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Abstract

Social inequalities are widened by climate change, which increases extreme temperature events that disproportionally affect the most vulnerable people. While the diseases impacted have been reviewed in the literature, how this reflects upon pharmaceutical consumption remains unknown. We assess that effect on a panel of the most prescribed drug classes in terms of volume in the National Health Service (NHS) database.

A retrospective econometric analysis of NHS prescription data was carried out, focusing on antibiotics, antidepressants and bronchodilators (drugs associated to priority diseases in addition to being among the most prescribed ones) between 2011 and 2018. Data linkage enabled prescriptions to be related to the Index of Multiple Deprivation (IMD), Disability Adjusted Life-Years (DALYs) and temperature data. The analysis was then undertaken at Lower Layer Super Output Areas (LSOAs) level, using fixed-effect negative binomial regression models.

Our results show that prescription rates were higher across most deprived LSOAs, even after adjusting for the associated disease DALYs. In addition, prescription volume also progressively increased under colder temperatures below 15 degrees Celsius, with an exacerbated effect in most deprived areas.

Therefore, health inequalities in England affect prescription volumes, with higher levels in most deprived areas which are not fully explained by morbidity differences. Lowest temperature conditions appear to intensify vulnerabilities while hot temperatures do not increase these differences in terms of prescriptions. Populations residing in most deprived LSOAs could be more sensitive to environmental variables, leading to higher consumption of medicine under cold temperature and increased air pollution.

Keywords: health inequalities; medicine prescriptions; England, temperature; spatial analysis; general practices; NHS

INTRODUCTION

The socio-economic gradient combines multiple factors, such as education, income and housing environment, driving health inequalities [1]. Reducing health inequalities has become a legal duty since 2012 [2] and a growing body of literature illustrates its morbid and costly consequences in England. Despite awareness of this issue, a considerable health gap remains between poor and rich in the UK. The UK public is strongly averse to those persistent health inequalities between socio-economic groups, especially when it comes to life expectancy [3].

Research carried out by the Health Foundation, an independent charity carrying out research to improve health and the healthcare system in the UK and to inform effective policymaking, showed that people living in the most socio-economically deprived areas are more likely to develop multiple health conditions ten years earlier, and live nearly 19 fewer years in good health, than those living in the most privileged neighbourhoods [4, 5]. However, the focus has been on inequalities in access to services or in the outcomes, with less attention given to prescriptions. A 2016 survey report in England highlighted that medicine consumption was higher in more deprived areas [6]. In terms of health inequality, while it certainly highlights the inequalities in outcome, it is not clear whether it also reflects inequalities in access to care or if instead less healthy individuals are able to access the type of care they need. Answering this question requires taking into account deprivation as well as the economic burden of disease.

In this study, we explore how socio-economic gradient and temperature interact to further impact the prescription volume of medicines, an analysis motivated by the current issue of climate change increasing the frequency of extreme temperature events. Climate change and socio-economic inequalities are intrinsically linked. Their interaction, known as 'climate justice', remains an understudied topic of growing importance, especially when it comes to 'within-country' inequality – as opposed to 'across countries' inequalities. Climate change is expected to have a heterogeneous impact on populations [7] according to their level of wealth and health states and their access to healthcare, widening inequalities. By increasing the frequency and severity of heatwaves and cold spells, climate change affects the population's health and well-being in various ways.

For instance, the number of general practice (GP) consultations and emergency department visits doubles during heatwave years [8]. The number of admissions for respiratory conditions and the rate of cardiovascular mortality also increase with heatwave occurrences [9]. Cold temperatures increase the number of respiratory consultations by up to 19% for every decrease in one degree Celsius under 5 °C [10], as well as the mortality rate from cardiorespiratory causes, independently of seasonality [11]. It is also known that extreme temperatures can disrupt the fragile balance and increase the mortality rate of patients treated for long-term conditions, such as mental health illnesses [12]. However, if the impact of extreme temperatures on disease rates has been considered, how this reflects upon pharmaceutical consumption is not yet fully understood [13].

In terms of health expenditures, and in particular, pharmaceutical consumption, we observe that 1.12 billion prescription items were dispensed in England in 2019, resulting in a total cost of £9.08 billion for the National Health Service (NHS) (£248 million more than the previous year) [14]. Since 2010, the total spending on medicines rises, on average, by 5% a year [15].

The three drug classes we chose to analyse play a particularly important role in the economic burden of medicine in England: bronchodilators are essentially prescribed to treat the symptoms of long-term diseases, such as asthma and chronic obstructive pulmonary disease (COPD). Chronic diseases are an economic burden for individuals but also for society. They lead to direct costs from medical care, indirect costs due to loss of human resources (work loss, disability pensions, etc.), and intangible costs related to the psychological impact of the illness [16]. In the UK, respiratory diseases account for 6% of the total healthcare budget distributed between £9.9 billion direct costs and £1.2 billion indirect costs related to loss in productivity [17].

COPD, more specifically, affects around 1.2 million people in the UK, leading to a £1.9 billion treatment cost mostly represented by inhalers [18]. Indeed, four of the top 10 most dispensed chemical substances by total cost are bronchodilators [19].

Antidepressants are associated with an NHS spending of £780,000 a day [20], resulting in a total cost of £8.8bn in 2018. The overall number of antidepressant items prescribed has almost doubled in the last ten years, from 36 million in 2008 to 70.9 million prescriptions in 2018 [21]. Antidepressants have even shown the most important increase among all medicine classes for a number of consecutive years [22].

Finally, if antibiotics are considered to be relatively affordable medicines, the economic burden of antimicrobial resistance must now be taken into account. Resistance to antibiotics increases drug usage and hospital admissions as well as their length of stay [23]. Even though more research is needed to better assess the economic burden of antimicrobial resistance, it has been estimated by a recent systematic review to range from $21,832 per case to over $3 trillion in gross domestic product loss [24].

To better anticipate temperature-related health outcomes across the socio-economic gradient in England, and identify public health priorities, this paper aims to analyse high-volume NHS prescription data, including all GP practices over eight years, linked to socio-economic data captured by the Index of Multiple Deprivation (IMD), Disability-Adjusted Life Years (DALYs) from the global burden of disease (GBD) study [25] and temperature data from the MetOffice. Our hypothesis was that healthcare needs and therefore prescription volumes may increase during periods characterized by extremely high or low temperatures (U-shaped curve), and that this pattern could be emphasized in most deprived areas where individuals are most sensitive to environmental variables.

In addition, these medicine classes were chosen for their prescription volume being among the highest in the NHS database, and their association with a priority disease, according to the World Health Organisation (WHO). Reasons for inclusion are: the major threat of antimicrobial resistance for antibiotics; the lack of awareness associated with the high burden of depression in Europe for antidepressants; and finally, the increasing burden of disease (due to smoking and industrialization) and considerable financial cost of COPD [7, 26] and asthma [27] for bronchodilators.

Section 1 introduces the methods with a description of the data, their preparation, the regression model and the statistical analysis. Section 2 presents the results in two distinct paragraphs: the first one focuses on the association between socio-economic inequalities and pharmaceutical consumption in England, while the second paragraph presents how the interaction between deprivation level and temperature affects prescribing rates. The last section discusses our findings in light of the existing evidence and acknowledges the strengths and limits of our work.

METHODS

1. Data

Data linkage at lower layer super output (LSOA) geographical level enabled the combining of four data sources: NHS prescriptions; monthly average temperatures; Index of Multiple Deprivation (IMD); and DALYs.[1]

a. NHS prescription data

This is a retrospective analysis of prescribing data from all general practices in England, retrieved from the NHS Business Services Authority prescription database, from January 1, 2011 to December 31, 2018. [28]

The NHS prescription database consists of completely anonymized dispensed prescriptions at practice level, written by professional prescribers all over England. It gathers, on average, 10 million records per month of all medicines, dressings and appliances, defined by their unique 15-character British National Formulary (BNF). Our dependent variable is the average number of items dispensed per day, aggregated per LSOA, and normalized per thousand inhabitants to account for each LSOA's exact population. We focus on three medicine classes: the antidepressant category (section 0403 of the BNF classification), which includes tricyclic antidepressants, monoamine oxidase inhibitors and selective serotonin reuptake inhibitors; bronchodilators (BNF0301); and antibacterial drugs (BNF0501, including all antibiotic subclasses).

b. IMD data

Deprivation is captured by the IMD (2019 version) released by the Ministry of Housing, Communities and Local Government [29]. It covers seven weighted deprivation domains: income (22.5%); employment (22.5%); health deprivation and disability (13.5%); education (13.5%); crime (9.3%); barriers to housing and services (9.3%); and living environment (9.3%). The IMD is available at LSOA level, with each LSOA representing approximately 1,500 individuals. LSOAs are ranked according to their relative degree of deprivation compared to that of other areas. They can be further categorized into quintiles and assigned a value from 1 (most deprived) to 5 (least deprived) [30]. A postcode was missing from <0.1% of all practices and thus they could not be matched to their corresponding IMD quintile.

[1] Data sets can be accessed from the following links: https://digital.nhs.uk/data-and-information/publications/statistical/practice-level-prescribing-data for NHS prescribing data, https://www.metoffice.gov.uk/research/climate/maps-and-data/data/index for MetOffice temperature data, https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019 for IMD government data and http://ghdx.healthdata.org/gbd-results-tool for Global Burden of Disease data.

c. Temperature data

Daily diurnal air temperatures were obtained from the Meteorological Office database [31], keeping only observations with an approved quality control (referred to as Version 1) and excluding the other versions.

From daily observations, monthly mean temperatures were then computed for every temperature station, as long as they had a minimum of 20 different days measured within a single month (otherwise the station was considered as unreliable and dropped from the data).

For each practice, the closest temperature stations were identified by finding the smallest Haversine distances between this practice and the set of available weather stations. The Haversine formula calculates a distance between two sets of longitude and latitude coordinates. The practices' coordinates were retrieved using the centroid of postcodes linked to the practices in the NHS database.

A monthly average temperature was then calculated for each GP postcode by using the values of the five closest temperature stations and the inverse distance weighting (IDW). IDW and Haversine distance are typically used in the literature to provide local average weather information.

An average using the temperatures obtained for all GP practices located within each LSOA was then calculated.

It is known that weather variables often have a non-linear shape. To account for this specificity, the continuous temperature was transformed into a binned variable, assuming that the impact of temperature on prescriptions was constant in the range of each bin.

In order to allow the observation of threshold effects, ten equal-sized bins were created (each one representing a decile of the temperature distribution, extending from 1.5 and 26.9 degree Celsius). The reference bin was arbitrarily chosen as the one containing a temperature of 15 degrees Celsius, as this is the accepted global average surface air temperature on Earth.

d. DALYs data

In order to better understand whether differences in prescription volume across the social gradient are related to real differences in the population health or not, the model was further adjusted for DALYs. Disability Adjusted Life Years rates were obtained from the GBD tool [32]. For each model, the appropriate DALY was chosen to adjust for the disease (or cause of disease) related to the specific medicine class investigated. Namely, the model was adjusted for DALYs attributable to asthma, COPD and air pollution (including ambient particulate matter, ambient ozone and household air pollution) when investigating bronchodilators, for DALYs attributable to depressive disorders when analysing antidepressants and for DALYS attributable to enteric, sexually transmitted, skin, and respiratory infections when fitting the model investigating the antibiotic class. DALYs were available at local authority district (LAD) level only, therefore each LSOA was associated with its corresponding LAD before analysis. As a result, LSOAs located in a same LAD were attributed a similar DALY rate value.

e. Demographic data

Data linkage also enabled each LSOA to be linked to its exact population, the proportion of women and the proportion of inhabitants aged more than 65 years old. Having the exact population per LSOA allowed normalizing the dependent variable (number of items) and expressing it per thousand inhabitants. Both proportions of women and older individuals were included as categorical predictors in the full model, in order to avoid any bias due to LSOA different demographic structures.

No ethical approval was required as all data sets analysed are publicly available.

2. Model design and statistical analysis

The following fixed-effect negative binomial model with a maximum likelihood estimation was implemented, in order to account for the overdispersed structure of prescription data:

Let $Y_{p,m,y}$ denote the dependent variable, corresponding to the average number of items prescribed per day for a thousand inhabitants, in practices located in a given LSOA, over a specific month of a given year. The subscripts l, m, and y refer to the LSOA between 1 and 5, month between 1 and 12, and year between 2011 and 2018, respectively. $Y_{p,m,y}$ is assumed to follow a negative binomial probability distribution with mean $\mu_{l,m,y}$. In the case of a regression model, $\mu_{l,m,y}$ depends on explanatory variables in the following way:

$$\log(\mu_{l,m,y}) = \beta_0 + \beta_1 * IMD_l + \beta_2 * DALY_{ly} + \beta_3 * Pf_{ly} + \beta_4 * Pold_{ly} + \beta_5^{14} * temp\_bin_{lmy} + \alpha_m + \alpha_y + SE(\bar{Y})$$

Explanatory variables include IMD_l, the IMD quintile associated with a specific LSOA with the 5th quintile (least deprived) used as reference, $DALY_{ly}$ the Disability Adjusted Life Years rate, $temp\_bin_{lmy}$ a categorical variable with 10 levels representing the average temperature at each LSOA, Pf_{ly} the proportion of females per LSOA, $Pold_{ly}$ the proportion of individuals aged more than 65 years old per LSOA, α_m and α_y the time fixed-effects accounting for the month and the year, respectively, and $SE(\bar{Y})$ the error clustering at month level. Backward stepwise selection enabled choosing the explanatory variables included in the full model, which was run separately for the three drug classes analysed.

The analysis was then performed using three models for each medicine class (denoted, respectively, model (i), (ii) and (iii)): (i) the average number of items per day per thousand inhabitants in each LSOA (prescription volume) was modelled as a function of the IMD; (ii) the monthly average temperature and GBD explicative variables were added (full model); and (iii) the step-2 model (ii) was run separately on two subgroups of the data – IMD 1 LSOAs (most deprived) and IMD5 LSOAs (least deprived) – in order to focus on the differential impact of temperature on both ends of the socio-economic gradient. In all models, month and year fixed-effects were included in order to remove the impact of seasonality and other variables exhibiting trends over the years. All models were also adjusted for the proportion of women and individuals aged 65+ per LSOA.

The β coefficients were exponentiated to give an incidence rate ratio (IRR), which can be interpreted as the ratio of expected counts, and its 95% confidence interval (CI) .[2] An IRR greater than 1 (less than 1) refers to a higher (lower) prescription volume under the considered condition.

A variable with a p-value of less than 0.05 was considered significant. However, as we analysed a data set of very consequent sizes, we preferred to rely on the practical significance in terms of IRR instead of p-values. Indeed, in the context of very large data, small p-values are easily reached [33].The goodness of fit of each model was assessed by D^2 squared values, which represent the proportion of deviance explained by a generalized linear model.

Pearson's r squared between prescription volumes, DALY rates and IMD scores were also calculated.

All data analyses were conducted using R software (version 3.5.2).

[2] The β coefficients of a negative binomial regression can be interpreted as the difference between the logarithm of expected counts for one unit change in the predictor variable (a one decile change in IMD here). Since the difference of two logarithms is equal to the logarithm of their quotient, we can interpret the difference as the ratio of expected counts. The term 'rate' is relevant to the structure of our panel data (volume of prescription per time and space).

RESULTS

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Two types of results will be presented: first with regard to socio-economic gradient and pharmaceutical consumption; and second concerning socio-economic gradient and temperature interaction on pharmaceutical consumption.

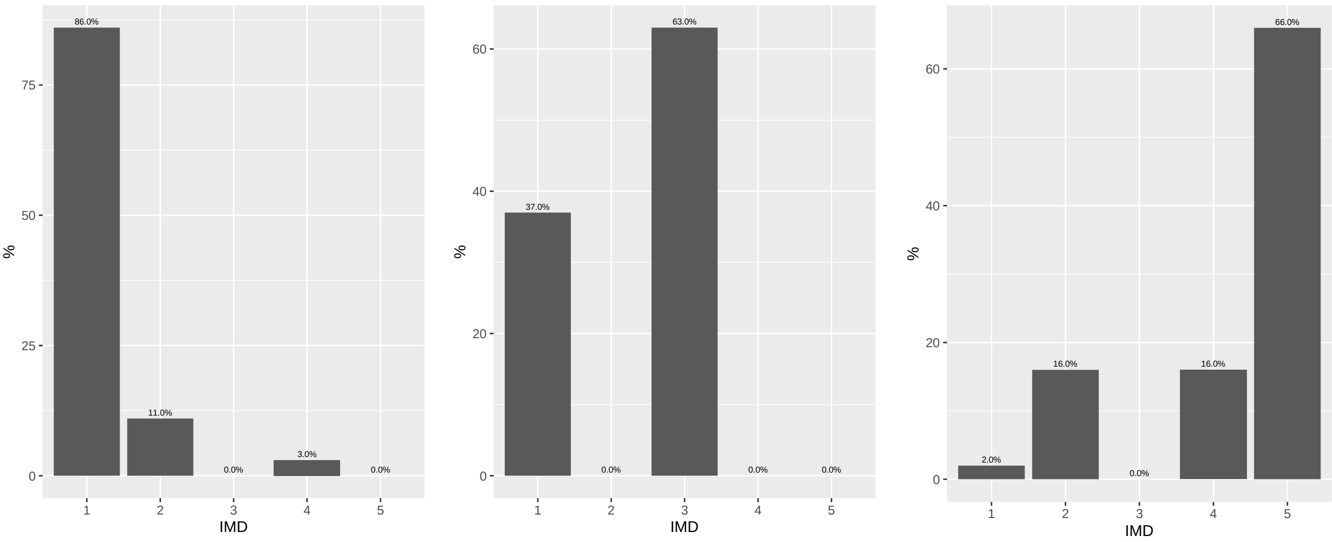
1. Socio-economic gradient and pharmaceutical consumption

a. General trends

Table 1 and Supplementary Tables 2 and 3 show the results (IRR with their confidence intervals) of the models, for antibiotics, bronchodilators and antidepressants, respectively.

After controlling for the exact population, the proportion of people aged 65+ and the proportion of women per LSOA, antibiotics, bronchodilators and antidepressants were all significantly more prescribed in deprived LSOAs, especially in the most deprived quintile (IMD1), where prescribing rates were, respectively, 24% (95% CI: 23–25), 105% (95% CI: 104–107) and 65% (95% CI: 64–66) higher than in IMD 5 LSOAs – see column 1 of Table 1, and Supplementary Tables 2 and 3. Figure 1 (a,b,c) shows how the 100 LSOAs prescribing the highest rates of antidepressants, bronchodilators and antibiotics, respectively, are distributed across the socioeconomic gradient: 86%, 37% and 2%, respectively, belong to the first (most deprived) IMD quintile. Therefore, a large majority of LSOAs prescribing the highest rates of antidepressants were located in the most deprived quintile. However, it should be noted that this graph does not take into account the age distribution of the population in each LSOA (while our regression model does). Since the proportion of elderly people, more sensitive to infections and their complications, tends to be higher in richer LSOAs (Pearson's correlation coefficient between IMD score and proportion of people aged 65+, r=0.35), this could explain why LSOAs prescribing the highest rates of antibiotics are mostly located in least deprived areas.

In the next subsections, the three medicine classes analysed are examined separately.



(a) Antidepressants (b) Bronchodilators (c) Antibiotics

Figure 1. IMD quintiles distribution of the 100 LSOA with the highest antidepressant, bronchodilator and antibiotic prescription rates

b. Antibiotics

Antibiotic prescription rates showed a 9% general decrease in England between 2011 and 2017, with a similar trend for most and least deprived areas.

Even after accounting for temperature and DALYs attributable to skin, sexually transmitted, enteric and respiratory infections, antibiotics remained more prescribed in deprived areas by 29% (95% CI 28–30) – see column 2 Supplementary Table 2. The fact that DALYs failed to explain the higher prescription volume in most deprived areas suggests that the excess in prescription could be unrelated to a proper health need.

c. Bronchodilators

The prescription volume of bronchodilators increased by 14% between 2011 and 2017. This increasing trend was homogeneously found across all socio-economic levels.

With regard to the prescription rate, IMD1 had an IRR) of 2.05 (95% CI, 2.04–2.07) compared with IMD5, corresponding to an increase in prescription of 105% (95% CI, 104–107) – see column 1 Table 1.

Air pollution DALY rate and prescription volume of bronchodilators were correlated (Pearson's r squared: r=0.26), especially in the most deprived areas (r=0.28 in IMD1 versus r=0.10 in IMD5).

Table 1 also shows that DALYs successfully explained part of the difference in prescription volume observed between IMD quintiles (model (ii)). Indeed, the IRR comparing most and least deprived areas was lowered from 2.05 (95% CI, 2.04–2.07) to 1.70 (95% CI, 1.69–1.70), while the D2 increased from 11% to 15%, suggesting a better goodness of fit of the model when controlling for the GBD variables (DALYs) and for the temperature. This suggests that higher DALY rates due to COPD and air pollution could partly explain the increased need for bronchodilators in most deprived areas.

Table 1: Models' estimate for bronchodilator prescriptions. (IRR and 95% confidence intervals)

	IMD model (i)	**IMD controlling for GBD and climate** model (ii)	**Focus on IMD1 (most deprived)** model (iii)	**Focus on IMD5 (least deprived)** model (iii)
Number of observations	561 023	561 023	140 374	86 880
IMD 1	2.05 (2.04–2.07)***	1.70 (1.69–1.71)***	X	X
IMD 2	1.46 (1.45–1.47)***	1.35 (1.34–1.36)***	X	X
IMD 3	1.22 (1.21–1.23)***	1.16 (1.15–1.17)***	X	X
IMD 4	1.11 (1.10–1.12)***	1.08 (1.07–1.09)***	X	X
IMD5	reference	reference	X	X
Prop 65+	14.95 (14.43–15.49)***	5.00 (4.92–5.08)***	11.22 (10.87–11.57)***	2.77 (2.72–2.82)***
Prop females	1.40 (1.37–1.42)***	2.38 (2.33–2.42)***	0.44 (0.42–0.45)***	3.4 (3.19–3.63)***
Year	Fixed effect	Fixed effect	Fixed effect	Fixed effect
Month	Fixed effect	Fixed effect	Fixed effect	Fixed effect
Asthma rate DALY	X	0.9997241 (0.9996918–0.9997564)***	0.9989604 (0.9988991 – 0.9990216)***	1.0000349 (1.0000027–1.0000672) *
Air pollution DALY rate	X	0.9998915 (0.9998643–0.9999187)***	X	0.9996709 (0.9996450–0.9996968) ***
COPD DALY rate	X	1.0007410 (1.0007260–1.0007559) ***	1.0008554 (1.000839–1.0008712)***	1.0004708 (1.0004543–1.0004873) ***
T1: Temp 1.5–7.3	X	NS	1.16 (1.06–1.26)***	NS
T2: Temp 7.3–8.8	X	NS	1.13 (1.06–1.21)***	NS
T3: Temp 8.8–10.2	X	NS	1.08 (1.03–1.15)**	NS
T4: Temp 10.2–12.3	X	1.03 (1.01–1.06)*	1.08 (1.05–1.11)***	NS
T5: Temp 12.3–14.4	X	NS	1.03 (1.01–1.05)**	NS
T6: Temp 14.4–16.3	**reference**	**reference**	**reference**	**reference**
T7: Temp 16.3–18	X	0.97 (0.94–0.99)*	0.93 (0.91–0.95)***	0.97 (0.95–0.99)*
T8: Temp 18–19.5	X	0.95 (0.91–0.99)*	0.91 (0.89–0.93)***	NS
T9: Temp 19.5–21.1	X	0.97 (0.94–0.99) *	0.88 (0.86–0.90)***	NS
T10: Temp 21.1–26.9	X	0.91 (0.88–0.95)***	0.84 (0.82–0.87)***	0.95 (0.91–0.99)*
D2	0.11	0.15	0.15	0.04

*** corresponds to variable significance of p<0.001.
'X' denotes non-included variables in the model.–

d. Antidepressants

Prescription volume of antidepressants rose by 45% between 2011 and 2017. This increase was found to be slightly sharper in most deprived LSOAs (47%) when compared to least deprived ones (43%).

As expected, the prescription volume of antidepressants was positively correlated with the prevalence of depressive disorders (Pearson's r = 0.16). DALYs from alcohol consumption were both correlated with antidepressant prescription volume (r= 0.12) and IMD score (r= 0.27). However, the volume of antidepressants prescribed per LSOA progressively increased with socio-economic deprivation, even after accounting for the prevalence of depressive disorders: +6% (95% CI, 5–7) in IMD4, + 13% (95% CI, 12–14) in IMD3, + 26% (95% CI, 24–27) in IMD2 and finally, individuals residing in most deprived areas (IMD1) were 1.65 times (95% CI, 1.64–1.66) more likely to get prescribed antidepressants compared with those residing in the least deprived quintile (see column 1 and 2 Supplementary Table 3).

Figure 2a shows the repartition of LSOAs prescribing the highest rates of antidepressants, which was found to overlap the distribution of LSOAs within the first IMD quintile – or most deprived neighbourhoods – located around Birmingham, Newcastle upon Tyne and in the north-west of England (Blackpool, Lancashire, Blackburn)[34], but spares the Greater London area, which was found to concentrate LSOAs prescribing the lowest rates of antidepressants (Figure 2b).

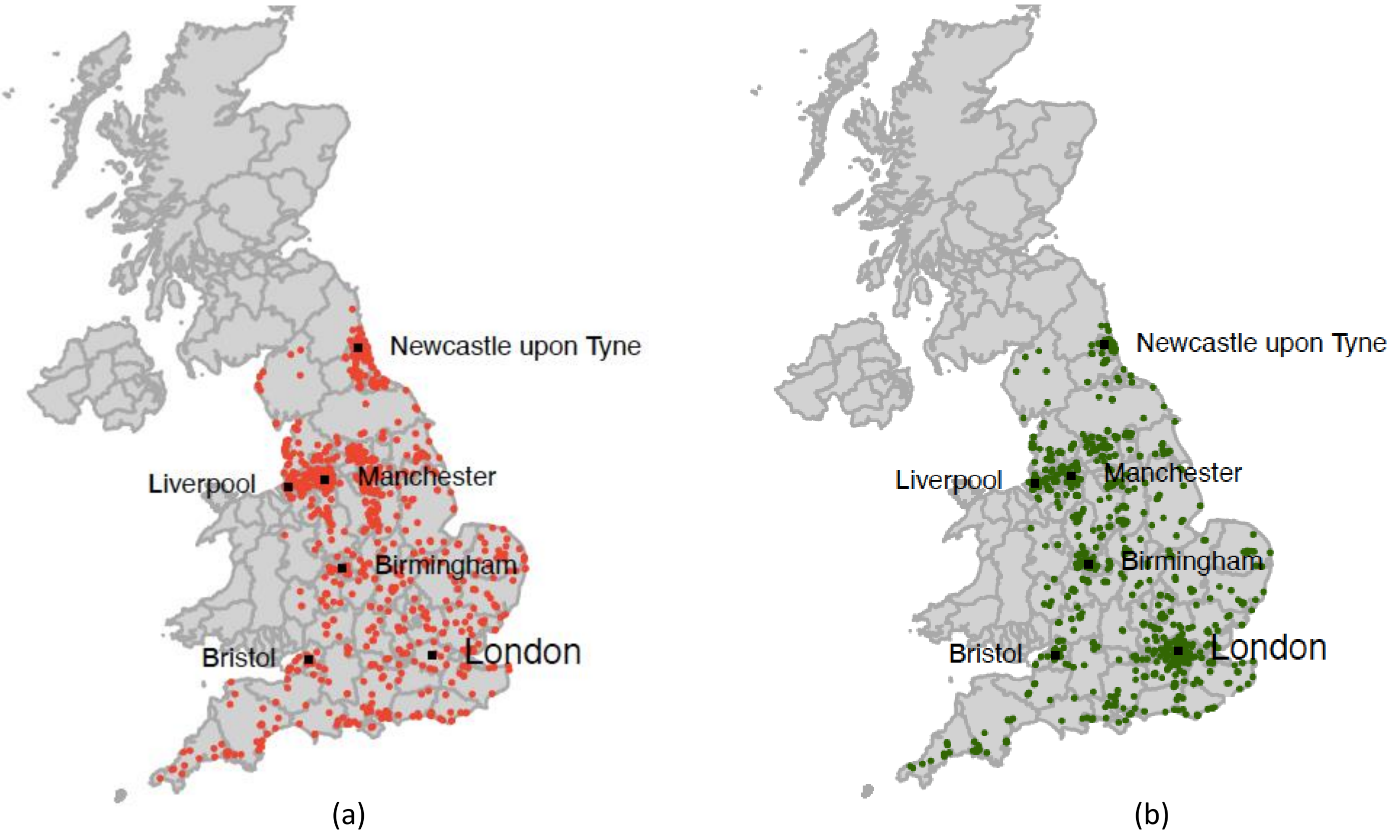


Figure 2. (a,b) Maps showing the geographical distribution of the 10% LSOAs where GPs prescribe the highest and lowest rates of antidepressants, respectively. Each dot represents a specific LSOA located with the coordinates (longitude and latitude) of its centroid.

If a positive correlation was observed between antidepressants prescription volume and IMD score (Pearson's r squared: r= 0.14), it is worth noting that out of the seven domains constituting the IMD score, health and employment domains were the most importantly correlated with the antidepressants volume (r=0.23 and r=0.20 respectively).

Therefore, health issues, unemployment and an important alcohol consumption could represent risk factors for a greater consumption of antidepressants.

2. Socio-economic gradient and temperature interaction on pharmaceutical consumption

Figure 3a shows a clear seasonal pattern for antibiotic prescriptions with a peak in winter (maximum in December) and a trough in summer (minimum in August). Bronchodilator and antidepressant prescription volumes tend to increase during winter months with a peak in December (Figures 3b and 3c, respectively).

For all three analysed medicine classes, prescription volumes followed similar seasonal patterns in all LSOAs, independently of their socio-economic level.

It should be noted that the seasonal patterns observed were only partly related to temperature fluctuations across the year. In order to isolate the effect of temperature, a month fixed-effect controlling for seasonality was included in the model and coefficients associated with temperature bins were analysed.

In Figure 4, those coefficients are plotted along with their respective 95% CI, separately for most (IMD1) and least (IMD5) deprived areas. Positive coefficients stand for an increased prescription volume under the given temperature bin – compared with the reference bin (bin 6: 14.4–16.3 degrees Celsius denoted °C) and vice versa (coefficients are exponentiated and translated into an IRR value in Tables).

Figure 4 shows that the effect of temperature on prescription volume does not follow the same pattern across the social gradient: when looking at antibiotics (Figure 4a and Supplementary Table 2 right bottom), decreasing temperatures were associated with progressively increased prescription volumes in most deprived areas but not in least deprived ones. In most deprived areas a temperature between 12.2 °C and 14.4 °C was associated with a 5% increase in antibiotic prescription volume compared with a temperature between 14.4 °C and 16.3 °C, a 10% increase was observed between 10 °C and 12.2 °C, 12% between 9 °C and 10 °C, 17% between 7 °C and 9 °C and finally below 7 °C antibiotic prescriptions increased by 21%. In least deprived areas it is only for temperatures below 10 °C that the antibiotic prescription volume showed a 4% increase, independent of the temperature drop. A temperature rise also had a greater effect in most deprived LSOAs: for temperatures above 21 °C a more important decrease in prescription volumes was observed in most deprived areas (-15%) than in least deprived areas (-7%).

For bronchodilators, the prescription rate was 16% (95% CI, 6–26%) higher under the lowest temperature bin (1.5–7.2 degrees Celsius) compared with the reference bin in most deprived areas. However, in least deprived areas, a temperature drop had no significant effect (see Table 1).

Likewise, when investigating prescription rates of antidepressants, coldest conditions saw a 45% (95% CI, 26–66%) rise in antidepressant prescriptions in most deprived areas while no significant effect was observed in least deprived areas. For temperatures above 21 degrees, antidepressant prescriptions decreased by 40% (95% CI, 35–44%) in most deprived LSOAs but only by 20% (95% CI, 17–23%) in least deprived ones.

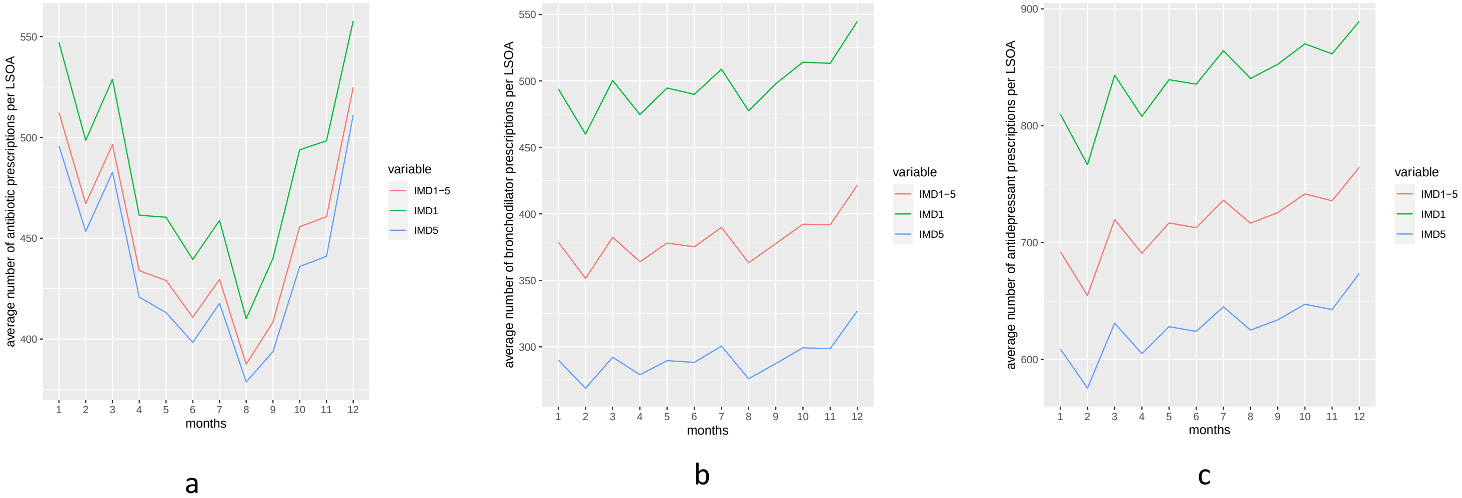
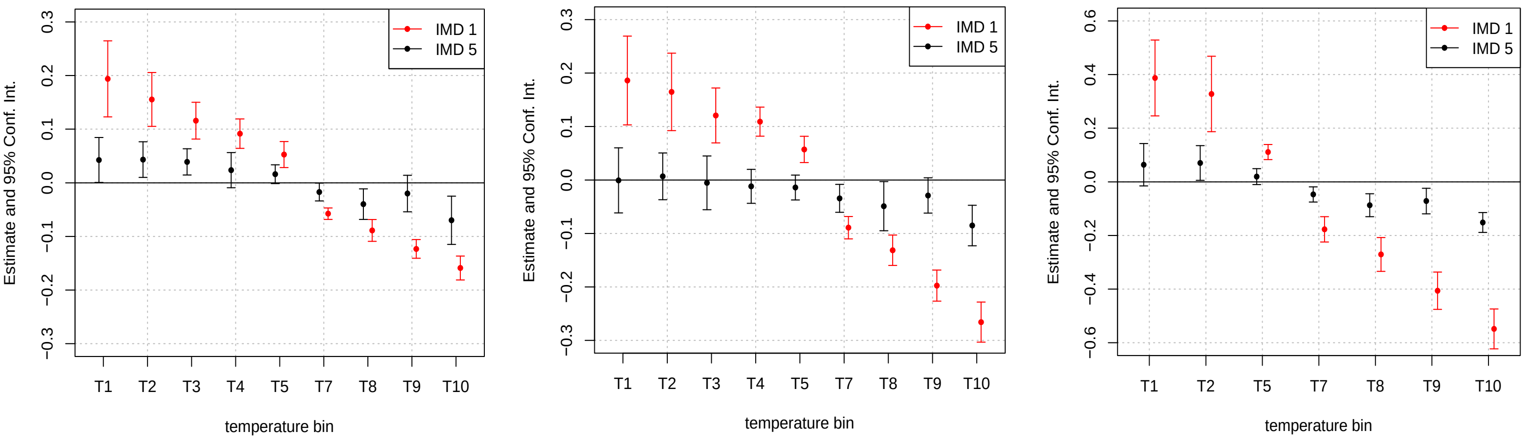


Figure 3 (a,b,c). Seasonality of antibiotic (a), bronchodilator (b) and antidepressant (c) prescriptions in England in all LSOAs (red), most (green) and least (blue) deprived ones.



(a) Antibiotics (b) Bronchodilators (c) Antidepressants

Figure 4 (a,b,c). Differential influence of temperature on antibiotic (a), bronchodilator (b) and antidepressant (c) prescription volumes in most (IMD1) and least (IMD5) deprived areas. Values for T1 to T10 are available in Table 1 and Supplementary Tables 2 and 3.

DISCUSSION

1. Socio-economic gradient and pharmaceutical consumption

We aimed to look at prescribing trends with regards to socio-economic deprivation, for three of the most important and commonly dispensed drug classes in England.

Results showed that antibiotics, bronchodilators and antidepressants are all prescribed at a higher rate in most deprived areas. The fact that the prescribing rate remains higher after accounting for the GBD suggests that the prescription excess observed in practices located in deprived neighbourhoods might not always be related to a real population need.

Our analysis of antibiotic prescription data showed a clear decreasing trend in the overall volume since 2012, thanks to numerous antibiotic stewardship campaigns [35, 36]. This evolution should follow the same downward trajectory in the next few years as a national five-year antimicrobial resistance action plan [37] has set the objective of a 15% reduction in human antibiotic use by 2024 in England. However, it is concerning that despite the general decreasing pattern, antibiotics remain more prescribed in deprived areas, especially since overconsumption is one of the risk factors for antimicrobial resistance. Our findings follow the same conclusion as results from a previous study conducted in England [38], where a 20% difference in antibiotic prescriptions between most and least deprived centile was observed. Findings in Scotland [39] had a larger magnitude (36.5% difference between most and least deprived quintiles), potentially related to the important health gap in this region [40]. The hypothesis of doctors' greater fear of complications among most deprived patients has been raised [41], and could explain why antibiotics prescription rates remain higher in these areas even after controlling for infection related DALYs.

As regards asthma, literature shows a disputed relationship between asthma and poverty [42]. Apart from hospital admissions for exacerbations, which are consistently associated with deprivation, other asthma-related outcomes appear to show a high level of inconsistency among studies. Supporting our results, the British Lung Foundation reported in 2012 a prevalence of asthma 11% higher in the most deprived areas when compared with the least deprived ones, partly explained by a higher level of precarious housing, with factors including more pollution, dampness and fungal spores [43]. An asthma UK report confirms this trend and also shows a poor access to asthma basic care in deprived areas with, for instance, less consultations for asthma review, and poor self-management due to lower health-literacy. Conversely, further evidence investigating children in Cardiff did not report any significant association between the proportion using inhaled bronchodilators or steroids and the Townsend index

[44]. The incidence of COPD is also associated with deprivation, and healthcare costs as well as mortality are higher among deprived COPD patients compared with non-deprived COPD patients.

As regards antidepressants, the positive correlation we found between the level of antidepressant prescriptions and socioeconomic deprivation was also highlighted in 2017 by Exasol [45]. The data analytics company showed important geographical disparities with the largest antidepressant prescribing rates found in the north and east of England, where the socio-economic level is at its lowest, and low prescribing rates in the Greater London area, consistent with our observations. In our models, the prevalence of depressive disorders from the GBD failed to explain the higher prescription volume of antidepressants in most deprived LSOAs. This suggests different prescribing behaviours: a potential use of antidepressant drugs unrelated to a true need and a treatment of depressive disorders relying more heavily on antidepressants rather than cognitive behavioural therapy in most deprived areas.

2. Socio-economic gradient and temperature interaction on pharmaceutical consumption

We observed higher prescription rates of antibiotics, bronchodilators and antidepressants associated with colder temperatures and a greater influence of temperature and air pollution on prescription volumes at the low end of the socio-economic spectrum, suggesting that individuals residing in most deprived areas could be more sensitive to environmental factors than the population living in least deprived neighbourhoods. This is confirmed by the goodness of fit of our statistical models: the temperature covariate systematically explained a much larger part of the variability when investigating the IMD1 subgroup compared with the IMD5 subgroup.

With global warming, extreme temperatures such as heatwaves or more and more severe winters are more commonly observed. Existing evidence already mentioned a potential increase in pharmaceutical consumption related to climate change and extreme temperatures [13]. A working paper from the Department of Economics and Social Affairs of the United Nations [7] showed that this pattern could be exacerbated in most deprived areas where individuals experience more exposure, a greater susceptibility and a reduced ability to cope with extreme weather conditions. The increasing exposure can be occupational, with more outdoors work among deprived individuals, while reduced financial resources to afford heaters, air conditioning or well-isolated accommodation challenges their capacity to adapt.

We were surprised to only find an association between prescription volume and decreasing temperature, instead of a U-shaped curve where healthcare needs would also increase with hottest weather conditions. However, this finding is in line with a previous meteorological analysis showing that the impact of an extremely cold winter is eight times more important than the impact of an excessively hot summer, in terms of mortality, related to a naturally higher mortality observed during the winter season. Despite the considerable increase in number of deaths observed during a heatwave, people remain more sensitive to cold temperatures via an increase in cardiovascular and respiratory mortality. Years with coldest winters are associated with an increased winter excess mortality. This same author showed a 200 deaths per day excess mortality for a 3 degrees difference between warmest and coldest winters in France [46], and therefore the significant impact in the most deprived areas.

It is known that cold temperatures can ease the replication of some viruses, alter our immune response and increase the risk of developing respiratory tract infections [14].

Previous work covering five years (2010–2015) of the same prescription data as the one we investigate also found that antibiotic prescriptions are highest in December and lowest in August, with a 59% difference [15]. Here, after controlling for seasonality, we observe a 39% increase in antibiotic prescriptions between coldest and warmest temperature bins. Interestingly, this gap was emphasized in most deprived areas (46%) and reduced in least deprived ones (22.5%), suggesting that antibiotic prescription volume is more importantly affected by temperature in deprived areas. The differential diagnosis between a bacterial or viral disease is often challenging, therefore antibiotics could be more easily prescribed to those at greatest risk, such as deprived individuals.

We also observed a higher consumption of antidepressants with colder temperature, an association exacerbated in deprived areas. The seasonal trend, however, was not found to be associated with social deprivation.

The presence of seasonal affective disorders during winter months could partly explain the higher consumption of antidepressants observed from October to December. An Austrian study [17] states that up to 0.9% of the population could be concerned by seasonal antidepressant prescriptions. Another paper reports 5 to 35% ($p<0.01$) more patients initiating an antidepressant therapy in winter rather than summer, observed in all groups except 18–30 and >60 years old [18]. In line with our findings, a study conducted in Sweden demonstrated a positive relationship between colder temperature during summer months and higher dispensation of selective serotonin reuptake inhibitors, a type of antidepressant [47].

Through a mechanism of bronchoconstriction, cold air triggers asthma attacks [48] and increases COPD exacerbation rate [49]. Mortality increases in particular when temperature drops below the normal average for a given location since it requires the body to adjust to unusual conditions [48].

Adaptation is even more challenging for older individuals [49] and those with less financial resources to cope with colder homes. Our findings suggest that colder temperatures are only associated with higher bronchodilator prescription rates (PRs) in most deprived areas and did not seem to affect neighbourhoods characterized by a higher socio-economic level. For those least deprived areas, seasonality seemed to matter more than temperature. This suggests that other characteristics associated with seasonality, such as the circulation of viruses, could explain the higher bronchodilators prescription rate in winter.

Our analysis also showed an association between air pollution DALYs and higher bronchodilator PRs, especially in deprived areas. It is known that respiratory symptoms increase with low air quality [49] associated with climate change, leading to an increase in pharmaceutical consumption . It has also been shown that a large part of the economic burden of asthma is attributable to air pollution exposure [50].

3. Strengths and limits

Our analysis is based on Big Data (on average 10 million records per month of all medicines, dressings and appliances), giving strong statistical significance. The prescription database provides all registered practices located in England including general practices but also prisons and training units, which makes it highly representative of trends at national level, and limits bias. Only dispensed medicines are analysed, and data gathering is highly reliable as it is obtained straight from pharmacy claims, which avoids any recall bias.

The panel of drugs investigated has a prescription-only status, also limiting bias. Indeed, over-the-counter (OTC) drugs are not captured in our data set, but it has been reported that practices serving a high percentage of income-deprived patients were associated with a higher volume of prescribed OTC medicines. Economically deprived patients would be more prone to consulting their GP to get prescriptions for OTC drugs in order to obtain them at no cost [51]. As a result, these drugs are less likely to act as a proxy for the population's health and more likely to only witness a lower financial status, creating bias.

The inclusion of time fixed-effects enables separating the influence of weather and IMD

on prescriptions from other potential drivers: the month fixed-effect enables seasonality to be controlled as well as any other differences between months such as bank holidays, that could influence the prescription volume. The year fixed-effect absorbs annual variations, country-wide trends, common to all LSOAs, such as new governmental prescriptions policies.

However, some limitations should be noted. The database does not include private prescriptions, which excludes a small part of dispensed medicines in England, targeting a population with a potentially high socio-economic level.

DALY variables from the GBD had a lower granularity (LAD level) compared with the other variables that were at LSOA level. The lower precision in DALY values may have lowered the impact of variables from the GBD.

We only included outdoor air temperature, but indoor temperature could also be of influence. Finally, the impact of climate change is limited to the effect of temperature. Many other variables could have been included to describe weather such as hours of sunshine, barometric pressure, wind… However, rainfall data were considered but removed early in the model building due to their lack of significance.

Conclusion

Health and social inequalities remain in England and also impact medicine consumption, in particular, with higher prescription rates of bronchodilators, antibiotics and antidepressants in most deprived areas, even after accounting for the disease DALYs. Severe winters characterized by unusually low temperatures could also be responsible for greater use of these three medicine classes.

We also show that social inequality and climate change are closely related, with individuals residing in the most deprived areas being potentially more sensitive to temperature change than those living in the least deprived neighbourhoods. Therefore, climate change could disproportionately impact on deprived individuals, increase their medicine consumption, and eventually widen socio-economic inequalities within developed countries.

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