Antibiotic use and deprivation: An analysis of Welsh primary care antibiotic prescribing data by socio-economic status

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Abstract (max 250 words)

Objective: To examine the association between socioeconomic status (SES) and antibiotic prescribing, controlling for presence of common chronic conditions and other potential confounders and variation amongst General Practitioner (GP) practices and clusters.

Patients and Methods: This was an electronic cohort study using linked GP and Welsh Index of Multiple Deprivation (WIMD) data. Setting was GP practices contributing to Secure Anonymised Information Linkage (SAIL) Database 2013–2017. The study involved 2.9 million patients nested within 339 GP practices, nested within 67 GP clusters.

Results: Approximately 9 million oral antibiotics were prescribed between 2013 and 2017. Antibiotic prescribing rates were associated with WIMD quintile, with more deprived populations receiving more antibiotics. This association persisted after controlling for patient demographics, smoking, chronic conditions, and clustering by GP practice and cluster, with those in the most deprived quintile receiving 18% more antibiotic prescriptions than those in the least deprived quintile (Incidence rate ratio [IRR] 1.18; 95% CI 1.181–1.187). We found substantial unexplained variation in antibiotic prescribing rates between GP practices (Intra cluster correlation [ICC] 47.31%) and GP clusters (ICC 12.88%) in the null model which reduced to ICCs of 3.5% and 0.85% for GP practices and GP clusters respectively in the final adjusted model.

Conclusion: Antibiotic prescribing in primary care is increased in areas of greater SES deprivation, and this is not explained by differences in the presence of common chronic conditions or smoking status. Substantial unexplained variation in prescribing supports the need for ongoing antimicrobial stewardship initiatives.

Introduction

The overuse of antibiotics contributes to the development of antimicrobial resistance,[1] and the majority of antibiotics used for humans are prescribed in primary care.[2] Many antimicrobial stewardship initiatives have been implemented in an attempt to reduce antibiotic prescribing.[3]

People from more socioeconomically deprived backgrounds are known to have more health problems,[4 5] and on average receive worse healthcare.[6-8] Previous studies from Scotland, Wales and England have found an association between socioeconomic status (SES) and antibiotic prescribing, with those coming from more deprived settings receiving more antibiotics.[9-12] Increased use of antibiotics in people experiencing socioeconomic deprivation could be an appropriate response to a greater prevalence of chronic conditions leading to an increased risk of adverse outcomes, or could be unnecessarily exposing those with the greatest needs to an increased risk of adverse effects and antimicrobial resistance. Previous studies have not controlled for chronic conditions, so it is not possible to determine the degree to which greater use in those with lower SES simply reflects a greater incidence of chronic conditions.

Several studies have previously been conducted on factors associated with a high rate of antibiotic prescribing in the United Kingdom (UK).[10 11 13-18] Some of these studies concentrated on individual-level factors alone[15 16] while others have focussed on contextual (GP practices/clusters and areas) level factors.[10 11 13 14 17] Moreover, research conducted at the individual or aggregate level alone may lead to individualistic and ecological fallacies respectively. Studies that include a combination of individual and aggregate-level factors may help elucidate a more accurate picture of the risk factors associated with high antibiotic prescribing in the UK. Such an understanding can help inform population level health policies to reduce high antibiotic prescribing rates. Crucially, aggregate-level factors tend to be more amenable to intervention, and more sustainable in the longer term.

We therefore set out to examine the association between antibiotic use and SES in Wales, controlling for common chronic conditions and other potential confounders using an electronic cohort study with a hierarchical design.

Patients and methods

Welsh General Practitioner (GP) data for the 5-year period 01/01/2013 to 31/12/2017 were extracted from the Secure Anonymised Information Linkage (SAIL) Databank. Virtually all of the population of Wales are registered with a general practitioner, and most primary care is provided by general practices. General practitioners and other primary care prescribers (such as nurses with prescribing qualifications) issue prescriptions and these are almost exclusively done electronically. Electronic prescriptions are recorded in primary care electronic medical records (EMR), and this data, along with other coded data such as diagnoses, symptoms and test results, are extracted from consenting general practices and included in the SAIL databank. Prescriptions issued by specialist doctors would generally not be recorded in the primary care EMR, but specialist would seldom issue antibiotics to ambulatory patients. Approximately 80 per cent of the population of Wales are registered at a practice that contributes data to SAIL. The patient level data fields extracted included the patient's age at study entry (any participant born after 1 January 2013 went into age group <10) and sex, the GP practice they are registered with (and start and end dates of the registration), Read code, version 2, (recording diagnoses, medications prescribed, smoking status) and related dates. We used the first practice that patients were registered with during the study period. Residents of England and Wales are coded to a Lower Layer Super Output Area (LSOA), which is a geospatial area of approximately 1,500 people, which is used by the Office of National Statistics and the Welsh Demographic Data Service for statistical analysis, and for the purpose of this study was used to obtain a rating of socioeconomic status (SES).[19] Only patients with a Welsh LSOA code were eligible for inclusion.

Outcome and exposure

The outcome variable was the total number of prescriptions of the specified oral antibiotics to an individual between years 2013–2017. Prescribed medicines were categorised by both British National Formulary (BNF) subsection and approved name and we included only medicines in BNF section 5.1 (antibacterial drugs), excluding 5.1.9 (antituberculosis drugs) and 5.1.10 (antileprotic drugs, except streptomycin). We excluded any intramuscular, intravenous and topical antibiotics so that only antibiotic prescriptions administered through the oral route were included.

The main exposure of interest was socioeconomic status (SES) as defined by the Welsh Index of Multiple Deprivation (WIMD). WIMD is a multidimensional neighbourhood-level indicator of socioeconomic deprivation for LSOAs that combines multiple area-level socioeconomic indicators into a single deprivation score.[20] Participants were categorised into a WIMD quintiles (with 1 representing the most deprived quintile and 5 the least deprived), based on the whole population of Wales and using data from 2011, and based on participants' first registered address in the period 2013–17.

Covariates

Based on previous findings,[9 21-23] baseline age, sex, smoking status, and chronic conditions (cerebrovascular disease, cancer, coronary heart disease, dementia, renal disease, liver disease, peripheral vascular disease, chronic pulmonary disease and diabetes mellitus) were considered as potential confounders. Chronic conditions were counted as being present if they were first coded prior to 01/01/2013. Analysis was based on complete cases: for all chronic conditions, less than 1 percent were missing data. We also conducted a sensitivity analysis by including all chronic conditions that developed (were first coded) during the follow-up period. Age was categorized into 10-year bands with a terminal band of 90 years and older. GPs in Wales are grouped in geographic areas into GP clusters.[24 25] The composition of the clusters changed slightly over 2013–17. We used the first cluster to which a GP practice belonged during the study period.

Statistical Analysis

We calculated the total number of oral antibiotics prescribed per person year over the period 2013–17. The denominator for the rate was number of years patient contributed during the study period. Person-time was calculated by including one year of person-time for each calendar year that a participant was registered with a participating GP practice for one or more days during that year.

We specified a three-level multilevel model with a patient (level 1) nested within GP practice (level 2) within GP cluster (level 3) due to the hierarchical nature of the datasets. We constructed four models. The first model, a null model without any predictor variables, was specified to decompose the amount of variance that existed between the GP practice and GP cluster levels. The second model contained the exposure of interest (SES), and individual-level demographic variables (sex, age group, WIMD quintile and smoking status). The third model included the chronic conditions, and the fourth controlled for all the covariates simultaneously. A mixed effect Poisson regression model was utilized to test the association between the covariates and antibiotic prescription rates. All variables were assessed independently, with significant predictors utilized in the multivariable models. The results of fixed effects (measures of association) were shown as incidence rate ratios (IRRs) with their 95% confidence interval (CI). Measures of random effects included an intra-cluster correlation (ICC), a variance partition coefficient [26] and median rate ratio (MRR).[27 28] MRR is the median relative change in the rate of the occurrence of the event when comparing identical subjects from 2 randomly selected different clusters that are ordered by rate[27]. The Akaike information criterion (AIC) was used to judge the goodness-of-fit of the models while variance inflation factor (VIF) was used to check for multicollinearity. All multilevel modelling was performed using R statistical software for Windows version 3.5.1[29] using the multilevel, lme4 and glmer packages. We used maximum likelihood estimation (MLE) for the multilevel Poisson regression models. The α-significance level for all tests were set at 0.05. We conducted a sensitivity analysis to examine the effects of developing comorbidities during the study period.

Results

We identified 2,873,959 individuals (Level 1) nested within 339 GP practices (Level 2) from 67 GP clusters (Level 3) that were included in the SAIL database during the period 2013-2017. Of these, 3,893 (0.1%) had no data recorded prior to 2013 and therefore it was impossible to assess for the presence of chronic conditions and smoking. This left 2,870,066 individuals (Level 1) nested within 339 GP practices (Level 2) from 67 GP clusters (Level 3) available for the regression analysis. The characteristics of the study population are presented in table 1. Slightly more than one-fifth (21.5%) of the participants were categorized within the most deprived WIMD quintile, indicating that practices contributing to SAIL data include a slightly greater proportion of people coming from the most deprived quintile than in the total population of Wales. The rate of oral antibiotic prescribed per 1000 registered patients per year was 771.4, 766.4, 732.0, 722.0 and 692.9 for the years 2013, 2014, 2015, 2016 and 2017 respectively. We observed a similar pattern within each class of antibiotics apart from quinolones and cephalosporins (see Table 2).

Antibiotic prescribing rates declined over the study period (from 854 prescriptions per 1000 registered patients per year to 770) for the most deprived WIMD quintile, and (from 681 prescriptions per 1000 registered patients per year to 612) for the least deprived WIMD quintile) (Figure 1). Antibiotic prescribing rates across all study years were higher for women than men across all deprivation quintiles (Figure 2). Antibiotic prescribing also varied by age group, with rates generally increasing with age, but with children aged 0-9 having slightly higher rates than those aged 10-19 or 20-29 years (Figure 3).

Antibiotic prescribing by levels of deprivation

Antibiotic prescribing rates varied by level of SES, with those in the most deprived areas receiving the most antibiotic prescriptions per person. Mean antibiotic prescribing rates for the most to the least deprived quintiles were 820.3, 773.5, 737.4, 692.2 and 649.5 prescriptions per 1000 registered patients per year respectively, for the period 2013–2017. We found a similar trend, with increasing deprivation by quintile being associated with increasing antibiotic prescribing rates, for each individual class of antibiotics (Table 2). The association between deprivation and antibiotic prescribing persisted after controlling for demographic variables, smoking, chronic conditions, and clustering by GP practice and GP cluster (Table 3). Those living in areas in the most deprived quintile in Wales received 18% more antibiotic prescriptions (IRR 1.18; 95% CI 1.181–1.187) than those with similar demographics, chronic conditions and smoking status but living in areas in the least deprived quintile (Table 3).

Variation in antibiotic prescribing by practice and cluster

There was significant variation in antibiotic prescribing rates between GP practices (ICC) 47.31% and GP clusters (ICC) 12.88% in Wales, which remained statistically significant after controlling for socio-demographic factors (in Model 2), comorbidity factors (in Model 3) and both factors simultaneously (in Model 4). We found a practice-level MRR of 1.98 in model 1 (base model with no variable adjusted) indicating that individuals in a practice with a highest propensity for prescribing antibiotics received nearly twice as many antibiotic prescriptions as individuals in a practice with the lowest propensity for prescribing antibiotics. Controlling for social and comorbidity factors reduced the unexplained heterogeneity between GP practices to an MRR of 1.19 in the final model.

Sensitivity analyses

Adjusting for comorbidities developed during the study period as well as before the study period did not significantly change the findings from our main analysis (Supplementary table S1 is available at JAC Online).

Discussion

In this analysis of routine healthcare and associated socio-demographic data from Wales, we found that there was significant variation in antibiotic prescribing in primary care by SES, with the mean antibiotic prescribing rate over 2013–17 for those in the most deprived quintile being 35% greater than for those in the least deprived quintile. This variation persisted after controlling for age, gender, smoking, comorbidities and variations by GP practice and cluster, with people in the most deprived quintile having a prescribing rate 18% higher than those in the least deprived quintile.

Prescribing is almost always done electronically in primary care in Wales and therefore ascertainment of antibiotic prescribing is high. Age and gender are accurately recorded as part of patient registration details and most of the chronic conditions included as co-variates are generally well coded as many have been associated with quality improvement incentives which require accurate coding.[30] We used a large dataset which provided adequate power for our analyses.

Although we controlled for many potential confounders, we were not able to control for the severity of the infection that the patient presented with, propensity to consult or calendar year. People in lower SES groups consult more frequently in general,[31] and it is possible the higher prescribing rates seen in lower SES groups may be because patients consult more frequently for infections.[32] We were able to demonstrate a reduction in antibiotic prescribing over the period of the study and were not able to control for this our model. However, as SES is relatively stable over short periods of time, we do not anticipate that calendar time is likely to have a significant confounding effect on the association between SES and antibiotic prescribing. Finally, in an observational study like this we are not able to comment on the appropriateness of the antibiotic prescribing.

Other possible reasons for increased prescribing in those from more deprived backgrounds include concern amongst prescribers about an increased risk of complications, pressure from patients, and greater time pressures. A grounded theory interview study on antibiotic prescribing for sore throat found that primary care clinicians were more likely to prescribe antibiotics to people from more deprived backgrounds because of concern about an increased risk of complications.[32] Perceived pressure from patients has been shown to be associated with increased propensity to prescribe antibiotics in several studies.[32-34] Shorter consultations times, which may result from reduced resources in more deprived settings, have been shown to result in a lower threshold to prescribe.[35]

Another important finding from this study was the significant variation in prescribing at both practice and cluster levels, that was present even after controlling for socio-demographic and clinical factors amongst patients. Although general practice ‘Clusters’ are unique to Wales, similar approaches are being implemented in other settings, for example with the implementation of ‘Primary Care Networks’ in England. Significant variation in antibiotic prescribing by practice, Clinical Commissioning Group (CCG) and region has been previously demonstrated in England.[10,17] Prescribers experience and confidence, as well as system factors, contribute to variation in antibiotic prescribing.[36] However, the ongoing unexplained variation found in our study and previous studies suggests the need for further antibiotic stewardship activities to reduce the unnecessary use of antibiotics that is driving antibiotic resistance.

Our findings of associations between antibiotic prescribing and SES, age and gender, were very similar to the findings of a similar study conducted in Scotland.[9] However, we were also able to demonstrate that the association between SES and antibiotic prescribing persisted after controlling for chronic conditions and smoking. A study of primary care antibiotic prescribing hot spots in England also identified an association between higher prescribing and lower SES, but also did not control for chronic conditions.[17] An ecological study looking at the association between income and antibiotic use in European countries found an effect in the opposite direction – with wealthier countries using more antibiotics than poorer countries.[37] However, this is very different from looking at individual use within countries. A study of regional differences in antibiotic consumption in Hungary found a positive association between the proportion of the population receiving social assistance and antibiotic use.[38]

It is nearly 50 years since Julian Tudor Hart first described the Inverse Care Law, where those with greatest need have the least access to good medical care.[8] We found that people from the lowest social classes were receiving the most antibiotics, but this is highly unlikely to represent high levels of access to medical care. Many antibiotic prescriptions in primary care are unnecessary,[39] and overuse of antibiotics promotes antimicrobial resistance.[1] It is therefore highly likely that the excess 'care' in this instance is likely to be harming those with the greatest need. It is therefore imperative that the reasons for the excess use of antibiotics in people with lower socio-economic status identified in this study are further investigated and, if necessary, steps are taken to address this variation in use. The findings of this study may be generalizable to other countries with similar settings and health care delivery system.

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Ethical approval: Not needed.

Data sharing statement: The data used in this study are available in the SAIL databank at Swansea University, Swansea, UK. SAIL has established an application process to be followed by anyone who would like to access data via SAIL, https://www.saildatabank.com/application-process. All proposals to use SAIL data are subject to review by an independent Information Governance Review Panel (IGRP). Before any data can be accessed, approval must be given by the IGRP. The IGRP gives careful consideration to each project to ensure proper and appropriate use of SAIL data. When access has been granted, it is gained through a privacy-protecting safe haven and remote access system referred to as the SAIL Gateway. Relevant information to allow acquisition of a replicable data set is available in the paper and its Supporting Information files or can be requested from the authors. Please contact SAILDatabank@swansea.ac.uk for more detail on data access requests.

Transparency: The authors affirm that the manuscript 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. R code for fitting the multilevel Poisson model has been provided as supplementary data. All authors confirm that they do not have any financial conflicts of interest and the funder has not played any decision-making role in the research.

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Table 1. Characteristics of the study population

Parameter	Number (%)
Sociodemographic factors (N=2,873,959)	
Sex	
Male	1,430,087 (49.8)
Female	1,443,872 (50.2)
Age	
0-9 years	438,440 (15.3)
10-19 years	348,459 (12.1)
20-29 years	411,398 (14.3)
30-39 years	338,618 (11.8)
40-49 years	376,892 (13.1)
50-59 years	335,361 (11.7)
60-69 years	304,340 (10.6)
70-79 years	195,875 (6.8)
80-89 years	102,577 (3.6)
90+ years	21,999 (0.7)
WIMD	
Quintile 5 (least deprived)	583,681 (20.3)
Quintile 4	516,667 (18.0)
Quintile 3	581,932 (20.2)
Quintile 2	573,809 (20.0)
Quintile 1 (most deprived)	617,870 (21.5)
Smoking status (N=2,870,066)	
Non smoker	1,979,825 (69.0)
Ex-smoker	500,087 (17.4)
Current smoker	390,154 (13.6)
Long term conditions (N=2,870,066)	
Cancers	

No	2,741,138 (95.5)
Yes	128,928 (4.5)
Cerebrovascular Diseases	
No	2,810,370 (97.9)
Yes	59,696 (2.1)
Coronary Heart Diseases	
No	2,764,670 (96.3)
Yes	105,396 (3.7)
Peripheral Vascular Diseases	
No	2,845,382 (99.1)
Yes	24,684 (0.9)
Diabetes	
No	2,725,317 (95.0)
Yes	144,749 (5.0)
Dementia	
No	2,855,711 (99.5)
Yes	14,355 (0.5)
Renal Diseases	
No	2,756,769 (96.1)
Yes	113,297 (3.9)
Liver Diseases	
No	2,864,096 (99.8)
Yes	5,970 (0.2)
Chronic Pulmonary Diseases	
No	2,421,698 (84.4)
Yes	448,368 (15.6)

WIMD – Welsh Index of Multiple Deprivation

Table 2. Mean antibiotics prescription per 1000 registered patients per year by selected BNF subsection, stratified by WIMD quintile (2013-2017)

Antibiotics	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Cephalosporins	28.7	29.7	28.7	28.5	27.5
Macrolides	100.5	92.2	86.1	80.2	72.5
Metronidazole	17.2	15.6	15.3	14.2	11.9
Phenoxymethylpenicillin	54.7	51.3	48.1	46.1	44.7
Broad spectrum Penicillins	255.0	240.5	228.2	204.0	176.2
Penicillinase resistant Penicillins	91.1	85.7	82.2	76.0	72.4
Quinolones	14.6	14.0	15.0	15.1	14.7
UTI antibiotics	133.7	130.5	128.0	123.3	124.0
Tetracyclines	122.0	111.4	103.3	102.2	103.4
Others	2.7	2.6	2.6	2.6	2.3
Total antibiotics	820.3	773.5	737.4	692.2	649.5

UTI – Urinary Tract Infection (including sulphonamides and trimethoprim);

Others (including antipseudomonal penicillin and aminoglycosides, clindamycin and lincomycin)

Quintile 1 – Most deprived; Quintile 5 – Least deprived

Table 3: Multilevel Poisson regression model for rates of antibiotics prescription in Wales

	Model 1	**Model 2**	**Model 3**	**Model 4**
Parameter	**IRR (95%CI)**	**IRR (95%CI)**	**IRR (95%CI)**	**IRR (95%CI)**
Fixed-Effects				
Sex				
Female vs. Male		1.63 (1.627 – 1.631)		1.66 (1.653 – 1.658)
Age				
0-9 years		1.00 (reference)		1.00 (reference)
10-19 years		0.91 (0.909 – 0.914)		0.82 (0.820 – 0.825)
20-29 years		0.78 (0.774 – 0.778)		0.70 (0.699 – 0.703)
30-39 years		0.78 (0.777 – 0.782)		0.72 (0.718 – 0.723)
40-49 years		0.86 (0.861 – 0.866)		0.80 (0.796 – 0.800)
50-59 years		1.05 (1.044 – 1.050)		0.93 (0.931 – 0.937)
60-69 years		1.35 (1.345 – 1.353)		1.12 (1.120 – 1.126)
70-79 years		1.79 (1.780 – 1.790)		1.32 (1.312 – 1.320)
80-89 years		2.18 (2.176 – 2.190)		1.47 (1.465 – 1.475)
90+ years		2.57 (2.559 – 2.588)		1.71 (1.701 – 1.721)
WIMD				
Quintile 5 (least deprived)		1.00 (reference)		1.00 (reference)
Quintile 4		1.05 (1.052 – 1.057)		1.04 (1.040 – 1.045)
Quintile 3		1.09 (1.089 – 1.094)		1.07 (1.069 – 1.074)
Quintile 2		1.15 (1.150 – 1.156)		1.12 (1.118 – 1.123)
Quintile 1 (most deprived)		1.24 (1.233 – 1.239)		1.18 (1.181 – 1.187)
Smoking status				
Non smoker		1.00 (reference)		1.00 (reference)
Ex-smoker		1.49 (1.488 – 1.493)		1.34 (1.337 – 1.342)
Current smoker		1.44 (1.437 – 1.443)		1.36 (1.360 – 1.365)
Comorbidities				
Cancers (No vs. Yes)			1.56 (1.554 – 1.562)	1.25 (1.250 – 1.256)
CVD (No vs. Yes)			1.51 (1.505 – 1.515)	1.28 (1.279 – 1.287)
CHD (No vs. Yes)			1.50 (1.491 – 1.499)	1.28 (1.272 – 1.279)
Diabetes (No vs. Yes)			1.54 (1.532 – 1.538)	1.33 (1.331 – 1.338)
Dementia (No vs. Yes)			2.05 (2.039 – 2.064)	1.53 (1.524 – 1.543)
Renal diseases (No vs. Yes)			1.58 (1.580 – 1.588)	1.22 (1.217 – 1.224)
Liver diseases (No vs. Yes)			1.68 (1.667 – 1.698)	1.56 (1.547 – 1.577)
CPD (No vs. Yes)			1.82 (1.821 – 1.827)	1.78 (1.780 – 1.785)
PVD (No vs. Yes)			1.40 (1.391 – 1.404)	1.22 (1.217 – 1.224)
Random-Effects				
GP clusters				

Variance (SD)	0.204(0.451)	0.094(0.097)	0.015(0.121)	0.009(0.093)
Explained variation (%)	Reference	53.80	92.80	95.70
Intra-clusters correlation, %	12.88	0.90	1.42	0.85
MRR	1.54	1.34	1.12	1.09
GP practices				
Variance (SD)	0.517(0.719)	0.037(0.192)	0.039(0.198)	0.035(0.187)
Explained variation (%)	Reference	92.90	92.40	93.20
Intra-practice correlation, %	47.31	3.69	3.95	3.50
MRR	1.98	1.20	1.21	1.19
AIC	24970277	22912954	23241295	22089908

IRR: Incidence Rate Ratio. AIC: Akaike Information Criterion. MRR: Median Rate Ratio. WIMD: Welsh Index of Multiple Deprivation. SD: Standard Deviation. CPD: Chronic Pulmonary Disease. PVD: Peripheral Vascular Disease. CHD: Coronary Heart Disease. CVD: Cerebrovascular Disease.

Figure 1 – Antibiotic Prescriptions by Deprivation (WIMD) and Year (2013-2017)

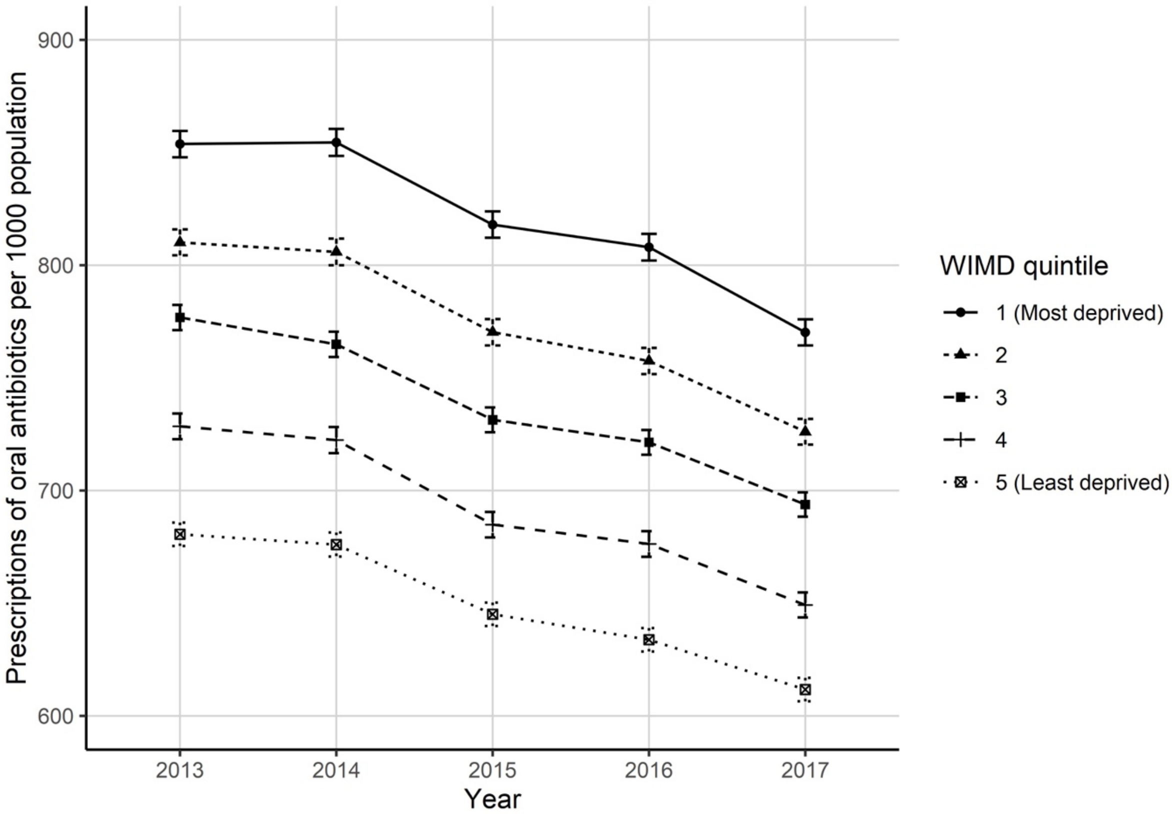

Figure 2 – Antibiotic Prescriptions by Deprivation (WIMD) and Sex

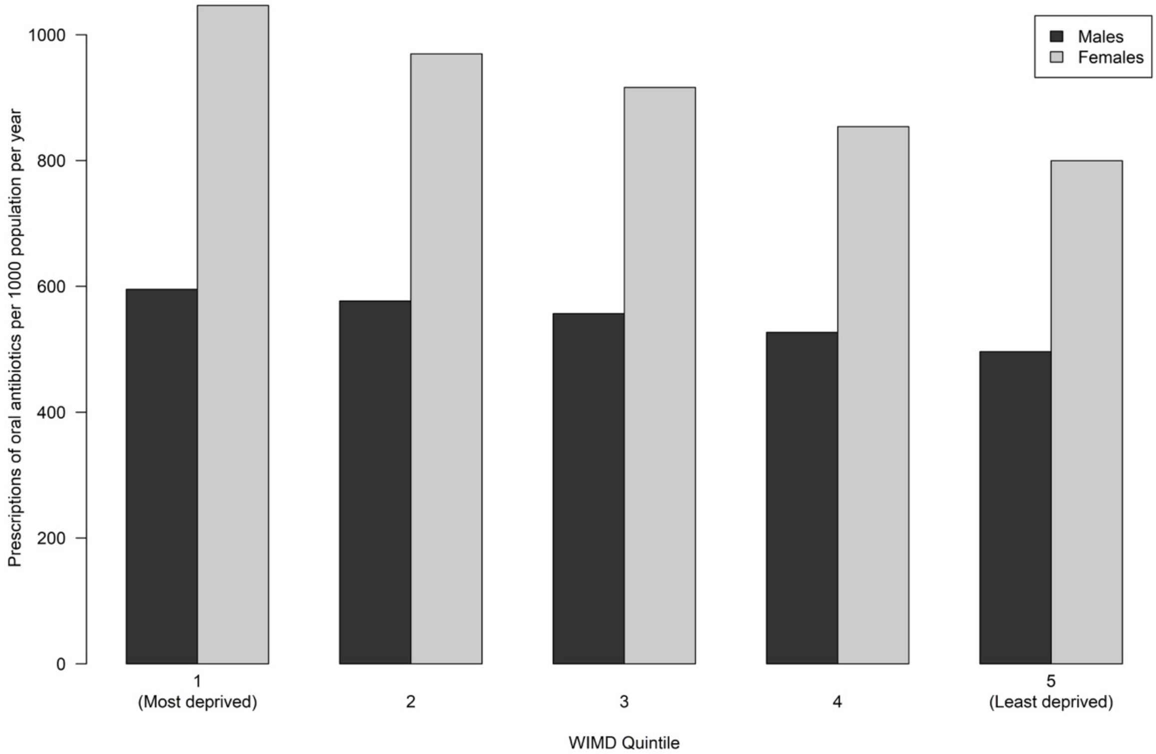

Figure 3 – Antibiotic Prescriptions by Deprivation (WIMD) and Age