Board across Scotland, where a reference value of $1 = e^0$ represents a null residual (i.e. there is no deviation from the model's predicted average). Each residual is specific to one individual anonymous GP practice. On an exponential scale, a value of 1 indicates a prescribing behaviour in line with the average as described by the statistical model across Scotland during the study period. A value below 1 indicates prescribing volumes higher than expected based

on the model, whilst a value larger than 1 indicates prescribing volumes lower than expected. Asymmetry around the reference value of 1, and/or multiple modes of distribution, suggests a different behaviour of individual GP practices within a Health Board compared against the national average across Scotland.

Using this statistical approach, we generally observed consistency in the prescription of drugs for BOO across Health Boards in Scotland, with most distributions appearing to be approximately unimodal and symmetric around the null residual (i.e. the reference value of $1 = e^0$). However, some interesting patterns of prescribing can be observed, such as the reduced level of BOO drug prescribing in some individual Health Boards (most notably Borders, Forth Valley, Tayside, Orkney and Shetland) compared to the average prescribing rate across Scotland. The reasons for these differences in prescribing pattern in these individual Health Boards are unclear and require further investigation.

Next, we examined the BOO drug prescribing patterns of GP practices with the aim of assessing and visualising possible spatial patterns. Once again using the model residuals, it was possible to identify individual anonymous practices at the extremes of the BOO prescribing distribution, and show their Health Board location on a map. This approach can be useful in order to detect geographic clusters of similar prescribing patterns, while accounting for temporal trends and other potential confounding factors that are already included in the model. For example, the policymaker might be interested in identifying clusters of GP practices where the rates of prescribing are either very low or very high with respect to the national average. We present the results of such analysis in **Figure 3** where, to preserve anonymity of the individual practices, we have aggregated the information at the Health Board level. We denote those GP practices with a model residual below the

2.5% percentile of the overall distribution of residuals as 'high-volumes prescribers', and those above the 97.5% percentile as 'low-volumes prescribers'. We stress that high- and low- are with respect to the national average as described by the model. Moreover, the quantile thresholds are arbitrary and can be adjusted according to the analytical need.

We observed that Highland is the Health Board with the largest percentage (~9.5%) of GP practices that were identified as being in the upper tail of prescribing volumes (identified by model residuals <2.5% percentile), followed by Lothian (~5.3%), Dumfries and Galloway (~3.2%), Grampian (~2.9%), Forth Valley (~2%) and Greater Glasgow and Clyde (~1.7%). No 'high-volume prescriber' GP practices were found within the remaining Health Boards. On the other hand, Tayside was identified as the Health Board with the largest percentage (~19%) of 'low-volume prescribers' (identified by model residuals >97.5% percentile). Shetland (10%), Borders (~8.7%), Grampian (~5.7%), Highland (~1.1%), Lothian (~1%), and Greater Glasgow and Clyde (~0.9%) also contained GP practices that prescribed far below the national average. The remaining Health Boards did not contain any 'low-volume prescribing' practices. The underlying reasons for these observations are currently unclear and require further investigation.

Discussion

This study has investigated possible differences in patterns of medical prescribing for the two most common classes of drugs (i.e. $\alpha - 1$ blockers and $5 - \alpha$ reductase inhibitors) used to treat BOO in Scotland over a recent 4-year period (October 2015 - November 2019) using publicly available data from individual GP practices across all Health Boards. In taking this approach, we have assumed that most BOO medication is prescribed by GPs, either practising alone or upon the advice of a specialist prescriber such as a urologist from specialist practice, as is the case throughout the UK. Nevertheless, using this approach and GP prescribing data with this assumption, we generated a study dataset by linking prescribing data to GP practice-specific information (such as their type of contract with the NHS, and their licence to dispense) and summary characteristics of their patient populations (such as patient age, and GP practice-associated levels of deprivation and rurality). To our knowledge, this is the first time that particular characteristics of a GP practice have been studied as potential factors influencing BOO drug prescribing patterns in Scotland. This has enabled us to identify trends in prescribing behaviour that may help inform future practice.

A trend of increased BOO drug prescribing practice was observed throughout the 4-year observation window consistent with an increased incidence of PCa (which is prevalent in men of the same age), an ageing Scottish population, increased awareness of male health issues amongst both patients and GPs, and increased referral of men to secondary care due to a raised PSA [21, 22]. Though gaining a definite understanding of this trend was outside the scope of this study, in order to fully understand the nature of this increase it would be pertinent to (i) identify the relative contribution (or otherwise) made by increased referral to secondary care with

suspected PCa (as identified by a raised PSA), which might result in increased BOO/BPH prescribing as a secondary consequence of a raised PSA referral, (ii) the currently unaccounted-for impact of increased GP and public awareness and public help seeking behaviour, and (iii) increased focus on PCa management, rather than BPH surgery which may have contributed to the increase in medical drug use for BOO, rather than definitive intervention, though this is speculative. Greater understanding of these issues will facilitate planning to meet demand in primary care services given ongoing capacity shortage, and also secondary care as increased pharmacological treatment could be indicative of future demand for surgery [23].

Whether practices were NHS or GP-run, or had a dispensing pharmacy present within the GP practice, were associated with higher and lower prescribing volumes respectively. While the individual characteristics of GP medical practices are known to differ by region [24] research accounting for these factors is relatively sparse; hence it is unclear why this difference exists. Furthermore, although regional prescribing behaviours were largely uniform, lower levels of prescribing were noted in some individual Health Boards. No clear explanation could be given for this observation, as no possible explanatory factor is common to these Health Boards. An investigation of factors listed above would be pertinent to understand regional differences evident in prescribing behaviours and guide intervention to reduce inequity.

This study found several GP practices operating at the extremes of prescribing, with practices across five Health Boards prescribing considerably more, and practices across seven Health Boards prescribing considerably less, of each drug than other Scottish practices. In particular, 19% of GP practices in Tayside were considered to be ‘low-volume prescribers’, which could partially explain why Tayside was found to

have lower overall levels of prescribing. However, there was otherwise no correlation between individual GP practice prescribing behaviours and overall volume of prescriptions within the Health Board. As such, this study found that factors other than GP list size or accepted sociodemographic and geographic measures may be contributing to inequalities in prescribing practice. Further research is needed to identify these factors, although individual GP attitudes and understanding of prostate diseases [9, 10], and Scotland's cultural diversity [7, 8, 18], may be potential explanations.

The data used in this research had several limitations. First, the available data only exists in the public domain at an aggregate level (i.e. individual GP practice or patient list), and further information would be helpful in order to identify the reasons why prescribing practices vary at a more granular level (perhaps by associating the prescribing practice with the presence or absence of a GP with a particular interest in men's health issues, as an example). Second, the use of summary data regarding levels of socio-economic deprivation and rurality of patients reduces the accuracy with which one can estimate the shape of their association with the outcome, with these factors likely to be important in terms of access to healthcare and prescribing. Third, not having information about specific GP practice catchment areas made it necessary to use an adjacency matrix based on postcodes, rather than actual distances, resulting in a sub-optimal method of accounting for underlying spatial processes. Fourth, we have not investigated how differences in GP prescribing practices for BOO may impact on the rates of surgical management of this condition. For example, a study in Australia identified regional differences in the surgical management of BOO secondary to BPH [23], and it would be interesting for future research to potentially link BPH prescribing practice with rates of surgical

management of this condition. For example, it might be the case that medical therapy can delay the need for surgery by a number of years, or reduced rates of BPH prescribing in any particular Health Board may be associated with higher rates of surgical intervention. These hypotheses require testing in datasets if they can be linked.

It would be interesting for future research to investigate trends and potential inequalities regarding all prostate-related conditions (both benign and malignant) over space and time in other settings and geographical locations. In particular, it would be interesting to investigate whether the trends observed in Scotland may similarly exist in other regions of the UK, and if so, are variations attributable to common factors such as urban/rural and socioeconomic status. Further research to investigate medical practice phenomena as complex as prescribing patterns using publicly available data will support identification of key limitations in practice, and inform data collection and data sharing in the future. In addition, the general nature of the statistical modelling framework we have proposed in this study may be extended to investigate other kinds of models, covariates, and medical conditions in a range of future studies.

Conclusions

The volume of prescriptions of drugs for LUTS secondary to BOO has steadily increased across Scotland during a recent 4-year observation period, consistent with trends in PCa, which similarly affects men of this age. Regional differences in the volume of prescribed drugs, and extremes in individual GP practice prescribing patterns, were found. Whilst prescribing patterns varied in relation to geographic and demographic factors and GP practice list size, this study identified considerable variations that could not easily be accounted for. Potential explanations for these variations include individual GP attitudes and understanding of prostate diseases [9, 10], and Scotland's cultural diversity [6, 7, 8].

Figure Legends

Figure 1:

Statistical model average number of daily doses of each BOO drug type prescribed per month, by individual Scottish Health Board and adjusted for GP practice patient roll size.

Figure 2:

Frequency histograms of the statistical model's exponentiated residuals for each Scottish Health Board. The vertical dashed line represents the null residual (value=1 on the exponentiated scale), and each small black square represents the average number of daily prescriptions of BOO drugs (combined $\alpha - 1$ blockers and $5 - \alpha$ reductase inhibitors) per month per individual anonymous GP practice within each Health Board. The boxplot below each histogram illustrates the same data distribution (the white point marks the median, the thick line represents the usual box, and the thin line represents the whiskers). Ideally the exponentiated residuals for each GP practice would lie around the null residual (i.e. value=1), however the heterogeneity in prescribing practice is illustrated by increased spread to the left and right of the null residual. A shift of GP practice distributions to the right of the null residual, as seen in Health Boards such as Borders, Fife, Orkney, Shetland and Tayside, illustrates less prescribing of these medications than would be expected.

Figure 3:

Maps of Scotland highlighting the Health Board locations of anonymous GP practices at the extremes of the distribution of BOO drug prescribing. The left panel shows the percentage of GP practices within each Health Board that have been identified (via model residuals) as being high in prescribing volumes with respect to

the national average (i.e. model residuals <2.5% percentile). Similarly, the right panel shows the percentage of GP practices low in prescribing volumes with respect to the national average (i.e. model residuals >97.5% percentile).

References

[1] European Association of Urology. EAU guidelines on non-neurogenic male LUTS. 2019.

[2] Patel ND, Parsons JK. Epidemiology and etiology of benign prostatic hyperplasia and bladder outlet obstruction. Indian J Urol 2014;30:170—6.

[3] Allemani C, Matsuda T, Di Carlo V et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): Analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018; 391:1023–75.

[4] NHS National Services Scotland. Cancer waiting times. NHS National Services Scotland. 2019.

[5] Lee SWH, Chan EMC, Lai YK. The global burden of lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a systematic review and meta-analysis. Sci Rep. 2017;7(1):7984. doi: 10.1038/s41598-017-06628-8.

[6] Taulbut M, Walsh D, McCartney G et al. Spatial inequalities in life expectancy within post-industrial regions of Europe: A cross-sectional observational study. BMI Open. 2014; 4.

[7] Walsh D, McCartney G, Collins C, Taulbut M, Batty GD. History, politics and vulnerability: explaining excess mortality in Scotland and Glasgow. Public Health. 2017; 151:1—12.

[8] Cowley J, Kiely J, Collins D. Unravelling the Glasgow effect: The relationship between accumulative bio-psychosocial stress, stress reactivity and Scotland's health problems. Prev. Med. Rep. 2016; 4:370-375.

[9] Public Health England. Prostate cancer risk management programme: overview. 2016.

[10] Clements A, Bukach C, Rai T, Shine B, Austoker J, Watson E. What influences men's decision to have a prostate-specific antigen test? A qualitative study. Family Practice. 2007; 24.

[11] Bajic P, Montgomery J, Nelson M et al. (2020). 133 comparisons fo BPH medication prescribing among sexagenarians with Medicare an private insurance. J Sex Med. 2020; 17(1):37—38.

[12] Fu Y, Han S, Wang L, Geo W, Cao X, Wang J. Comparison of characteristics of benign prostatic hyperplasia (BPH) patients treated with finasteride and alpha blocker combination therapy verses alpha blocker monotherapy in China: An analysis of electronic medical record data. Adv. Ther. 2018; 35:1191—1198.

[13] Moon HW, Yang JH, Choi JB, Bae WJ. Prescription pattern of alpha-blockers for management of lower urinary tract symptoms/benign prostatic hyperplasia. Sci Rep. 2018; 8.

[14] Scottish Government. Scottish Index Of Multiple Deprivation. [online] available at: http://www.gov.scot/Topics/Statistics/SIMD [accessed 9 Mar 2020].

[15] Scottish Government. Scottish Government Urban Rural Classification. [online] available at: https://www2.gov.scot/Topics/Statistics/About/Methodology/UrbanRuralClassification [accessed 9 Mar 2020]

[16] National Institute for Health and Care Excellence. LUTS in men. National Institute for Health and Care Excellence. 2019.

[17] McConnell JD, Roehrborn CG, Bautista OM et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. Clinical Trial N Engl J Med. 2003 Dec 8;349(25):2387-98. doi: 10.1056/NEJMoa030656.

[18] R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria 2019. URL https://www.R-project.org/.

[19] H. Rue, S. Martino, and N. Chopin. Approximate Bayesian inference for latent Gaussian models using integrated nested Laplace approximations (with discussion). Journal of the Royal Statistical Society, Series B. 2009; 71(2):319--392.

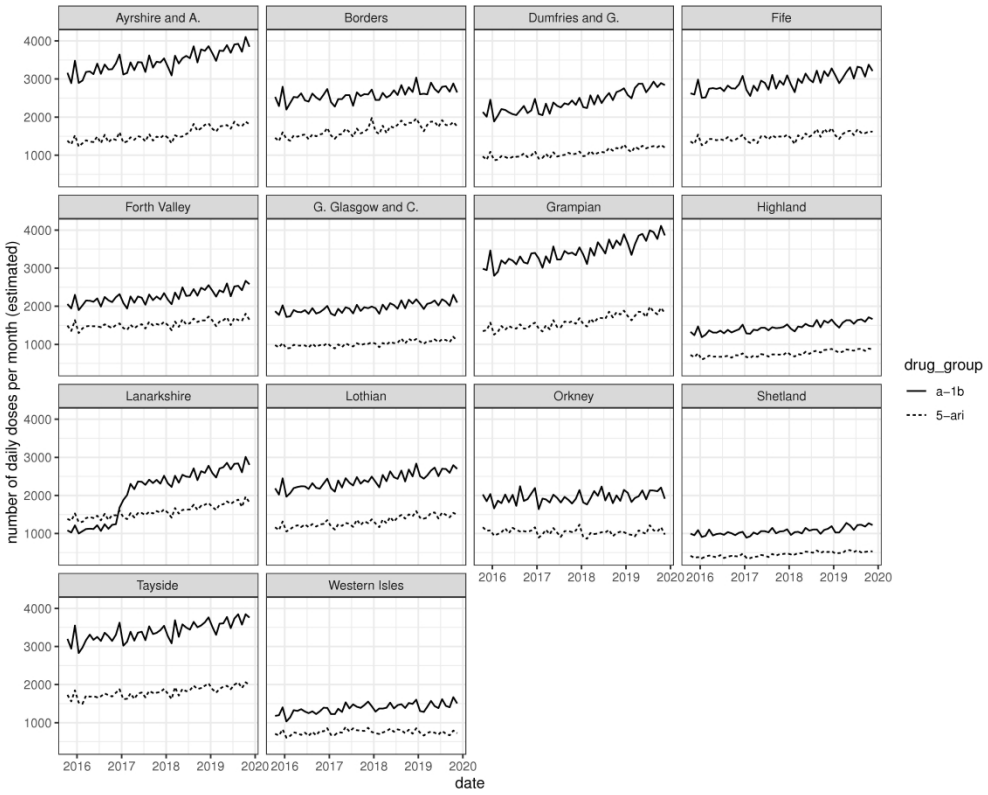
[20] Andreis F. Github repository for code, data and shapefiles to reproduce the analyses in the paper. URL https://github.com/federicoandreis/prescribing_bmjopen/blob/main/README.md

[21] National Records of Scotland. Mid-year population estimates Scotland, Mid-2018. 2019.

[22] European Association of Urology. EAU guidelines on prostate cancer. 2019.

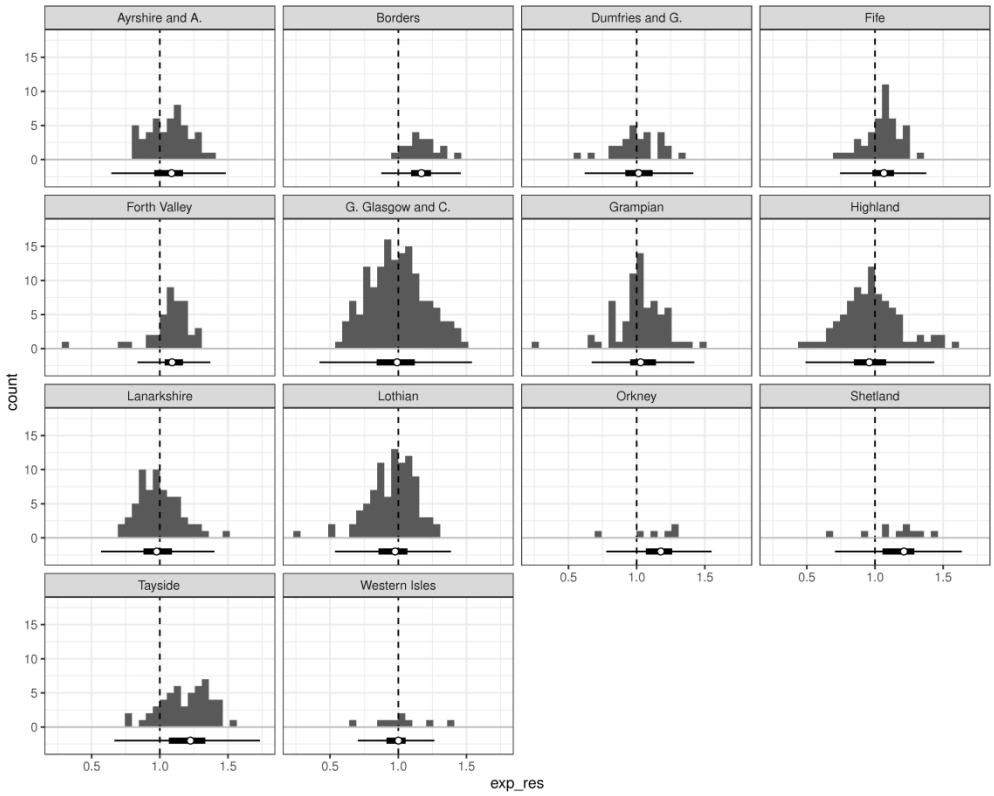
[23] Morton A, Williams M, Perera M, et al. Management of benign prostatic hyperplasia in the 21st century: temporal trends in Australian population-based data. BJU International. 2020 Sep;126 Suppl 1:18-26. DOI: 10.1111/bju.15098.

[24] Burgess L. Primary Care in Scotland. The Scottish Parliament. 2018.



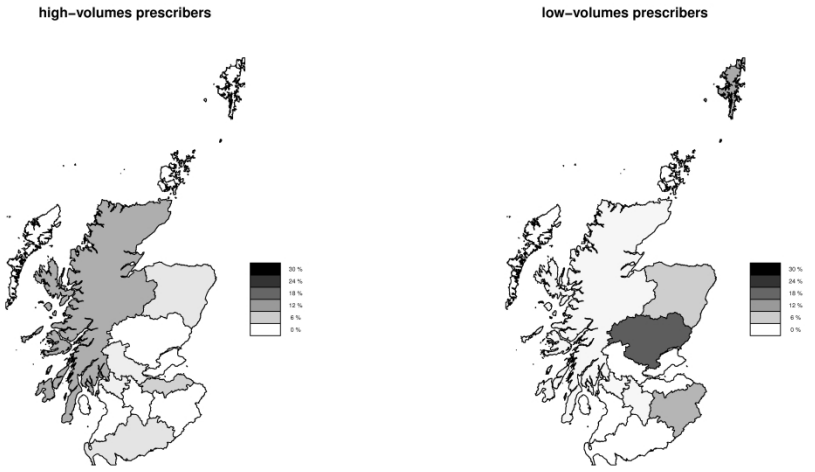
Statistical model average number of daily doses of each BOO drug type prescribed per month, by individual Scottish Health Board and adjusted for GP practice patient roll size.

254x203mm (600 x 600 DPI)



Frequency histograms of the statistical model's exponentiated residuals for each Scottish Health Board. The vertical dashed line represents the null residual (value=1 on the exponentiated scale), and each small black square represents the average number of daily prescriptions of BOO drugs (combined α-1 blockers and 5-α reductase inhibitors) per month per individual anonymous GP practice within each Health Board. The boxplot below each histogram illustrates the same data distribution (the white point marks the median, the thick line represents the usual box, and the thin line represents the whiskers). Ideally the exponentiated residuals for each GP practice would lie around the null residual (i.e. value=1), however the heterogeneity in prescribing practice is illustrated by increased spread to the left and right of the null residual. A shift of GP practice distributions to the right of the null residual, as seen in Health Boards such as Borders, Fife, Orkney, Shetland and Tayside, illustrates less prescribing of these medications than would be expected.

254x203mm (600 x 600 DPI)



Maps of Scotland highlighting the Health Board locations of anonymous GP practices at the extremes of the distribution of BOO drug prescribing. The left panel shows the percentage of GP practices within each Health Board that have been identified (via model residuals) as being high in prescribing volumes with respect to the national average (i.e. model residuals <2.5% percentile). Similarly, the right panel shows the percentage of GP practices low in prescribing volumes with respect to the national average (i.e. model residuals >97.5% percentile).

355x203mm (600 x 600 DPI)

Technical supplement for the paper "Prescribing patterns for medical treatment of suspected prostatic obstruction: a longitudinal register-based study the Scottish Health and Social Care Open Data"

Authors: Federico Andreis, Richard Bryant, Emanuele Giorgi, Andrea Williamson, Ashleigh Ward

We employ a Bayesian hierarchical Poisson model that estimates spatial and temporal structured patterns. The outcome of interest is the number of daily doses prescribed in a month at a general practice in Scotland, between October 2015 and November 2019. Let n_{jti} denote the number of prescriptions of drugs belonging to group $j \in \{\alpha - 1\text{b}, 5 - \alpha\text{ri}\}$, for practice $i = 1, \dots, 903$, in month $t = 1, \dots, 50$.

Conditionally on a set of random effects $\alpha_{[i]}$, $\alpha_{[ji]}$ and $\alpha_{[t]}$, let n_{jti} follow a Poisson distribution with parameter λ_{jti}, modelled with an additive linear predictor on a natural logarithm scale:

$$n_{jti} \sim \text{Poisson}(\lambda_{jti})$$

$$\log(\lambda_{jti}) = \alpha + \alpha_{[i]} + \alpha_{[ji]} + \alpha_{[tji]} + \beta_1 \log(\text{list size}_{ti}) + \beta_2 \text{drug group} + \beta_3 \text{contract}_i + \beta_4 \text{dispensing}_i + \beta_5 \text{males 45p}_{ti} + \beta_6 \text{deprived 15}_{ti} + \beta_7 \text{remote}_{ti}$$

The random effects, as described in Table 3 in the paper, relate to:

- A structured component accounting for spatial correlation ($\alpha_{[i]}$)
- An unstructured component accounting for potential interactions between individual practice and type of drug ($\alpha_{[ji]}$)
- A component accounting for temporal correlation, grouped by health board and type of drug ($\alpha_{[t]}$).

To model the spatial component $\alpha_{[i]}$, we employ an intrinsic Conditional Auto Regressive (iCAR [1,2,3]) structure that exploits an adjacency matrix based on location of the practices. The postcodes are linked to Easting/Northing coordinates and Voronoi tessellation is used to find nearest neighbours and their distances (this was done using the caramellar package, available from github via devtools::install_github("barryrowlingson/caramellar")). In this way, the model allows the borrowing of strength of information across neighbouring regions.

The component accounting for potential interactions between the individual medical practice and the type of drug prescribed $\alpha_{[ji]}$ is modelled in an unstructured way, using *iid* gaussian terms with common precision parameter [3].

The temporal component $\alpha_{[t]}$ is modelled using a first-order autoregressive process [1], allowing grouping by health board and drug type. This approach allows the estimation of a common temporal autocorrelation structure for practices in the same health board and with respect to the same drug group type.

An Integrated Nested Laplace Approximation [4] approach is used to approximate the posterior distribution and obtain the estimates, using the inla package in R; default prior distributions are used for all parameters. To make estimation computationally easier, a cheap Gaussian approximation is first used and the resulting estimates employed as reasonable starting values for the actual model fitting procedure (details in the R code in Supplement 2). Kullback-Leibler divergence statistics [3] indicate a satisfactory approximation to all marginal posterior densities.

Figure 1 contains the summary of the model fit, while Table 1 contains a summary of estimated posterior distributions for the random effects in terms of standard deviations, rather than precision parameters (as in Figure 1). Estimation took

approximately 7 hours on an AMD Ryzen 7 2700x processor with 32GB DDR4 RAM, under Windows 10.

Figure 1. Summary of model fit

```
Call:
   c("inla(formula = formula_mod_IV, family = \"poisson\", data = df_joint, ", " verbose = TRUE,
   control.compute = control$compute, control.predictor = control$predictor, ", " control.inla =
   list(diagonal = 10), control.results = control$results, ", " control.fixed = list(prec.intercept =
   0.1), control.mode = list(result = mod_inla_approx_IV, ", " restart = TRUE))")
Time used:
    Pre = 0.612, Running = 24085, Post = 4.97, Total = 24091
Fixed effects:
                  mean    sd 0.025quant 0.5quant 0.975quant   mode kld
(Intercept)     -1.570 0.040     -1.648   -1.570     -1.492 -1.570   0
drug_group5-ari -0.625 0.017     -0.658   -0.625     -0.591 -0.625   0
gp_runY          0.238 0.033      0.174    0.238      0.302  0.238   0
dispensingY     -0.086 0.026     -0.138   -0.086     -0.035 -0.086   0
log(list_size)   0.915 0.002      0.911    0.915      0.919  0.915   0
prop_m_45p       4.816 0.032      4.754    4.816      4.879  4.816   0
p_15             0.017 0.007      0.003    0.017      0.030  0.017   0
ur_codeRemote    0.002 0.000      0.002    0.002      0.003  0.002   0

Random effects:
  Name    Model
    postcode_n Besags ICAR model
   time_n AR1 model
   gp_drug IID model

Model hyperparameters:
                           mean    sd 0.025quant 0.5quant 0.975quant   mode
Precision for postcode_n  4.353 0.328      3.753    4.337      5.039  4.302
Precision for time_n     29.235 5.693     18.647   29.144     40.766 29.217
Rho for time_n            0.899 0.013      0.871    0.900      0.923  0.901
GroupRho for time_n       0.685 0.043      0.604    0.683      0.771  0.676
Precision for gp_drug    20.286 0.802     18.736   20.277     21.895 20.269

Expected number of effective parameters(stdev): 4095.95(1.50)
Number of equivalent replicates : 22.01

Deviance Information Criterion (DIC) ...............: 4371157.00
Deviance Information Criterion (DIC, saturated) ....: 3605454.27
Effective number of parameters .....................: 4097.92

Watanabe-Akaike information criterion (WAIC) ...: 4488316.21
Effective number of parameters .................: 159926.14

Marginal log-Likelihood:  -2217597.61
CPO and PIT are computed

Posterior marginals for the linear predictor and
 the fitted values are computed
```

Table 1. Summary of estimated posterior distributions for random effects. SD denotes the standard deviation.

	mean	Sd	2.5%	50%	97.5%	mode
SD of $\alpha_{[i]}$ (spatial)	0.480	0.018	0.446	0.480	0.516	0.480
SD of $\alpha_{[ji]}$ (unstructured)	0.222	0.004	0.214	0.222	0.231	0.222
SD of $\alpha_{[tji]}$ (temporal)	0.188	0.019	0.157	0.185	0.231	0.178
ρ_1 of $\alpha_{[tji]}$ (autocorrelation)	0.899	0.013	0.871	0.900	0.923	0.901
ρ_2 of $\alpha_{[tji]}$ (group correlation)	0.685	0.043	0.604	0.683	0.771	0.676

References

[1] Banerjee S, Carlin BP, Gelfand AE. Hierarchical Modeling and Analysis for Spatial Data. 2nd ed. Boca Raton: Chapman & Hall. 2015.

[2] Paciorek CJ. Understanding Intrinsic Gaussian Markov Random Field Spatial Models, Including Intrinsic Conditional Autoregressive Models. University of California, Berkeley. 2009. http://www.stat.berkeley.edu/~paciorek/research/techVignettes/techVignette5.pdf.

[3] Rue H, Held L. Gaussian Markov Random Fields: Theory and Applications. Boca Raton: Chapman & Hall. 2005.

[4] H. Rue, S. Martino, and N. Chopin. Approximate Bayesian inference for latent Gaussian models using integrated nested Laplace approximations (with discussion). Journal of the Royal Statistical Society, Series B. 2009; 71(2):319--392.

```
#######################################################################
# Code to reproduce the analyses and the plots in the the manuscript  #
# "Prescribing patterns for medical treatment of suspected prostatic  #
#  obstruction: a longitudinal register-based study the Scottish      #
#  Health and Social Care Open Data" (2020)                           #
# Authors: Federico Andreis, Richard Bryant, Emanuele Giorgi,         #
#          Andrea Williamson, Ashleigh Ward                           #
#######################################################################

##############################
# Code by: Federico Andreis #
##############################

#############
# libraries #
#############
library(tidyverse)    # to manipulate data objects

library(rgdal)        # to deal with spatial objects
library(sf)
library(raster)

library(caramellar)   # to build the adjacency matrix, not on CRAN
                      #
devtools::install_github("barryrowlingson/caramellar")

library(INLA)         # to fit the model
library(brinla)       # to manipulate inla objects

#######################################
# load the dataset and the shapefile #
#######################################
dataset <- read_csv('dataset.csv')

map_scotland_hb <- readOGR('SG_NHS_HealthBoards_2018.shp')

############################
# create adjacency matrix #
############################

# create adjacency matrix and transform it into an inla graph
adjacency_graph <- voronoi_adjacency(dataset %>%
                                       group_by(postcode_n) %>%
                                       slice(1) %>%

dplyr::select(postcode_n,Easting,Northing) %>%
                                       ungroup,

postcode_n~Easting+Northing)$Adjacencies %>% inla.read.graph

#################
# fit the model #
#################

# set inla controls
control <-list(predictor=list(compute=TRUE,link=1),
               results=list(return.marginals.random=TRUE,
                            return.marginals.predictor=TRUE),
```

```
                compute=list(hyperpar=TRUE, return.marginals=TRUE,
                             dic=TRUE, mlik=TRUE, cpo=TRUE, po=TRUE,
                             waic=TRUE, graph=TRUE, gdensity=TRUE))

# model specification
model <- n_daily_doses~drug_group+gp_run+dispensing+     # fixed effects
                 log(list_size)+prop_m_45p+p_15+ur_code+ # fixed effects
  f(postcode_n,model='besag',graph=adjacency_graph)+     # structured
spatial component (iCAR)
  f(time_n,model='ar1',group=hb_drug)+                   # temporal
component (grouped AR1)
  f(gp_drug,model='iid')                                 # unstructured
spatial component (iid)

# fit the model using a cheap Gaussian approximation to obtain reasonable
starting values
# run time ~18 minutes on a AMD Ryzen 7 2700x processor with 32GB DDR4
RAM, under Windows 10
cheap_approximation <- inla(model,
                            family='poisson',
                            data=dataset,
                            control.inla=list(diagonal=100,
                                              strategy="gaussian",
                                              int.strategy="eb"),
                            control.compute=control$compute,
                            control.predictor=control$predictor,
                            control.results=control$results,
                            verbose=TRUE)

# use the command
#
# model_fit <- cheap_approximation
#
# and ignore the following model fit block to be able to use the rest of
the
# code without having to wait for the more accurate approximation to be
obtained
# Note: if you use this approach, the resulting estimates and plots will
differ
# from those in the paper


# fit the model using the cheap approximation estimates as starting
values
# note: this step takes ~7 hours on the machine described earlier
model_fit <- inla(model,
                  family='poisson',
                  data=dataset,
                  control.inla=list(diagonal=10),
                  control.fixed = list(prec.intercept = 0.1),
                  control.compute=control$compute,
                  control.predictor=control$predictor,
                  control.results=control$results,
                  control.mode=list(result=cheap_approximation,
                                    restart=TRUE),
                  verbose=TRUE)

rm(adjacency_graph,control,
```

```
   model,cheap_approximation) # clean up

########################################
# post-processing of the model output #
########################################

# add the fitted values to the dataset and make health board names into
factors
dataset <- dataset %>%
  mutate(fitted=model_fit$summary.fitted.values$mean,
         hb_name=factor(hb_name))

# obtain predictions by health board and drug group
average_fitted <- dataset %>%
  group_by(time=time,hb_name,drug_group) %>%
  summarise(avg_fitted=mean(fitted),
            avg_observed=mean(n_daily_doses))

# extract the exponentiated spatial residuals and add them to the dataset
exp_residuals <- numeric(length(model_fit$marginals.random$postcode_n))

for (i in 1:length(exp_residuals)) {

  tmp <- model_fit$marginals.random$postcode_n[[i]]

  exp_residuals[i] <- inla.emarginal(exp,tmp) # exponentiate the spatial
residuals

}

rm(tmp,i) # clean up

# make the residuals  into a tibble that also contains the practice
postcodes
# and health boards names
exp_residuals <- data.frame(postcode_n=1:length(exp_residuals),
                            postcode=unique(dataset$postcode),
                            exp_residuals=exp_residuals) %>%
  mutate(postcode=as.character(postcode)) %>%
  left_join(.,dataset %>%
              dplyr::select(postcode,hb_name),
            by=c('postcode','postcode')) %>%
  group_by(postcode) %>%
  slice(1)

# add the exponentiated residuals to the dataset
dataset <- left_join(dataset,
                     exp_residuals %>%
                       dplyr::select(postcode_n,exp_residuals),
                     by='postcode_n')

# set up the shapefile and data needed to to plot the map in Figure 3
geo_df <- dataset
coordinates(geo_df) <- ~Easting+Northing
crop_map_hb <- crop(map_scotland_hb,geo_df)

rm(map_scotland_hb) # clean up
```

```
# obtain the quantiles of the exponentiate residuals distribution
# residuals are constant for each GP practice, extract only one line each
dataset_singletons <- dataset %>%
  group_by(gp_code) %>%
  slice(1) %>%
  ungroup

exp_residuals_quantiles <- quantile(dataset_singletons$exp_residuals,
                                    p=seq(0,1,by=.025))

##################################
# produce the plots in the paper #
##################################

# Figure 1
average_fitted %>%
  ggplot(aes(x=time))+
  geom_line(aes(y=avg_fitted,linetype=drug_group))+
  theme_bw()+facet_wrap(~hb_name)+
  xlab('date')+ylab('number of daily doses per month (estimated)')

# Figure 2
exp_residuals %>%
  group_by(hb_name) %>%
  mutate(q1=quantile(exp_residuals,.25),
         q2=quantile(exp_residuals,.5),
         q3=quantile(exp_residuals,.75),
         w=1.5*(q3-q1)) %>%
  ungroup %>%
  ggplot()+geom_histogram(aes(exp_residuals))+
  geom_vline(xintercept = 1, lty=2)+
  ylim(-3,18)+
  geom_hline(yintercept=0,col='grey')+
  geom_segment(aes(y=-2,yend=-2,x=q1-w,xend=q1))+
  geom_segment(aes(y=-2,yend=-2,x=q1,xend=q3),lwd=2)+
  geom_segment(aes(y=-2,yend=-2,x=q3,xend=q3+w))+
  geom_point(aes(y=-2,x=q2),lwd=2,pch=16,col='white')+
  geom_point(aes(y=-2,x=q2),lwd=2,pch=1)+
  theme_bw()+facet_wrap(~hb_name)

# Figure 3

# change quantiles as needed
lower_quantile <- 2   # corresponding to 2.5% in the quantiles vector
upper_quantile <- 40  # corresponding to 97.5% in the quantiles vector

# create the proportions of GP practices meeting the quantile
requirements
prop_q_by_hb <- dataset_singletons %>%
  group_by(hb_name) %>%
  summarise(HBCode=first(hb_code),
            prop_l_q2.5=mean(exp_res<quant_res[2]),
            prop_g_q97.5=mean(exp_res>quant_res[40]))

crop_map_hb@data <- crop_map_hb@data %>%
  left_join(prop_q_by_hb,by='HBCode')

# define a scaling factor for the grey scale: the max observed proportion
```

```
# is slightly less than 0.2, rescaling aids visualisation
scale_factor <- .3

par(mfrow=c(1,2))
plot(crop_map_hb,
     main='high-volumes prescribers',
     #border='black',
     col=grey(1-crop_map_hb$prop_l_q2.5/scale_factor))

for (i in 0:5) {

  rect(470000,750000+i*20000,520000,750000+(i+1)*20000,
       col=grey(seq(1,0,length.out=6))[i+1])
  text(x=545000,y=760000+i*20000,
       paste0(round(scale_factor*seq(0,1,length.out=6)[i+1]*100,2),' %'),
       cex=.5)
}

plot(crop_map_hb,
     main='low-volumes prescribers',
     #border='black',
     col=grey(1-crop_map_hb$prop_g_q97.5/scale_factor))

for (i in 0:5) {

  rect(470000,750000+i*20000,520000,750000+(i+1)*20000,
       col=grey(seq(1,0,length.out=6))[i+1])
  text(x=545000,y=760000+i*20000,
       paste0(round(scale_factor*seq(0,1,length.out=6)[i+1]*100,2),' %'),
       cex=.5)
}
par(mfrow=c(1,1))

rm(prop_q_by_hb,scale_factor,
   lower_quantile,upper_quantile) # clean up

###################################
# posterior distributions summary #
###################################

# table of fixed effects posterior estimates
model_fit$summary.fixed

# table of random effects posterior estimates
model_fit$summary.random        # expressed in terms of precision
bri.hyperpar.summary(model_fit) # expressed in terms of standard
deviation
```