Controlling antibiotic usage—A national analysis of General Practitioner/Family Doctor practices links overall antibiotic levels to demography, geography, comorbidity factors with local discretionary prescribing choices

Michael Stedman1 | Mark Lunt2 | Mark Davies1 | Erin Fulton-McAlister3 | Abid Hussain4 | Tjeerd van Staa5 | Simon G. Anderson2,6 | Adrian H. Heald2,7

1Res Consortium, Andover, UK
2The School of Medicine and Manchester Academic Health Sciences Centre, University of Manchester, Manchester, UK
3Centre for Molecular Bacteriology and Infection, Imperial College London, London, UK
4Heart of England NHS Trust, Birmingham, UK
5School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK
6The George Alleyne Chronic Disease Research Centre, University of the West Indies, Cavehill, Barbados
7Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, UK

Correspondence
Adrian Heald, Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford M6 8HD, UK.
Email: adrian.heald@manchester.ac.uk

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Abstract

Introduction: Ecological studies show association between antimicrobial resistance (AMR), and inappropriate oral antibiotics use. Moderating antibiotic prescribing requires an understanding of all drivers of local prescribing. The aim was to quantify how much is determined by external factors compared with discretionary clinical choices.

Methods: Oral antibiotic usage taken from England General Practitioner/Family Doctor practice prescribing data was aggregated using WHO/ATC defined daily doses (DDDs). The average annual antibiotic daily prescribing rate (AAADPR) in each practice was the total DDD of oral antibiotics divided by registered population and 365. The AAADPR of English practices in 2017_18 was linked by regression to factors including demographics, geography, medical comorbidities, clinical performance, patient satisfaction, medical workforce characteristics and prescribing selection. The regression coefficients for modifiable prescribing selection factors were applied to the difference between the median and top decile practice values to establish overall reduction opportunities through changing prescribing behaviour.

Results: Twenty five factors accounted for 58% of the AAADPR variation in 5889 practices supporting 49.8 million patients. Non-modifiable factors linked increased AAADPR to more northerly location, higher prevalence of diabetes, COPD, CHD, and asthma; higher white ethnicity; higher patient satisfaction and lower population density. Modifiable behaviour accounted for 11% of the variation in AAADPR, with increases associated with a wider range of antibiotics, higher proportion taken as liquids, higher doses in each prescription, lower guideline compliance, lower targeted antibiotics, lower spend/dose, and less seasonal variation. If all practices achieved the level of modifiable factors of the top decile, this model suggests that overall AAADPR could reduce by 31%.

Conclusion: Such analysis is associative and does not infer causation. However, demographics, location, medical condition of the population, and prescribing selection are drivers of overall antibiotic prescribing. This analysis provides benchmarks for...
both non-modifiable and modifiable factors against which practices could evaluate their opportunities to reduce antibiotic prescribing.

1 | INTRODUCTION

Most people living in Europe and North America receive their antibiotics in primary care.1 Curtis et al have previously described variations in antibiotic usage across primary care, linked to key factors such as General Practitioner (GP) Practice size, deprivation and age mix of General Practitioner/Family Doctor (GP/FD) lists.2 Additional factors linked to inappropriate antibiotic use3,4 also include general practitioner knowledge, patient pressure and pharmaceutical industry influences. Furthermore, different actors are involved in antimicrobial prescribing, namely, physicians, patients, pharmacists and health authorities. This is an area that health ministries and prescribing monitors recognise as a priority for change in many countries.5

Resistance to antibiotics is a critical public health threat, which is aggravated by high volumes of use and at times inappropriate clinical targeting, along with a lack of development of new antimicrobial agents.6,7 For example, ecological studies suggest that there is a clear association between the use of antibiotics (penicillin and fluoroquinolones) and resistance rates.8,9

The Public Health England English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)10 was established in 2013 to support the delivery of the UK Five Year Antimicrobial Resistance (AMR) Strategy 2013-2018. The aims include robust surveillance of both antimicrobial use and resistance and identification of processes to optimise antimicrobial prescribing. The 2018 report10 highlights reductions being achieved in antibiotic prescribing in primary care. However, despite this antibiotic-resistant infections continue to increase.

In 2016 the UK Government set a target to halve inappropriate antibiotic prescribing by 2020. Achieving this requires a detailed understanding of prescribing behaviour. Currently, there is continuing debate about the association between the use of antibiotics and the spread of AMR, with inappropriate prescription of antibiotics being one of the reported potential enhancing factors7-9 for this. Previously a number of interventions have already been aimed at addressing inappropriate prescribing of antibiotics and, ultimately, improving the quality of such prescribing although not always with success.11,12

NICE recommendations state that when antimicrobials are necessary to treat an infection that is not life-threatening, a narrow-spectrum antibiotic should generally be first choice.1 Indiscriminate use of broad-spectrum antibiotics creates a selective advantage for bacteria resistant even to these ‘last-line’ broad-spectrum agents and kills normal commensal flora leaving people susceptible to antibiotic-resistant harmful bacteria such as Clostridium difficile (C. difficile). The Chief Medical Officer

What’s already known about this topic?

- There is significant evidence around the effect of local population demography on levels of antibiotic prescribing, which in general cannot be changed by clinicians.
- The assumption may be that other variations are the responsibility of clinicians.

What does this article add?

- We have shown that while choice is an important factor in antibiotic prescribing performance, non-discretionary factors such as demographics, location and comorbidities of the local population are also associated with antibiotic prescribing patterns in General Practitioner (GP) practices.
- By addressing certain modifiable discretionary factors, or ‘simple rules’, there is a potential opportunity to reduce antibiotic prescribing in primary care by 31% or the equivalent of 10 million prescriptions/year in England, equivalent to all practices achieving the same antibiotic prescribing profile as the top decile practices in this study. In turn, this could build a more sustainable approach to the use of antibiotics.

Review criteria: How did you gather, select and analyse the information you considered in your review?

- We used national published public GP practice level data from various sources Prescribing, Quality and Outcomes Framework, population age/gender, workforce, patient survey and associated it with other local population data, ethnicity, deprivation, urban/rural etc and then linked that to specific prescribing behavioural indicators. We then restricted analysis to only those factors that were found to be significant within the model.

Message for the clinic: What is the ‘take-home’ message for the clinician?

- Evaluating personal prescribing behaviours against the national prescribing levels will give clinicians insight into their basic local population’s requirements and indicate where changes would be most appropriate in reducing their own personal antibiotic prescribing.
Annual report 2011 makes it clear that for infections that are not life-threatening, broad-spectrum antibiotics (for example, co-amoxiclav, quinolones and cephalosporins) need to be reserved for second-choice treatment when narrow-spectrum antibiotics are ineffective. This aligns with NICE compliance as measured by a lower percentage of total antibiotic prescriptions for quinolones and cephalosporins.1

The aim of our study was to quantify the impact of local discretionary (behavioural) and external non-discretionary factors on levels of antibiotic prescribing choices within GP/FD practices by analysis of their 2017-2018 prescribing, demographic, geographic, medical condition and patient satisfaction data for the whole of England.

2 | METHODS

English national prescribing data for antibiotics at a GP/FD practice level was analysed from 2013/14 to 2017/18.12,14

The conventional method for comparing levels of prescribing between practices is to relate the number of prescriptions to Specific Therapeutic group Age-sex Related Prescribing Units (STAR-PU) population,14 which standardises the local population by an agreed set of age and gender factors derived specifically for antibiotic usage. However, our paper uses an alternative model, with additional indicators such as prescription dose variation and certain socioeconomic and demographic factors found to increase model reliability.

The antibiotic dose was converted to a defined daily dose (DDD) using the conversion factors as laid down in the WHO/ATC.15

The annual average antibiotic daily prescribing rate (AAADPR) was then established by dividing the total DDD of oral antibiotics in each year by the population and 365 (days in the year). AAADPR was taken for the outcome in all the statistical models. The relation in AAADPR of each practice between 2016-17 and 2017-18 was used to establish a baseline level of short-term variation.

Public data for each GP/FD practice in 2017-18 was assembled including data published by NHS Digital for levels of patient comorbidity and condition control in the Quality and Outcomes Framework (QOF)13 and medical workforce characteristics from General Practice Workforce.16 Additional data included practice demographics and social deprivation analysis published by the Office of National Statistics.17 The patient experience data were collected from the annual NHS England GP patient Survey which also provided the ethnicity of responders, which was assumed to be representative of the whole practice.18 The longitude (East-West) and latitude (North-South) and local population density were also established for the postal code of the practice.

2.1 | Prescribing behaviour

The discretionary prescribing behaviour in each practice was characterised through selection of a number of factors over which clinicians may have control through choice, including the total number of unique different oral antibiotics being prescribed, the range of different dose strengths and formulations, the percentage of doses prescribed in liquid form, the compliance with NICE guidelines to reduce the percentage of quinolones, the average number of doses associated with each prescription, the average cost/dose and percent doses that are targeted to specific conditions.

All these factors were grouped into three classes:

- Population and location: Covering demographic data including practice population age (Percent<15 and Percent>65), gender, ethnicity (Percent Black and Minority Ethnicity), social deprivation index of multiple deprivation score, location data including latitude/longitude, average population density (population/square kilometre) in the practice address area.
- Practice characteristics: Practice size, medical comorbidity prevalence in 10 major long-term conditions, including diabetes/asthma/COPD, clinical outcomes as levels of glycaemic control achieved in diabetes and blood pressure in hypertension, overall patient experience satisfaction levels taken from the GP patient survey, and medical workforce characteristics (age, gender, country of qualification).
- Prescribing behaviour: Number of different unique antibiotic combination dose and delivery, the percentage used as a liquid, percentage use targeted on specific conditions, compliance with NICE antibiotic stewardship minimising percent of co-amoxiclav, cephalosporins & quinolones, number of doses included in each prescription, average cost/dose and seasonal variation in prescribing.

2.2 | Statistics

An MS-Excel 64-bit power pivot table was used to consolidate the various prescribing and population data and then Analyse-it add-in used to carry out the regression analysis. Multi-variate regression was used on the complete population of GP/FD practices in England in 2017-18. The number of practices was then restricted to those with sufficient patient numbers (>2000) to restrict sample outlier effect. Data were obtained from a variety of different sources for the same period and included the potential major sources of confounders on population demographics and local clinical behaviour. While this brought in some potential errors, both the variance captured by the statistical models and confidence levels achieved were high.

Factors in each of the above three classes were run initially together to establish the impact of each class on the in-year variability.

All the factors were then run backwards stepwise and those factors with p-value >0.01 were removed. The strength of the link between the factor and outcome in terms of antibiotic prescribing was identified by standardised beta value.

The potential opportunity identified within the model, of moving within the modifiable prescribing behaviour class was quantified by applying the regression coefficient to the difference between the current median level of performance to the level achieved by the top decile of GP/FD practices for each of the factors.
The trends in these prescribing behaviour factors over the last 5 years were examined and the 2017_18 regression coefficient was applied to see how this “optimal model” value compared with the observed overall reduction in oral antibiotic prescribing.

All data were publicly available and at a GP/FD practice level, with no patient-level data being utilised. As this was not an interventional study and no patient data or input was required, no ethics approval was applied for in regard to this study.

3 | RESULTS

3.1 | Cost and prescribing

Data from 9612 prescribing centres, with 33.5 million individual prescriptions, 419 million DDD, at an actual cost of £146 million were analysed. The reported total actual costs of the different antibiotics prescribed in 2017_18 are shown in Table 1. The greatest spend was on the antimicrobial treatment of urinary tract infections at £38 million, with the most prescribed class by DDD being broad-spectrum penicillin with 126 million DDD. In absolute numbers of unique different agents in different doses the total of 177 splits by 58 in broad-spectrum, 51 in targeted, 38 sparingly, and 30 in others.

Table 2 displays the variation across all the GP/FD practices whose data were analysed and highlights that the median practice uses 59 different unique agents/doses while the lowest decile uses 47 and highest decile practice uses 70.

We analysed in more detail data from 6988 practices recorded in QOF with more than 2000 patients on their register supporting a total recorded population of 58.7 million. The total spend on antibiotics in these practices was £136 million with 31 million prescriptions or 387 million DDDs. This was 3% lower in amount and 7% lower in value than the previous year 2016-2017. Dividing the total doses by the population and annual days of 365 gives a value

| TABLE 1 | National unique types and use and spend on different Antibiotics classes for the year 2017/18 |
|---------|---------------------------------------------------------------------------------------------|
| Type/class | Number antIB\(^a\) | Number formul. / dose\(^b\) | Number BNF codes\(^c\) | Total prescriptions | Total DDD | Total ACT cost |
| Broad | | | | | | |
| Broad-spectrum penicillins | 3 | 12 | 22 | 8 718 854 | 125 688 028 | £9 921 100 |
| Tetracyclines | 8 | 13 | 29 | 4 400 774 | 86 748 480 | £16 987 262 |
| Macrolides | 6 | 14 | 41 | 3 964 690 | 64 360 415 | £15 681 229 |
| Benzylpenicillin and phenoxymethyl-penicillin | 1 | 3 | 5 | 2 346 675 | 26 891 055 | £18 153 255 |
| Sulfonamides and trimethoprim | 5 | 16 | 19 | 2 600 104 | 21 268 961 | £3 557 998 |
| Targetted | | | | | | |
| Penicillinase-resistant penicillins | 2 | 6 | 10 | 3 965 503 | 31 750 525 | £16 633 031 |
| Urinary-tract infections | 4 | 11 | 26 | 3 636 635 | 23 637 265 | £37 776 986 |
| Metronidazole, tinidazole and ornidazole | 2 | 7 | 12 | 611 672 | 2 425 262 | £3 202 121 |
| Antituberculosis drugs | 8 | 21 | 31 | 50 753 | 949 433 | £1 699 005 |
| Antileprotic drugs | 3 | 6 | 6 | 27 442 | 638 599 | £1 849 033 |
| NICE guidelines (sparing) | | | | | | |
| Co-Amoxiclav | 1 | 8 | 14 | 1 430 897 | 19 301 384 | £3 162 405 |
| Quinolones | 6 | 12 | 22 | 646 146 | 6 665 202 | £3 480 726 |
| Cephalosporins | 7 | 18 | 44 | 834 165 | 4 877 924 | £1 652 430 |
| Other | | | | | | |
| Some other antibiotics | 12 | 19 | 27 | 59 258 | 1 808 194 | £9 908 714 |
| Mecillinams | 1 | 1 | 2 | 170 029 | 960 995 | £1 450 543 |
| Clindamycin and lincomycin | 1 | 7 | 11 | 77 286 | 841 047 | £1 737 261 |
| Aminoglycosides | 3 | 3 | 3 | 463 | 2 642 | £14 958 |
| Total | 73 | 177 | 324 | 33 541 346 | 418 815 410 | £146 868 066 |

Abbreviation: ACT, actual cost; BNF, British National Formulary; DDD, defined daily dose; NICE, National Institute for Health and Clinical Excellence.

\(^a\)Number of different unique antibiotic agents.

\(^b\)Number of different unique antibiotic agents plus dose level and formulation.

\(^c\)Number of different unique BNF codes.
**Table 2** Factors, their source, range and values that were initially tried in the multivariate analysis, plus those with low P values that were retained for the final model (overall model $R^2 = 0.58$, location factors alone model $R^2 = 0.3$, practice factors alone model $R^2 = 0.3$ and prescribing factors alone model $R^2 = 0.11$)

| Outcome                        | Source | Practice | Retained |
|--------------------------------|--------|----------|----------|
|                                | Source | Mean     | 10%ile   | 50%ile   | 90%ile   | Std β | P-value |
| **Values**                     |        |          |          |          |          |       |         |
| **Outcome**                    |        |          |          |          |          |       |         |
| AAADPR                         | GPP    | 0.018    | 0.013    | 0.018    | 0.023    |       |         |
| **Location**                   |        |          |          |          |          |       |         |
| Social deprivation (IMD)       | PHE    | 22.9     | 10.0     | 21.0     | 39.0     |       |         |
| Ethnicity BME                  | PHE    | 16.70%   | 0.60%    | 6.70%    | 50.60%   | -0.27 | <.001   |
| Population density /sq. km     | ONS    | 4197     | 190      | 3280     | 9400     | -0.11 | <.001   |
| Age % < 15                     | PHE    | 11.4%    | 8.9%     | 11.1%    | 14.3%    |       |         |
| Age % > 65                     | PHE    | 17.6%    | 8.7%     | 17.7%    | 25.9%    | 0.22  | <.001   |
| Gender % female                | PHE    | 50.0%    | 47.6%    | 50.3%    | 51.8%    |       |         |
| Latitude                       | ONS    | 52.40    | 51.11    | 52.25    | 53.80    | 0.11  | <.001   |
| Longitude                      | ONS    | -1.20    | -2.72    | -1.29    | 0.20     |       |         |
| **Practice**                   |        |          |          |          |          |       |         |
| List size                      | QOF    | 8470     | 3410     | 7560     | 14 390   | -0.23 | <.001   |
| %Register-cancer a             | QOF    | 2.7%     | 1.4%     | 2.8%     | 4.0%     |       |         |
| %Register-diabetes a           | QOF    | 7.1%     | 5.0%     | 7.0%     | 9.3%     | 0.19  | <.001   |
| %Register-Rh. arthritis a      | QOF    | 0.8%     | 0.5%     | 0.8%     | 1.1%     | 0.04  | <.001   |
| %Register-stroke TIA a         | QOF    | 1.8%     | 0.9%     | 1.8%     | 2.6%     |       |         |
| %Register-depression a         | QOF    | 9.8%     | 5.4%     | 9.4%     | 14.8%    | 0.03  | <.001   |
| %Register-chronic heart a      | QOF    | 3.2%     | 1.8%     | 3.2%     | 4.5%     | 0.07  | =.002   |
| %Register-chronic kidney a     | QOF    | 4.2%     | 1.9%     | 3.9%     | 6.9%     | -0.05 | <.001   |
| %Register-asthma a             | QOF    | 6.0%     | 4.3%     | 6.0%     | 7.5%     | 0.06  | <.001   |
| %Register-COPD a               | QOF    | 2.0%     | 0.9%     | 1.9%     | 3.2%     | 0.10  | <.001   |
| %Register-hypertension a       | QOF    | 14.3%    | 9.9%     | 14.5%    | 18.4%    |       |         |
| Control DM HbA1c % < 59 a      | QOF    | 71.6%    | 59.8%    | 72.8%    | 81.3%    | -0.04 | <.001   |
| Control HYP BP% < 150/90 a     | QOF    | 82.9%    | 76.0%    | 83.3%    | 88.8%    |       |         |
| Overall patient experience % good | GPPS  | 48.00%   | 29.0%    | 47.0%    | 68.0%    | 0.10  | <.001   |
| LTC patient confidence managing conditions % yes | GPP5  | 29.7%    | 19.0%    | 29.5%    | 40.6%    |       |         |
| MED WF-FTE/1000 patients       | GPW    | 0.518    | 0.296    | 0.495    | 0.748    |       |         |
| MED WF-FTE gender % male       | GPW    | 54.1%    | 22.2%    | 52.7%    | 100.0%   | 0.02  | =.007   |
| MED WF-HC age% < 40            | GPW    | 27.8%    | 0.0%     | 25.0%    | 60.0%    | -0.06 | <.001   |
| MED WF-HC age% > 55            | GPW    | 25.8%    | 0.0%     | 20.0%    | 57.1%    |       |         |
| MED WF-COQ %non UK             | GPW    | 28.9%    | 0.0%     | 16.7%    | 100.0%   | 0.02  | =.087   |
| **Prescribing**                |        |          |          |          |          |       |         |
| DDD/item                       | GPP    | 12.5     | 11.1     | 12.4     | 13.9     | 0.16  | <.001   |
| Spend/DDD                      | GPP    | £0.35    | £0.27    | £0.34    | £0.43    | -0.11 | <.001   |
| % Non-compliance               | GPP    | 7.2%     | 4.1%     | 7.0%     | 10.7%    | 0.02  | =.009   |
| % Targeted                     | GPP    | 14.1%    | 10.9%    | 14.0%    | 17.5%    | -0.13 | <.001   |
| % Liquid                       | GPP    | 25.4%    | 17.5%    | 24.6%    | 34.5%    | 0.29  | <.001   |
| Seasonality                    | GPP    | 1.2      | 1.1      | 1.2      | 1.4      | -0.03 | =.011   |
| Different antibiotics          | GPP    | 26.6     | 21       | 27       | 32       |       |         |
| Different antibiotics dose method | GPP    | 59.0     | 47       | 59       | 70       | 0.38  | <.001   |

Abbreviations: AAADPR, average annual antibiotic daily prescribing rate; BME, Black and Minority Ethnicity; DDD, defined daily dose; GP, Practice Characteristics; GPP, General Practice Prescribing; GPPS, General Practice Patient Survey; GPW, General Practice Workforce; IMD, Index of Multiple Deprivation; ONS, Office for National Statistics; PHE, Public Health England; QOF, Quality Outcomes Framework.

*P% Prevalence as reported in the Practice Disease Register in QOF.
of 1.8%, which assuming no waste, is the average percent spend on antibiotics at any one time. Dividing the total number of prescriptions issued and assuming no repeat or nurse prescriptions then the 33,807 full-time equivalent GPs during 2017-18 wrote on average 4.5 antibiotic prescriptions each working day.

There was data missing for some practices for some data sources restricting the final analysis to 5889 practices which supported 49.8 million patients in total. Data omission could be because of incomplete reporting and errors in database compilation in the data reporting pathway.

Figure 1A highlights the wide variation in AAADPR with top decile of practices prescribing more than twice as much / head population as those in the bottom decile.

Figure 1B shows the AAADPR relation in each practice between 2016_17 and 2017_18, where correlation with previous year prescribing accounted for 78% of the variation. This suggests that while each individual prescription is written for a specific incident, most of the local sources of variations in prescribing are coming from factors that are continuing over time.

We also found an underlying seasonality in the antibiotic prescribing year on year between 2013/14 and 2017/18 (Figure 2) with a mean 21% higher prescribing in the autumn and winter quarters (1st quarter is April-June 2nd quarter is July-September 3rd quarter is October-December and 4th quarter is January-March). This phenomenon was consistent year on year.

The separate multi-variate cross-sectional analysis by factors associated with location, practice and prescribing classes is shown in Table 2. Factors covering location and local population accounted for 30% of the variation in antibiotic prescribing, while factors covering practice characteristics and comorbidities also accounted for 30%, while factors covering prescribing behaviour accounted for 11% of the variation in prescribing.

The list of factors included in the regression analysis and those that remained with sufficiently low P values are shown in Table 2. This model (Figure 3) accounted for 58% of the overall variation in antibiotic prescribing. Practices with GREATER levels of prescribing in 2017/18 are associated with HIGHER use of percent liquid antibiotic, number of different antibiotic types, proportion of older patients on the GP list, proportion of people on the long-term condition register (Diabetes, COPD, Asthma, Depression, Rheumatoid Arthritis), doses of antibiotic/item, patient satisfaction, percent NICE compliance with antibiotic prescribing and a more northerly latitude.

Practices with LOWER levels of prescribing in 2017/18 are associated with HIGHER non-white ethnicity, practice size, population density, percent targeted antibiotics, spend/DDD, percent of diabetes patients with glycaemia on QOF target, percent younger GPs in the practice and greater seasonal variation summer to winter in antibiotic prescribing.

### 3.2 Potential behavioural change opportunities

Based on this analysis there is an opportunity for GP practices to review and improve their antibiotic prescribing behaviour in line with the top decile of GP practices (Table 3). Aspirationally, if all GP practices were to align with top decile practice behaviour, there is a national opportunity to reduce overall antibiotic prescribing by 31%

These top decile behaviours or ‘simple rules’ include:

(i) Reduce the total number of different unique oral antibiotics classified by medication, dose and method being prescribed to 47 (-12%)
(ii) Reduce the amount of liquid antibiotics to 18% of the total (-6%) 
(iii) Reduce average dosage in each prescription to 11 DDD (-4%)
(iv) Increase targeted antibiotics ie linking antibiotic prescribing to a specific diagnosis to 18% of the total (-4%)
(v) Reduce low-cost antibiotics and so increase average spend/DDD antibiotics to £0.43 (-3%)
(vi) Reduce NICE non-compliance to 4% (-1%)
(vii) Reduce prescribing in spring/summer to increase seasonal variation to 137% (-1%)

Year on year change analysis (Figure 4) shows the trends over the last 5 years in prescribing behaviour. These highlight decreases of 3% in the variety of unique antibiotic formulations being used along with a decrease in 10% in numbers of antibiotic prescriptions resulting in a 4% fall in doses, because of a 6% increase in doses/prescription. Growth in percent of liquids and percent of targeted antibiotics was steady over the 5-year period.

A model expected prescribing value was calculated by applying the regression coefficients from this years statistical model to value for each factor in previous years to estimate how much the annual changes in those annual factor values affected overall prescribing, this analysis shows that actual prescribing is declining faster than this model would predict, suggesting that other changes outside the scope such as updated guidelines and closer monitoring are having an impact.

### 4 DISCUSSION

We have found that differences between GP practices in terms of antibiotic prescribing are associated with non-discretionary factors outside clinicians’ control including older age of people on the practice list, a higher proportion of white ethnicity; higher numbers of people on the long-term condition register, lower population density and more northerly latitude. Variation in the gender and age profile of the population, as traditionally reflected in the STAR-PU measure, contributes only a minor part of that effect with most influence coming from ethnicity, location and general health of the local population.

In relation to these non-modifiable factors, the link between the age profile percent>65 years old of the practice and more antibiotic prescribing is not unexpected. We accept that one of the consequences of the Covid-19 pandemic will be that anyone in the older age groups is going to be very concerned about the potential for infections to be life-changing or life-threatening and therefore may...
well want to have antibiotics in any circumstances. However, clinician judgement remains a significant factor in modulating antibiotic prescribing.

That practices with a higher proportion of BME individuals prescribed less antibiotics, with greater white ethnicity associated with higher antibiotic prescribing, reflects behavioural prescribing trends reported by Public Health England in ESPAUR. This report also identifies a similar degree of seasonal variation as found in this study.

The link between more northerly latitude and greater antibiotic prescribing at a GP practice level is significant and suggests factors such as climatic and cultural differences across the latitudes of England may play a role. This is consistent with other studies that have found a link between climatic temperature and antibiotic resistance. Access to GP training day updates in more outlying rural areas of the north could also be a factor. Practices in areas of higher population density as found in towns and cities vs more rural locations prescribe relatively less antibiotics which given higher infection transmission risk rates appears counter-intuitive. This effect has been previously identified and been linked to the increasing use of antibiotics in animals creating a more resistant environment. Further systematic qualitative exploratory work is required in order to elucidate the potential causes for these and the other demography related differences that we report.

A younger workforce (GPs under the age of 40) was also associated with less antibiotic prescribing. This has been described in an important paper by Ahluwalia et al. GP training practices prescribed fewer antibiotics, representing a reduction of 6.2% from the median.
A thorough evaluation of antibiotic prescribing was conducted by van Staa’s group, who studied more than 8 million patient records in the UK. Findings were similar to this study in that much of the variation came from the environmental factors. However, other factors such as the type of antibiotic/patient survey/age/gender of the doctor were not included in the model. The authors showed that GPs with a higher workload are more likely to prescribe antibiotics. The researchers saw that 50% of the variation in prescribing rates between practices could be explained by differences in the incidence of common infections such as respiratory tract infections and urinary tract infections. Nevertheless, practice location, duration of GP consultation and number of GPs per thousand consultations also accounted for 40% of the variation in prescription rates.

Antibiotic choice in prescribing is a complex process influenced by factors affecting all the actors involved, including physicians, other healthcare providers, the healthcare system and the general public. These factors closely interact with each other. However, this should be put in the context of a 13% drop in GP prescribing of antibiotics over the last 5 years.

As we found, in the recently published study by Dolk et al in 2018, antibiotic prescribing rates vary considerably between GP practices. In the Dolk study, 46% of prescriptions were linked to conditions of the respiratory tract, with infections of the urogenital tract and skin/wounds accounting for 22.7% and 16.4%, respectively. In terms of antibiotics prescribed, penicillin accounted for 50% of all prescriptions, followed by macrolides (13%), tetracyclines (12%) and trimethoprim (11%).

One difference of this study from previous studies is the inclusion of not just the number of prescriptions, which is the standard way of aggregating prescribing, but also the actual amount of drug being prescribed, as measured by DDD for that molecule. This indicates that each prescription for liquid antibiotic contains four times as much in dose terms than tablets/capsules, meaning non-consumption may result in significant wastage.

From these results, a number of provisional recommendations can be drawn to inform and shape more sustainable antibiotic prescribing and lower future AMR rates. Achieving a prescribing profile that reflects that of the average top decile GP practice in terms of antibiotic prescribing could reduce antibiotic use by 31% or 10 million

| TABLE 3 Identification of potential opportunities in prescribing decision changes by applying regression coefficients to median and top decile values of prescribing behaviour factors |
|---------------------------------|--------------|----------------|-----------------|------------------|-----------------|
| **Regression coefficient.**     | **Median value** | **Target 10%ile value** | **Potential change in AAADPR** | **% Current AAADPR** |
| Decrease Distinct antibiotic, dose, methoda | 0.000 18 | 59 | 47 | −0.002 1 | −12 |
| Decrease Percent liquid | 0.0170 2 | 0.25 | 0.18 | −0.001 1 | −6 |
| Decrease DDD/prescription | 0.000 6 | 12.5 | 11.1 | −0.000 8 | −4 |
| Increase Percent targeted | −0.019 1 | 0.14 | 0.18 | −0.000 7 | −4 |
| Increase Spend £/DDD | −0.006 34 | 0.35 | 0.43 | −0.000 5 | −3 |
| Decrease Percent NICE non-compliant | 0.003 77 | 0.07 | 0.04 | −0.000 1 | −1 |
| Increase Seasonality + sum) | −0.000 66 | 1.21 | 1.37 | −0.000 1 | −1 |
| Total | −0.005 7 | 23 | 23 | −0.000 1 | −31 |

Abbreviations: AAADPR, average annual antibiotic daily prescribing rate; DDD, defined daily dose.

*aThis is related to an average practice.
prescriptions/year. Changes in discretionary prescribing behaviour could be achieved through a set of ‘simple rules’ including reducing the number of different antibiotic agents being chosen/prescribed, more limitations on the use of liquids, more careful evaluation of the number of doses within each prescription, reduction in use of broader spectrum antibiotics, reducing use of very low-cost agents and tighter controls on use of antibiotics in summer. The summer factor is linked to the finding that GP practices with higher seasonality of prescribing (ie higher relative prescribing in the winter) tend to prescribe less antibiotics overall. Those without seasonality effects appear to demonstrate relative over-prescribing in the summer, considering that winter prescribing should be associated with greater use of antibiotics including less appropriate use such as for viral infections.

Other factors that might be considered include:

- **Lack of time to access or comply with clear local guidelines** which could result in increased use of different variants and doses, increased use of less expensive more generic antibiotics showing up in lower spend per dose, lower use of targeted antibiotics and higher relative prescribing in summer (this might suggest antibiotics sometimes being used for other non-infectious symptoms such as allergies/hay-fever). Other guidelines often not achieved include national urinary tract infection 3-day dose targets, which can also contribute to higher usage and longer term AMR rates.

- **Overuse, leftovers, and wastage.** The number of doses in each liquid prescription is up to four times higher than in tablets, meaning higher liquid use could result in more residual left at the end of the course with consequent opportunities for future self-medication. However, liquid antibiotics could be associated with localities with higher age groups and subsequent higher numbers in end-of-life care which could require higher liquid antibiotic prescribing.

- **Increased use of point of care testing** to more accurately establish the need and validity of appropriate antibiotic prescribing.

- **Failure of strategic healthcare organisations** such as Clinical Commissioning Groups (CCGs) to fully implement antibiotic prescribing guidelines—a recent study by Croker et al found that localities in England with little evidence of prescribing change were associated with little or no active implementation of guidelines to primary care by Clinical Commissioning Groups.24

We suggest that the development of a benchmarking tool to inform GP practices of comparative antibiotic prescribing performance could enable reduced levels of antibiotic prescribing at an individual practice level and cumulatively at a national level, with a subsequent positive impact on AMR rates. A 50% or more reduction in antibiotic prescriptions is achievable but would require a fundamental change in prescribing patterns in primary care.

Our findings reflect a wider range of factors potentially influencing physicians’ antibiotic prescribing, revealing it to be a complex process associated with both discretionary (prescriber-related) and non-discretionary (environment-related) factors.

### 4.1 | Strengths

We were able to look at national-level data for prescribing in England across nearly 6000 GP practices in relation to all prescriptions issued. In the UK all systemic antibiotics can only be obtained with a prescription from an accredited healthcare professional. Primary care is responsible for around 80% of all antibiotic prescribing in the UK’s National Health Service.72

### 4.2 | Limitations

A caveat in any conclusions that are drawn from our work is that we have not been able to evaluate any (positive or negative) outcomes of
However, this does not necessarily equate to overall improved infection control and the optimal comparative level of antibiotic use which balances this control with reduced AMR rates is unknown. Furthermore, real-world studies cannot infer direct causality compared with, for example, randomised controlled studies. However, real-world data modeling provides greater insight into actual service performance that could not be achieved with controlled studies. With this real-world analysis methodology, there are also potential confounding factors that are inherent in any retrospective study, although this study was designed to minimise the potential impact of such factors.

Healthcare systems influence antibiotic prescription, both directly, via implemented policies/guidelines, and indirectly through the impact of the short duration of clinical appointments and patients’ perceptions of their healthcare needs. We hope that this paper will inform policy-makers in healthcare both in the UK and elsewhere in the world in terms of enabling improved antibiotic use.

5 | CONCLUSIONS

We have shown that while choice is an important factor in antibiotic prescribing performance, non-discretionary factors such as demographics, location and comorbidities of the local population are also associated with antibiotic prescribing patterns in GP practices. The authors acknowledge the daily challenges that GPs face, with often conflicting tensions of healthcare policy, prescribing guidelines, overcrowded surgeries and patient demands. However, by addressing certain modifiable discretionary factors, or ‘simple rules’, there is a potential opportunity to reduce antibiotic prescribing in primary care by 31% or the equivalent of 10 million prescriptions/year in England, equivalent to all practices achieving the same antibiotic prescribing profile as the top decile practices in this study. In turn, this could reduce future AMR rates and build a more sustainable approach to the use of antibiotics.

By shedding new light on the antibiotic prescribing process, we hope to contribute to the development of new and more effective strategies and tools to optimise antibiotic prescribing, while also addressing in some small way global concern about current and future antibiotic resistance.

CONFLICT OF INTEREST

None of the authors has anything to disclose in relation to competing interests. No external funding was received in connection with the research and compilation of this paper.

AUTHOR CONTRIBUTION

MS, MD, and AHH conceived the study. MS collected the data. MS and ML conducted the data analysis. MS, ML, MD, EFM, AB, TVS, SGA and AHH all contributed to the writing of the paper. SGA, EFM, AB and TVS provided review and feedback on the manuscript.

TRANSPARENCY STATEMENT

Dr Heald as the corresponding author affirms that this is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ETHICS STATEMENT

As we used publicly available and GP level data, it was not necessary to seek Ethics Approval for this study. This was not a clinical trial.

ROLE OF THE SPONSOR

There was no research sponsor for this study.

DISSEMINATION OF STUDY RESULTS TO PARTICIPANTS

Dissemination to specific participants will not be possible as all data were anonymised and at the GP practice level.

PATIENT CONSENT

This was not applicable.

DATA AVAILABILITY STATEMENT

We used publicly available data for the analysis and findings that we report in this paper.

ORCID

Adrian H. Heald https://orcid.org/0000-0002-9537-4050

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