Socioeconomic status and benzodiazepine and Z-drug prescribing: a cross-sectional study of practice-level data in England.

[Accepted Submission to *Family Practice*]

Running title: Socioeconomic status, benzodiazepines and Z-drugs

Article category: Epidemiology

Stephanie Soyombo[1], Rhian Stanbrook[2], Harpal Aujla[1], David Capewell[3], Mary Shantikumar[4], Farah Kidy[1], Daniel Todkill[1], Saran Shantikumar[1]

[1] Warwick Medical School, University of Warwick, Coventry, UK.

[2] Medwyn Surgery, Surrey, UK

[3] Outwood Park Medical Centre, Wakefield, UK

[4] Central Surgery, Rugby, UK

Correspondence to:

Dr S Shantikumar, Clinical Lecturer in Public Health

Room B163, Warwick Medical School

University of Warwick, Coventry, UK. CV4 7AL

saran.shantikumar@warwick.ac.uk

Abstract Word Count: 243 words

Manuscript Word Count: 2554 words (excl. abstract, figures, appendices and references)

KEY MESSAGES

- Benzodiazepine prescribing is higher in practices with underserved populations
- This association is seen more strongly in certain drugs of this class
- Other determinants of prescribing variation exist and need to be explored

ABSTRACT

Background

Benzodiazepines and Z-drugs (such as zopiclone) are widely prescribed in primary care. Given their association with addiction and dependence, understanding where and for whom these medications are being prescribed is a necessary step in addressing potentially harmful prescribing.

Objective

To determine whether there is an association between primary care practice benzodiazepine and Z-drug prescribing and practice population socioeconomic status in England.

Methods

This was a cross-sectional study. An aggregated dataset was created to include primary care prescribing data for 2017, practice age and sex profiles, and practice Index of Multiple Deprivation (IMD) scores – a marker of socioeconomic status. Drug doses were converted to their milligram-equivalent of diazepam to allow comparison. Multiple linear regression was used to examine the association between IMD and prescribing (for all benzodiazepines and Z-drugs in total, and individually), adjusting for practice sex (% male) and older age distribution (% >65s).

Results

Benzodiazepine and Z-drug prescribing overall was positively associated with practice-level IMD score, with more prescribing in practices with more underserved patients, after adjusting for age and sex (p<0.001), although the strength of the association varied by individual drug. Overall, however, IMD score, age and sex only explained a small proportion of the overall variation in prescribing across GP practices.

Conclusion

Our findings may, in part, be a reflection of an underlying association between the indications for benzodiazepine and Z-drug prescribing and socioeconomic status. Further work is required to more accurately define the major contributors of prescribing variation.

Keywords: anti-anxiety agents, benzodiazepines, general practice, hypnotics and sedatives, prescriptions, socioeconomic factors

Background

Benzodiazepines and Z-drugs are classes of medication with similar pharmacological mechanisms of action, both being functional at $GABA_A$ receptors. Benzodiazepines are used for a wide range of indications and durations, with different drugs within the class being more suited to different situations (such as chlordiazepoxide for alcohol withdrawal, and clobazam for epilepsy). In primary care, common indications for use include insomnia, anxiety and acute back pain. Benzodiazepines have been in common use since the 1960s, when they were initially thought to be less addictive and safer than alternatives in the treatment of anxiety and insomnia[1]. It is now appreciated that benzodiazepines have a high risk of dependency and withdrawal symptoms even at normal doses[2]. Indeed, they are thought to be at least as addictive as opiates, and the duration of withdrawal may be longer[3]. Z-drugs are a group of non-benzodiazepine medications, the most well-known of which is zopiclone, which are frequently prescribed for insomnia. Whilst this class of medications were reportedly considered safer than benzodiazepines[4], long-term Z-drug use is also associated with tolerance and dependence[5],[6]. This poses difficult questions regarding the management of dependency and withdrawal, which have frequently been cited as a national priority in the UK and USA[7].

Around 300,000 people in the UK are on long-term prescriptions for benzodiazepines[8], and zopiclone prescription rates continue to increase, particularly in the elderly population[4]. Significant medical and social concerns arise from use of these medications long-term: benzodiazepines have been associated with an increased risk of falls causing significant injury[9], traffic accidents[10], cognitive impairment[11] and dementia[12]. These effects may be especially marked in the elderly[13]. There is also a significant market in illicit benzodiazepine and Z-drug sale and use[14].

In light of a landmark review currently being undertaken by Public Health England into prescription drugs likely to lead to dependence and withdrawal[15], it has never been more important for us to understand the geographic and demographic distribution of prescriptions in primary care. In the UK and the USA, benzodiazepines and Z-drugs are more commonly prescribed in the elderly population and in females[16,17]. A study conducted in 2004/5 suggested that practice-level benzodiazepine prescribing may be related to socioeconomic status, as defined by Index of Multiple Deprivation (IMD) scores[18]. However, this study did not consider Z-drugs, and only looked at benzodiazepine prescribing as a whole. It may be that some benzodiazepines, but not others, are driving the apparent overall association with low socioeconomic status. Furthermore, the proportion of patients being prescribed benzodiazepines has gradually declined since this time[19]. This may reflect a shift in prescribing habits.

Here, we use recent primary care prescribing data from England to explore associations between primary care practice-level benzodiazepine and Z-drug prescribing and socioeconomic status (SES). The associations were tested for these classes of drugs as a whole, as well as for individual drugs.

Methods

Data Sources

This is a cross-sectional study of monthly prescribing data for primary care practices in England in 2017, which were downloaded from NHS Digital (https://digital.nhs.uk)[20]. This gives information for each GP practice and their Clinical Commissioning Group (CCG – regional bodies that are responsible for planning and commissioning healthcare services for their local area), and for each drug preparation: (1) the number of items prescribed that month; and (2) the total quantity prescribed that month (i.e. number of tablets or total in milligrams if the preparation is a liquid). The total quantity prescribed was chosen as the primary outcome measure, rather than the number of items, as it gives a more accurate picture of how much of each drug was prescribed. Private prescriptions are not recorded in these datasets. Information on GP practice list sizes (from January 2017), including stratification by sex and 5-year age bands, was also retrieved from NHS Digital[21], as were British National Formulary (BNF) drug codes[22]. BNF codes are unique for each drug preparation; for example, the codes for diazepam 5mg tablets, diazepam 10mg tablets, and diazepam 10mg/ml in oral solution are all different.

Information about the equivalence of benzodiazepines and Z-drugs is published in the BNF[23]. It gives, for each drug, the approximate dose which is equivalent to 5mg of diazepam, thus allowing comparisons to be made across the different drugs in these classes. The equivalences used are given in *Supplementary Material 1*.

Data on practice-level and CCG-level socioeconomic status were obtained from Public Health England's National General Practice Profiles[24]. Socioeconomic status was quantified using the Index of Multiple Deprivation (IMD) score from 2015. The IMD score combines information from seven domains to produce an overall relative measure of SES. The domains are combined using the following weights[25]: income deprivation (22.5%); employment deprivation (22.5%); education, skills and training deprivation (13.5%); health deprivation and disability (13.5%); crime (9.3%); barriers to housing and services (9.3%); and living environment deprivation (9.3%).

Data Processing

Primary care prescribing data for each month in 2017 were aggregated by BNF drug code to give the total number of items and total quantity prescribed under each BNF code per practice over a year. Practices with fewer than 1000 patients were excluded. All oral formulations (tablet and solution) of benzodiazepine and Z-drugs were included. In order to standardise the quantities of different drugs prescribed, all drug doses were converted into their milligram-equivalent of diazepam. The total prescribed quantities (in mg-equivalent of diazepam) were then aggregated, by practice, for each drug irrespective of the initial preparation. Information on the following were added to the aggregated prescribing dataset: practice-level IMD score, total list size, the proportion of males in the practice list, and the proportion of over-65s (calculated from the age-stratified practice list size dataset). Prescribing in each practice was then calculated in milligram equivalents of diazepam per 1000 patients.

Practice-level prescribing is presented by IMD decile, showing the mean and 95% confidence interval (CI), where decile ten represents the practices with the highest IMD score. To process the data for presentation on a regional map by CCG, the same process was followed as above, but aggregating prescribing and list sizes by CCG rather than by practice. NHS Manchester CCG was formed in April 2017 as a merger of three separate CCGs (North, Central and South Manchester CCGs). For this case, all data from the three superseded CCGs (i.e. prior to April 2017) were recoded as being from NHS Manchester CCG. Prescribing was then stratified by decile and plotted on choropleth maps of England, using CCG boundary shapefiles published by the Office for National Statistics (ONS)[26]. The same was done for CCG-level IMD scores. In order to display both IMD decile and prescribing level on a single

CCG map, bivariate choropleth maps were created by splitting each variable into tertiles and plotting each variable in a different colour.

The individual drugs studied included those which constituted more than 0.1% of items of benzodiazepines or Z-drugs prescribed across 2017. These were: chlordiazepoxide, clobazam, clonazepam, diazepam, lorazepam, nitrazepam, oxazepam, temazepam and zopiclone. Bromazepam and zaleplon (both < 0.01% of items) were excluded.

Statistical Analysis

The association between practice-level IMD score and benzodiazepine prescribing quantity per 1000 patients was testing using simple (univariate) linear regression. The assumptions of linear regression were satisfied, except that of a normal distribution of residuals. However, linear regression can still be appropriate in the absence of non-normally distributed residuals where the sample size is large, as in this study[27]. Multivariable linear regression was conducted using both the practice proportion of males and the proportion of over-65s as independent variables, to test whether practice-level IMD was associated with prescribing independently of practice age and sex distribution. The results of linear regression analyses are presented as unstandardized coefficients of regression (B), which denote the extra amount of mg-equivalent diazepam prescribed per 1000 patients for each one-point increase in practice IMD score, and adjusted R^2 values (the proportion of the variability in prescribing that is explained by the factors studied in the regression model). A p value < 0.05 is considered statistically significant. All data were analysed, and all plots generated, using the software R[7]. As all the data used were publicly available, no ethical approval was required.

Results

Association between socioeconomic status and total benzodiazepine and Z-drug prescribing

In 2017, over 14.6 million prescriptions of benzodiazepines and Z-drugs were written in England, totalling more than the equivalent of 2.3 billion milligrams of diazepam. Over a third of the items prescribed were for diazepam, with a similar proportion being for zopiclone (*Figure 1*).

The association between total benzodiazepine and Z-drug prescribing and practice IMD score decile was examined (*Figure 2*). This shows that prescribing was statistically significantly higher in decile 10 (the highest IMD scoring practices) compared to the lowest decile. Specifically, practices in the lowest IMD decile prescribed fewer benzodiazepines that those in every other decile.

On univariate analysis, there was a significant association between practice IMD score and prescribing (B = 164 [95% CI 119-209], $p < 0.001$). After accounting for sex distribution and the proportion of over-65s, this association was strengthened (B = 628 [95% CI 580-676)], $p < 0.001$). The combination of the three variables practice IMD score, proportion of males and proportion of over-65s explained almost a fifth of the variability in total benzodiazepine and Z-drug prescribing across practices (multiple R^2 = 18%).

Association between socioeconomic status and prescribing for individual drugs

In univariate analyses, all drugs except zopiclone were statistically significantly associated with practice IMD score. Once age and sex were taken into account in the multivariable model, IMD score was significantly associated with prescribing levels for all individual drugs, with more prescribing seen in practices with higher IMD scores. The combination of practice IMD score, age and sex accounted for between 6% and 13% of the variation seen in prescribing of individual drugs, leaving a significant proportion of the variation unaccounted for. A summary of the results of univariate and multiple linear regression tests for the association between the level of prescribing for each individual drug and practice IMD score is shown in *Table 1*. The varying strengths of association between prescribing and SES is unsurprising given that individual benzodiazepines are favoured for different indications. The strongest associations were seen with nitrazepam and clobazam (see *Supplementary Material 2*, which includes relevant plots for all individual drugs).

Geographical Variation in Prescribing

Choropleth maps showing deciles of prescribing rates by CCG for total benzodiazepine and Z-drug prescribing are shown in *Figure 3* (see *Supplementary Material 2* for a choropleth map of regional CCG IMD deciles). Rates of benzodiazepine prescribing are highest in the East of England, as well as in dispersed coastal regions around the UK. Interestingly, CCGs with the highest prescribing rates do not necessarily coincide with those with the highest IMD scores. Similarly, there is no clear north/south divide in CCG-level benzodiazepine and Z-drug prescribing.

In order to simultaneously display CCG-level prescribing and socioeconomic status, and to visualise any correlations, a bivariate choropleth map was created (*Figure 4*). This visualisation suggests that, at the CCG level, coastal areas tend to have lower IMD scores but more prescribing. Indeed, very few CCGs have both high IMD scores and high prescribing. The finding of higher prescribing in coastal regions warrants further study, but it is notable that coastal regions also tend to have a higher proportion of elderly people.

Conclusions

In this study, we examined the association between benzodiazepine and Z-drug prescribing and socioeconomic status in England. We have found that practices with a higher IMD score tend to have higher prescription rates, after adjusting for age and sex, although these three factors alone only explain a relatively small percentage of the total variation in benzodiazepine and Z-drug prescribing. The prescription of benzodiazepines and Z-drugs is subject to large geographical variation in England; for example, we found a preponderance of higher prescribing rates in coastal regions, but no clear north-south divide. Social status alone cannot explain this geographic variation. The strength of the association between IMD scores and prescribing rates was not replicated for each individual drug, likely as an expression of the diverse indications for these medications. For example, chlordiazepoxide – used to manage alcohol withdrawal – showed unique geographical patterning, being prescribed at a relatively low rate in some relatively underserved areas. It may be that cultural influence is important in this case, as the Muslim population, who generally do not drink alcohol, are a sizeable proportion of some these regional subpopulations[28,29]. It is likely that the study of prescribing stratified by indication (e.g. anxiety) may help to improve the relevance of associations with SES.

A recent study in Ireland analysing benzodiazepine and Z-drug prescribing in adults nationally found a third of patients receiving these drugs were on longer-term prescriptions (over 90 days), with prescribing rates highest in older women[30]. Whilst the association with age and sex is in line with our findings, and that of other studies[31,32], the authors did not consider socioeconomic status. A Scottish population-based study of adults over the age of 65 years found that 12% were prescribed one or more benzodiazepine and Z-drug, although care-home residents were three-times as likely to be on this class of drugs[16]. This more convincingly highlights the impact of age as a predictor of prescription. A study examining the relationship between patient and practice factors and anxiolytic and hypnotic prescribing using data from 2004/5 in England also found a relationship with low socioeconomic status, as well as increased prescribing in practices with a lower proportion of ethnic minorities[18].

Whilst we found that the relationship persists in 2017 with respect to benzodiazepine and Z-drug prescribing overall, we also demonstrated that the strength of the association differed between drugs within these classes.

Strengths and Limitations

We evaluated the prescribing of benzodiazepines and Z-drugs in primary care practices across England, thus removing selection bias. Aggregating data across a calendar year avoided the potential effects of seasonal variation.

There are limitations to the presented study. IMD score is not a direct measure of socioeconomic status, and the IMD score attributed to a GP practice does not necessarily reflect the socioeconomic status of those patients who are prescribed benzodiazepines, so we cannot conclude that patients with a low socioeconomic status are more likely to be prescribed these medications. A further limitation of aggregated data is the lack of detail around the intended indications for prescribing. We did not consider prescriptions originating outside of primary care or private prescriptions, and these may have had an impact on results; for example if those in underserved populations are less likely to seek private prescriptions. Finally, the effects of patient- and practice-level factors (other than age and sex) on prescribing were not included in our regression model.

Implications for Research and Practice

We found an association between primary care practice-level socioeconomic status and practice-level prescribing of benzodiazepines and Z-drugs in England in 2017, although the combination of IMD score, age and sex only explained a small proportion of the variation in prescribing. Whilst it is possible that similar associations may be seen in other settings and countries, this would require direct investigation. Further work is required on individual-level datasets from primary care to determine which patient-level and practice-level factors are driving the prescription of these drugs, to help identify where future interventions to reduce prescribing should be targeted. Whilst Z-drugs and benzodiazepines are commonly prescribed and effective in specific situations, the side-effects and potential for abuse, as well as the propensity for addiction, mean closer scrutiny is required.

Additional Information

Funding

SS is supported by a National Institute of Health Research (NIHR) Clinical Lectureship, and FK by an NIHR Academic Clinical Fellowship. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the UK's Department of Health and Social Care. No specific funding was sought for the presented analysis.

Ethical Approval

This study used publicly available data only, so no ethical approval was required.

Competing Interests

The authors declare no competing interests

References

1. Lader M. Antianxiety drugs: clinical pharmacology and therapeutic use. *Drugs.* 1976;12(5):362-373.
2. Beaumont B. Care of drug users in general practice: a harm reduction approach. Second edition. CRC Press, 2004.
3. World Health Organisation. Chapter 4: Withdrawal Management *in* Clinical guidelines for withdrawal management and treatment of drug dependence in closed settings. Geneva: World Health Organisation; 2009.
4. Siriwardena AN, Qureshi Z, Gibson S, Collier S, Latham M. GPs' attitudes to benzodiazepine and 'Z-drug' prescribing: a barrier to implementation of evidence and guidance on hypnotics. *Br J Gen Pract.* 2006;56(533):964-967.
5. Griffin CE, 3rd, Kaye AM, Bueno FR, Kaye AD. Benzodiazepine pharmacology and central nervous system-mediated effects. *Ochsner J.* 2013;13(2):214-223.
6. Gunja N. The clinical and forensic toxicology of Z-drugs. *J Med Toxicol.* 2013;9(2):155-162.
7. R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/. [last accessed Nov 2018).
8. Davies J, Rae TC, Montagu L. Long-term benzodiazepine and Z-drugs use in England: a survey of general practice. *Br J Gen Pract.* 2017;67(662):e609-e613.
9. Pariente A, Dartigues JF, Benichou J, Letenneur L, Moore N, Fourrier-Reglat A. Benzodiazepines and injurious falls in community dwelling elders. *Drugs Aging.* 2008;25(1):61-70.
10. Thomas RE. Benzodiazepine use and motor vehicle accidents. Systematic review of reported association. *Can Fam Physician.* 1998;44:799-808.
11. Barker MJ, Greenwood KM, Jackson M, Crowe SF. Cognitive effects of long-term benzodiazepine use: a meta-analysis. *CNS Drugs.* 2004;18(1):37-48.
12. Billioti de Gage S, Moride Y, Ducruet T, et al. Benzodiazepine use and risk of Alzheimer's disease: case-control study. *BMJ.* 2014;349:g5205.
13. Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ.* 2005;331(7526):1169.
14. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European Drug Report 2017: Trends and Developments. EMCDDA, 2017. .
15. Public Health England. Prescribed medicines that may cause dependence or withdrawal. Available at: https://www.gov.uk/government/news/prescribed-medicines-that-may-cause-dependence-or-withdrawal [Accessed March 2019].
16. Johnson CF, Frei C, Downes N, McTaggart SA, Akram G. Benzodiazepine and z-hypnotic prescribing for older people in primary care: a cross-sectional population-based study. *Br J Gen Pract.* 2016;66(647):e410-415.
17. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. *JAMA Psychiatry.* 2015;72(2):136-142.
18. Tsimtsiou Z, Ashworth M, Jones R. Variations in anxiolytic and hypnotic prescribing by GPs: a cross-sectional analysis using data from the UK Quality and Outcomes Framework. *Br J Gen Pract.* 2009;59(563):e191-198.
19. Farias JC, Porter L, McManus S, et al. Prescribing patterns in dependence forming medicines. Public Health Research Consortium; 2017. .
20. NHS Digital. Practice level prescribing data. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/practice-level-prescribing-data. [Accessed March 2019].

21. NHS Digital. Patients registered at a GP practice. https://digital.nhs.uk/data-and-information/publications/statistical/patients-registered-at-a-gp-practice [Last accessed November 2018].
22. NHS Digital. Chemical names and BNF codes. https://data.gov.uk/dataset/176ae264-2484-4afe-a297-d51798eb8228/resource/bac33489-b3dc-47ec-b688-da9cf40e25bd [Last accessed November 2018].
23. British National Formulary. Hypnotics and anxiolytics. https://bnf.nice.org.uk/treatment-summary/hypnotics-and-anxiolytics.html [Last accessed November 2018].
24. Public Health England. National General Practice Profiles. https://fingertips.phe.org.uk/profile/general-practice [Last accessed November 2018].
25. Department for Communities and Local Government. English indices of deprivation 2015. https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015 [Last accessed November 2018].
26. Office for National Statistics. CCG boundaries (April 2017). https://data.gov.uk/dataset/91c26db1-926b-4215-8d88-2e922914bc00/clinical-commissioning-groups-april-2017-full-clipped-boundaries-in-england-v4 [last accessed Nov 2018].
27. Lumley T, Diehr P, Emerson S, Chen L. The importance of the normality assumption in large public health data sets. *Annu Rev Public Health.* 2002;23:151-169.
28. NHS Tower Hamlets Clinical Commissioning Group. Annual report and accounts 2017-2018. NHS Tower Hamlets CCG 2018. Available at: http://www.towerhamletsccg.nhs.uk/downloads/about/publications/annualreports/NHS-THCCG-Annual-report-and-accounts-2017-18-final.pdf [Last accessed May 2019].
29. NHS Newham Clinical Commissioning Group. Equality and information report 2017-2018. NHS Newham CCG 2018. Available at: http://www.newhamccg.nhs.uk/Downloads/News-and-Publications/Policies-and-procedures/NHS-NCCG-Equality-Information-report-2017-18-V1.pdf [Last accessed May 2019]

30. Cadogan CA, Ryan C, Cahir C, Bradley CP, Bennett K. Benzodiazepine and Z-drug prescribing in Ireland: analysis of national prescribing trends from 2005 to 2015. *Br J Clin Pharmacol.* 2018;84(6):1354-1363.
31. Tu K, Mamdani MM, Hux JE, Tu JB. Progressive trends in the prevalence of benzodiazepine prescribing in older people in Ontario, Canada. *J Am Geriatr Soc.* 2001;49(10):1341-1345.
32. Hollingworth SA, Siskind DJ. Anxiolytic, hypnotic and sedative medication use in Australia. *Pharmacoepidemiol Drug Saf.* 2010;19(3):280-288.

Figures

Figure 1. The prescribing level for each drug, as a proportion of total benzodiazepine and Z-drug prescribing in 2017 in England.

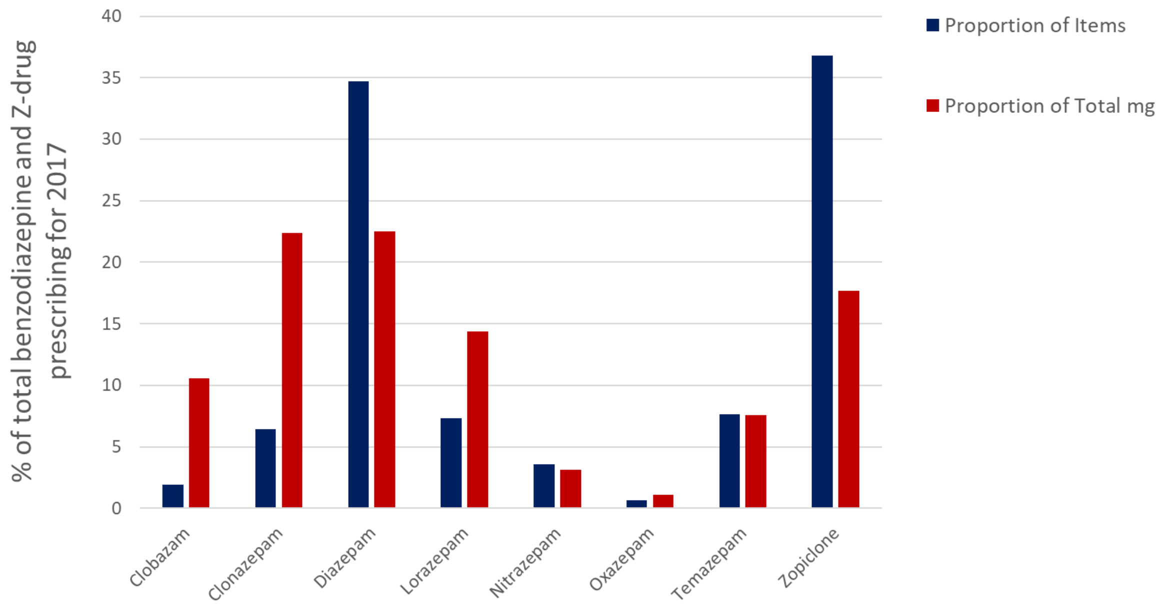


Figure 2. Benzodiazepine and Z-drug prescription levels per 1000 registered patients by practice Index of Multiple Deprivation Deciles in England (2017). For Index of Multiple Deprivation (IMD) deciles, 1 is the lowest scores (most underserved) and 10 is the highest scores. Bars and whiskers show the mean and 95% confidence interval for each decile.

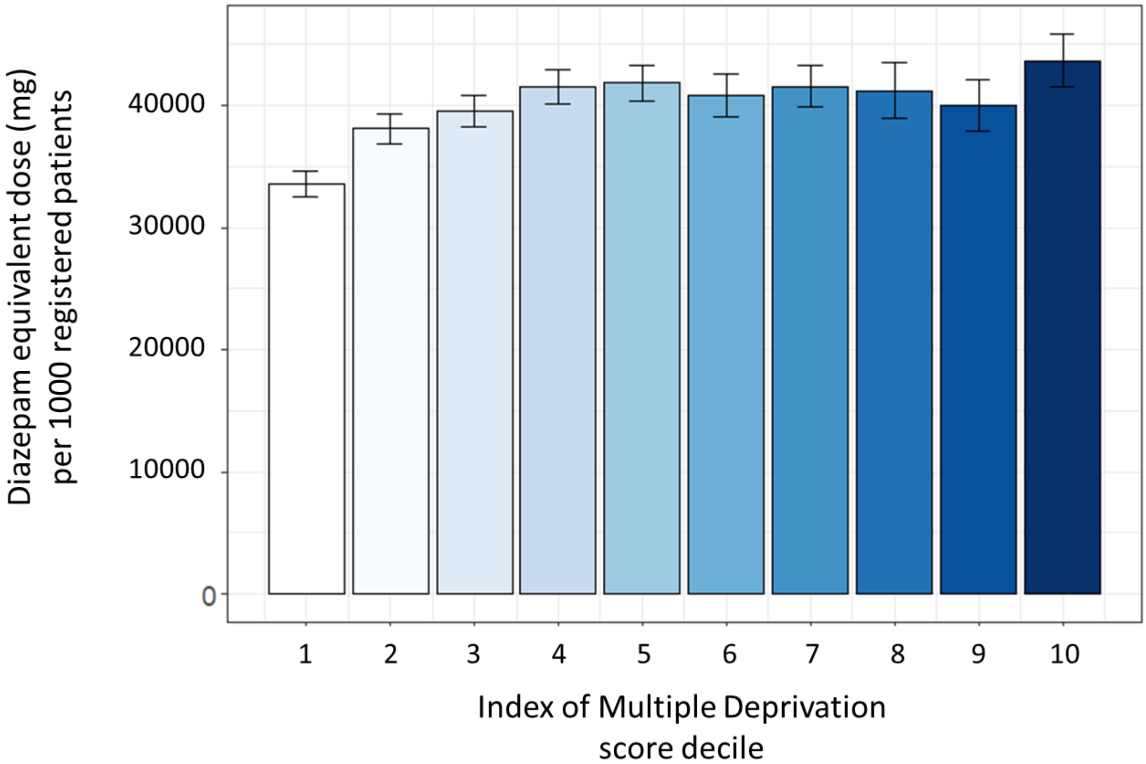


Figure 3: Benzodiazepine and Z-drug prescribing by region (by Clinical Commissioning Group in England, 2017).

Geographical choropleth map of England, categorising Clinical Commissioning Group regions according to deciles of benzodiazepine and Z-drug prescribing. Decile 1 is the lowest level of prescribing and 10 is the highest

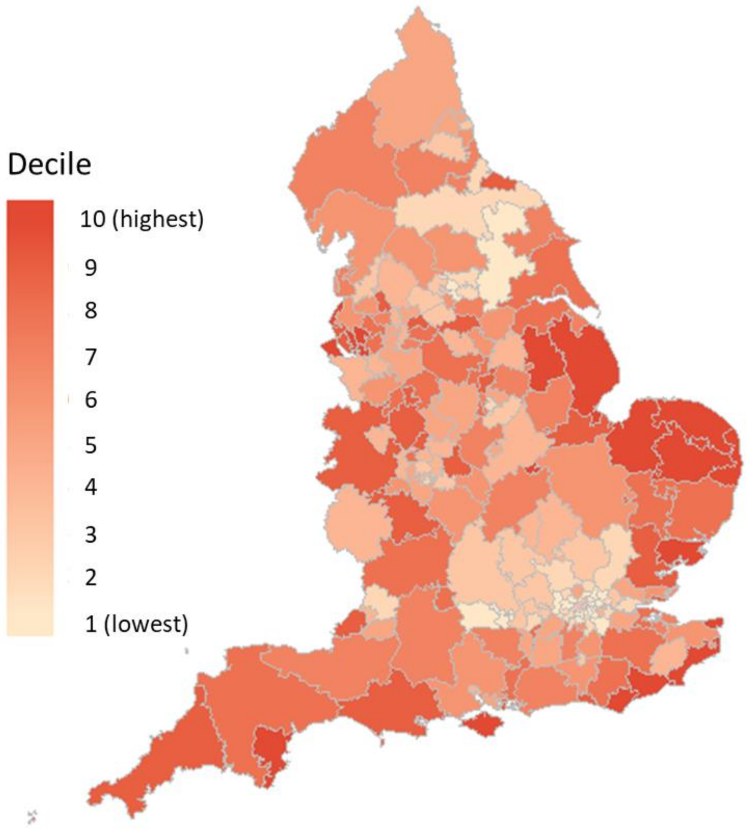
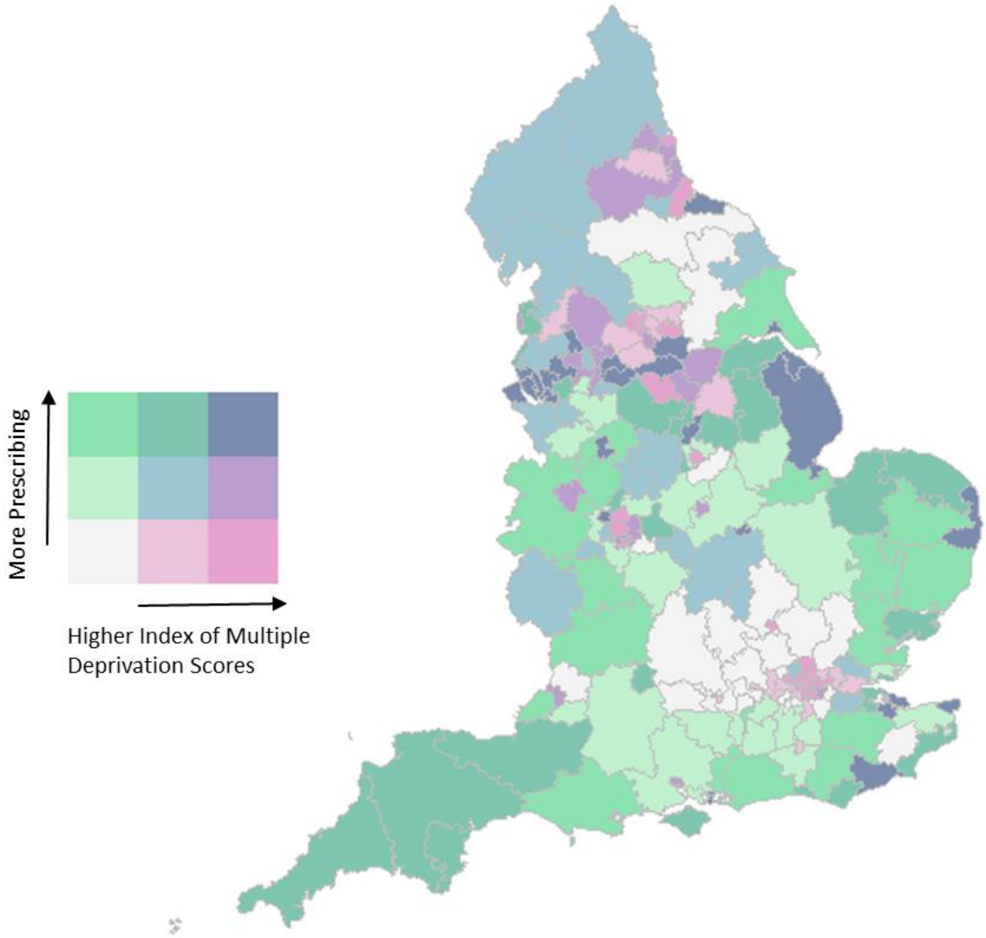


Figure 4. Benzodiazepine and Z-drug prescribing and Index of Multiple Deprivation scores by region (by Clinical Commissioning Group in England, 2017).

Bivariate choropleth map of England combining information on the rate of benzodiazepine and Z-drug prescribing and socioeconomic status as described by Index of Multiple Deprivation (IMD) scores (by tertiles). Where IMD scores and prescribing are in the same tertile, white or blue shading is given. Alternative shading represents either a higher tertile of IMD score than benzodiazepine prescribing (purple), or a higher tertile of prescribing than IMD score (green).



Table

Table 1. Summary of linear regression results for each individual drug, and all drugs in total, of the association between practice Index of Multiple Deprivation (IMD) score and benzodiazepine and Z-drug prescribing levels in England (2017). B coefficients are in mg-equivalent diazepam per 1000 registered patients. The multivariable model is adjusted for the proportion of males and the proportion of over-65s in each practice.

Drug		Univariate	Multivariable
All benzodiazepine & Z-drug prescriptions	B	164	628
	p value	< 0.001	< 0.001
	adjusted R^2	0.70%	18%
Chlordiazepoxide	B	22	20
	p value	< 0.001	0.003
	adjusted R^2	6%	13%
Clobazam	B	121	162
	p value	< 0.001	< 0.001
	adjusted R^2	8%	12%
Clonazepam	B	79	146
	p value	< 0.001	< 0.001
	adjusted R^2	1%	6%
Diazepam	B	73	164
	p value	< 0.001	< 0.001
	adjusted R^2	1%	7%
Lorazepam	B	50	114
	p value	< 0.001	< 0.001
	adjusted R^2	1%	11%
Nitrazepam	B	36	45
	p value	< 0.001	< 0.001
	adjusted R^2	6%	13%
Temazepam	B	37	55
	p value	< 0.001	< 0.001
	adjusted R^2	2%	8%
Zopiclone	B	4	83
	p value	0.47	< 0.001
	adjusted R^2	<0.1%	13%

Supplementary Material 1

Benzodiazepine and Z-drug equivalences

From the BNF: https://bnf.nice.org.uk/treatment-summary/hypnotics-and-anxiolytics.html

The following doses are approximately equivalent to 5mg of diazepam:

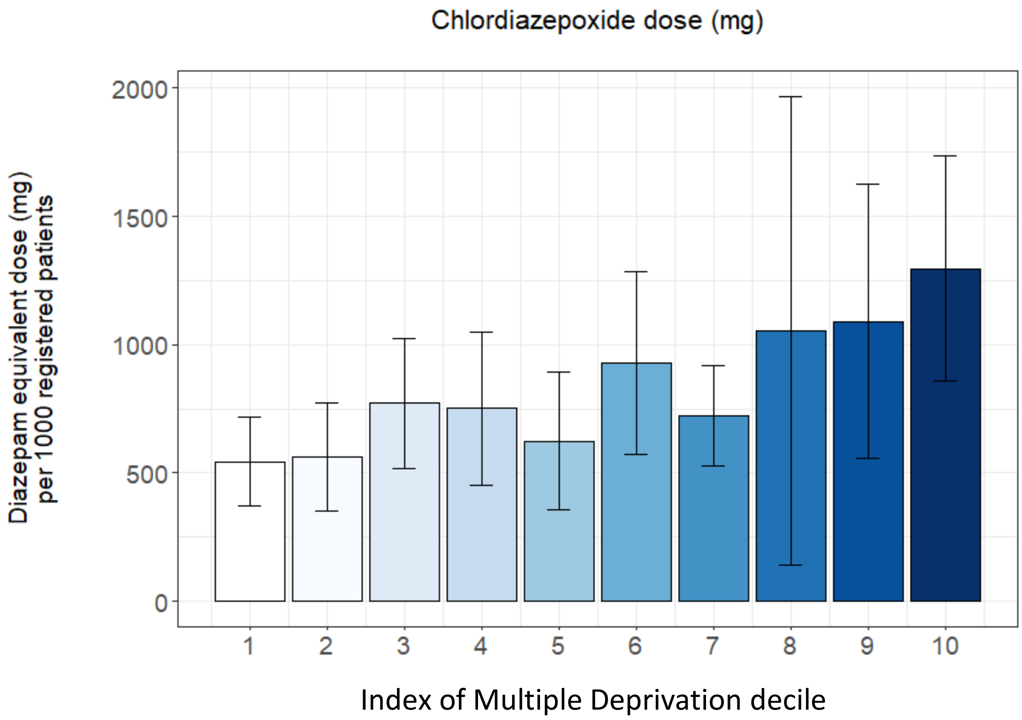
- Alprazolam 250 micrograms
- Clobazam 10 mg
- Clonazepam 250 micrograms
- Flurazepam 7.5 – 15 mg
- Chlordiazepoxide 12.5 mg
- Loprazolam 0.5 – 1 mg
- Lorazepam 500 micrograms
- Lormetazepam 0.5 – 1.0 mg
- Nitrazepam 5 mg
- Oxazepam 10 mg
- Temazepam 10 mg
- Zaleplon 10 mg
- Zolpidem 10 mg
- Zopiclone 7.5 mg

Supplementary Material 2

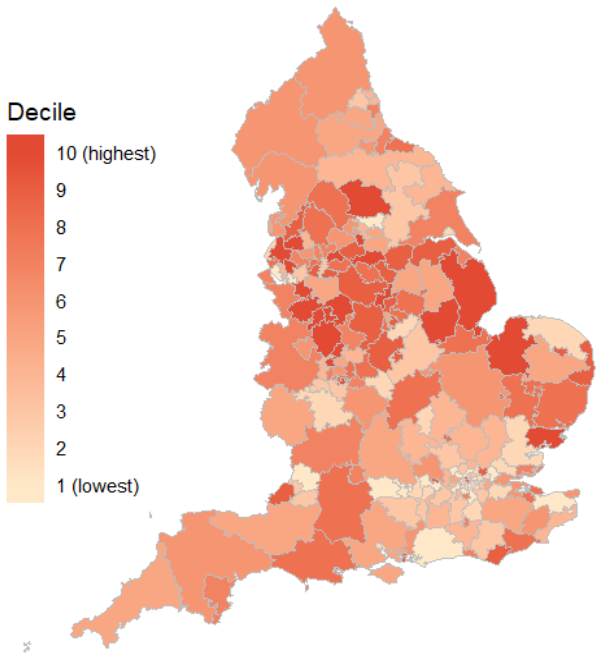
Plots for all individual drugs analysed, using data from England, 2017. For each drug is shown: (1) mean prescribing per 1000 patients (with 95% confidence intervals), for GP practices within each index of multiple deprivation (IMD) decile; (2) choropleth maps of prescribing deciles by Clinical Commissioning Group region (CCG), alongside a map of IMD deciles by CCG; and (3) bivariate choropleth maps simultaneously showing tertiles of prescribing and socioeconomic status by IMD score.

Chlordiazepoxide

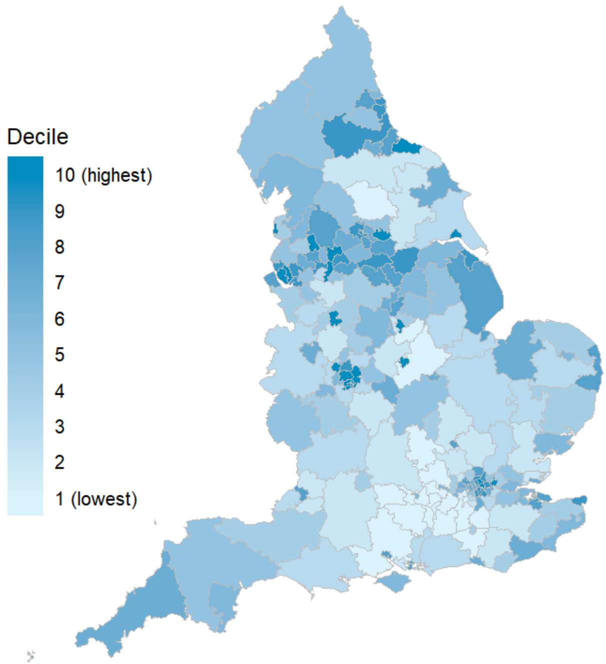
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



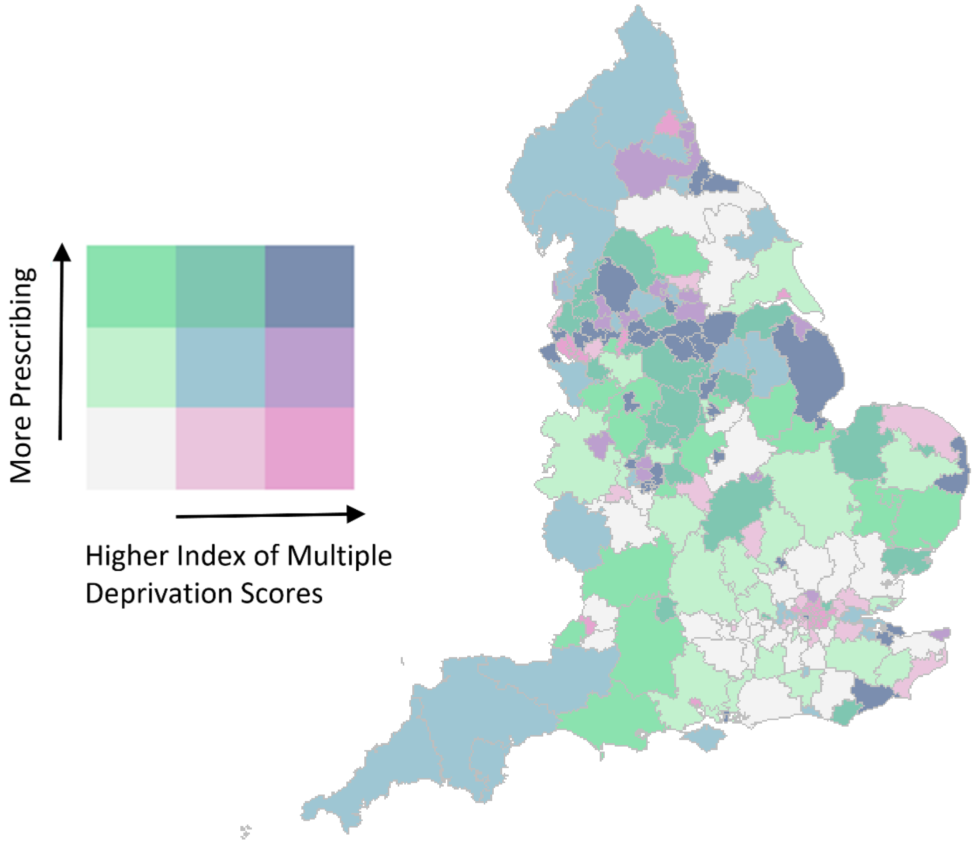
Chlordiazepoxide prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

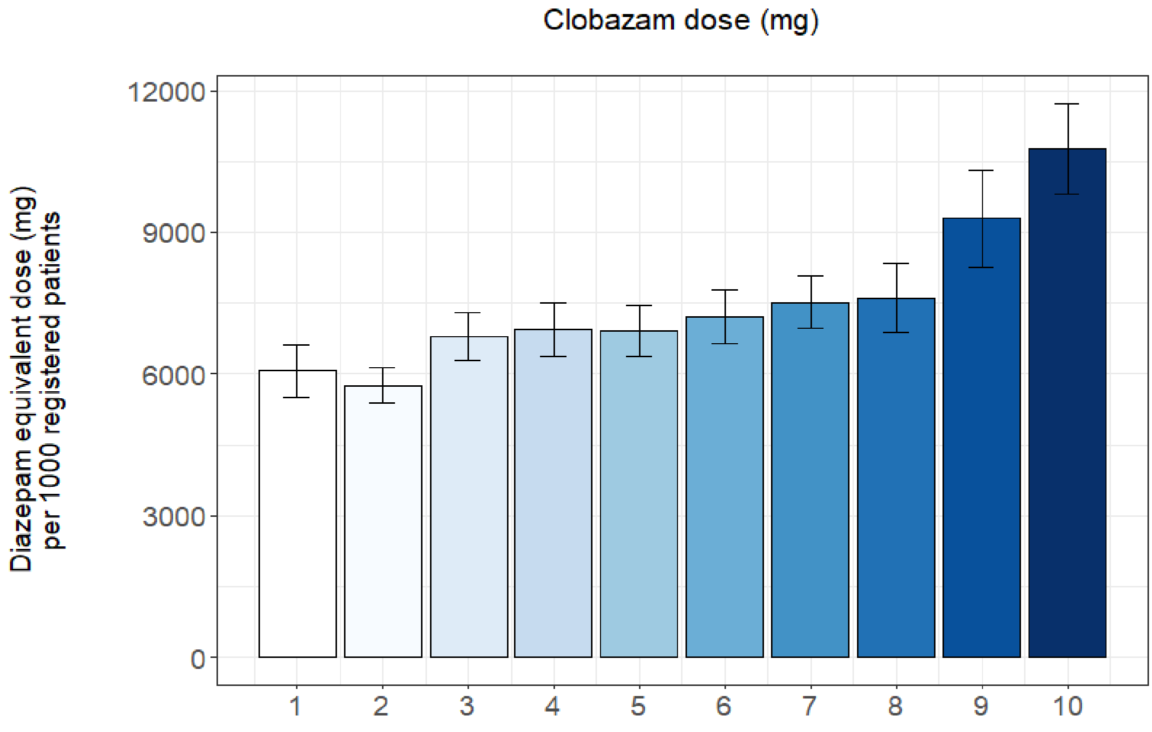


Chlordiazepoxide prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

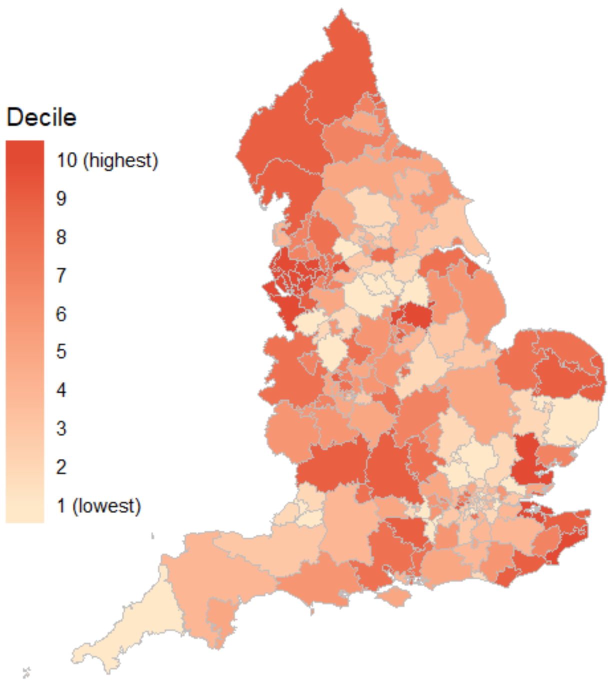


Clobazam

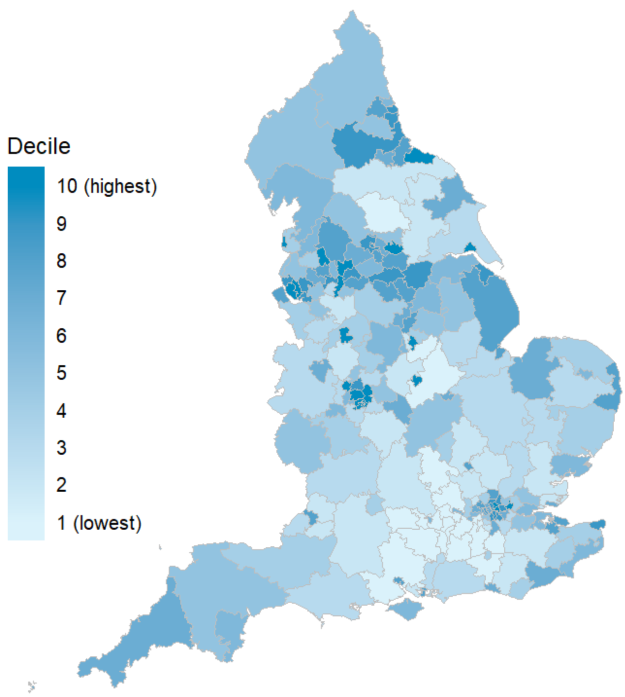
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



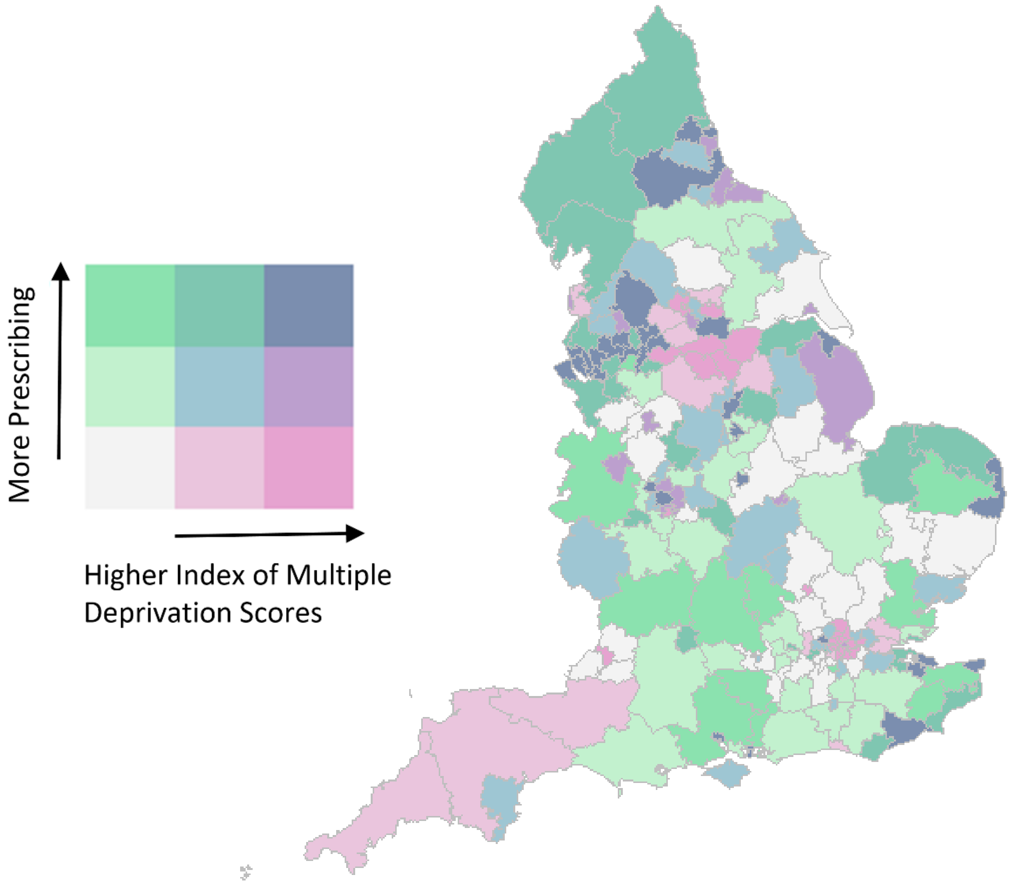
Clobazam prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

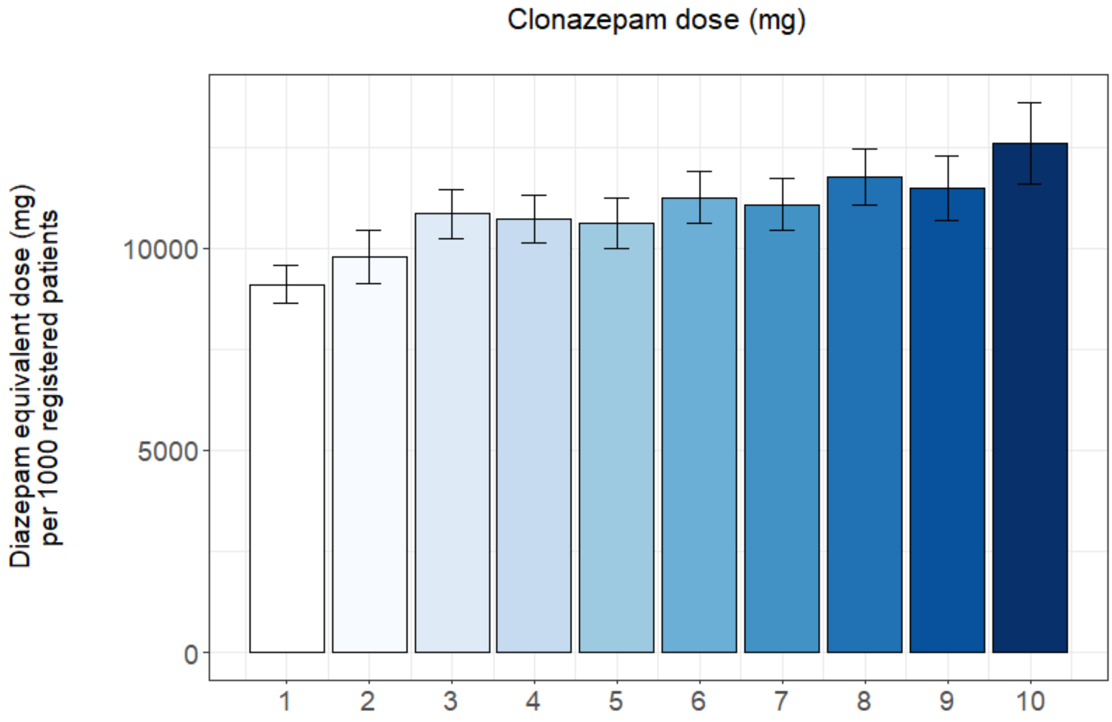


Clobazam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group



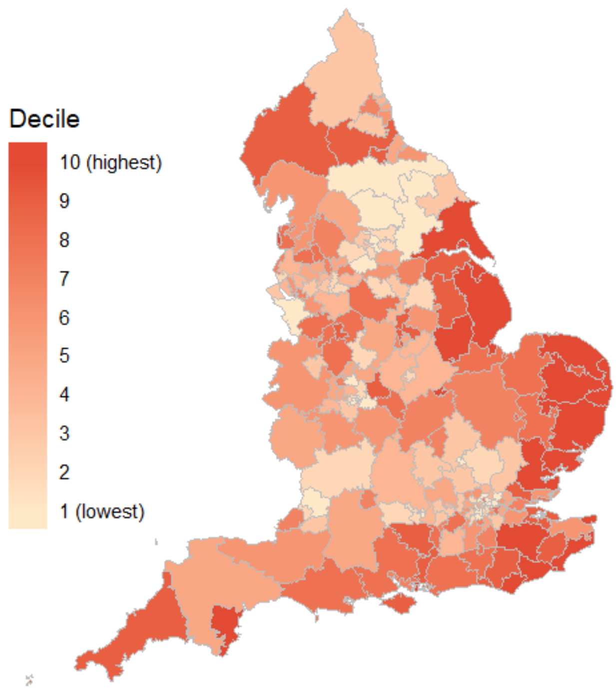
Clonazepam

Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):

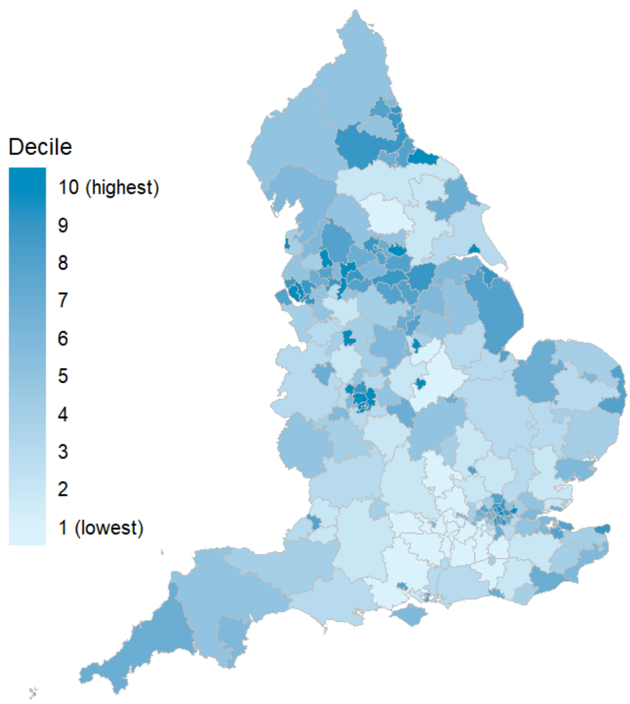


Index of Multiple Deprivation decile

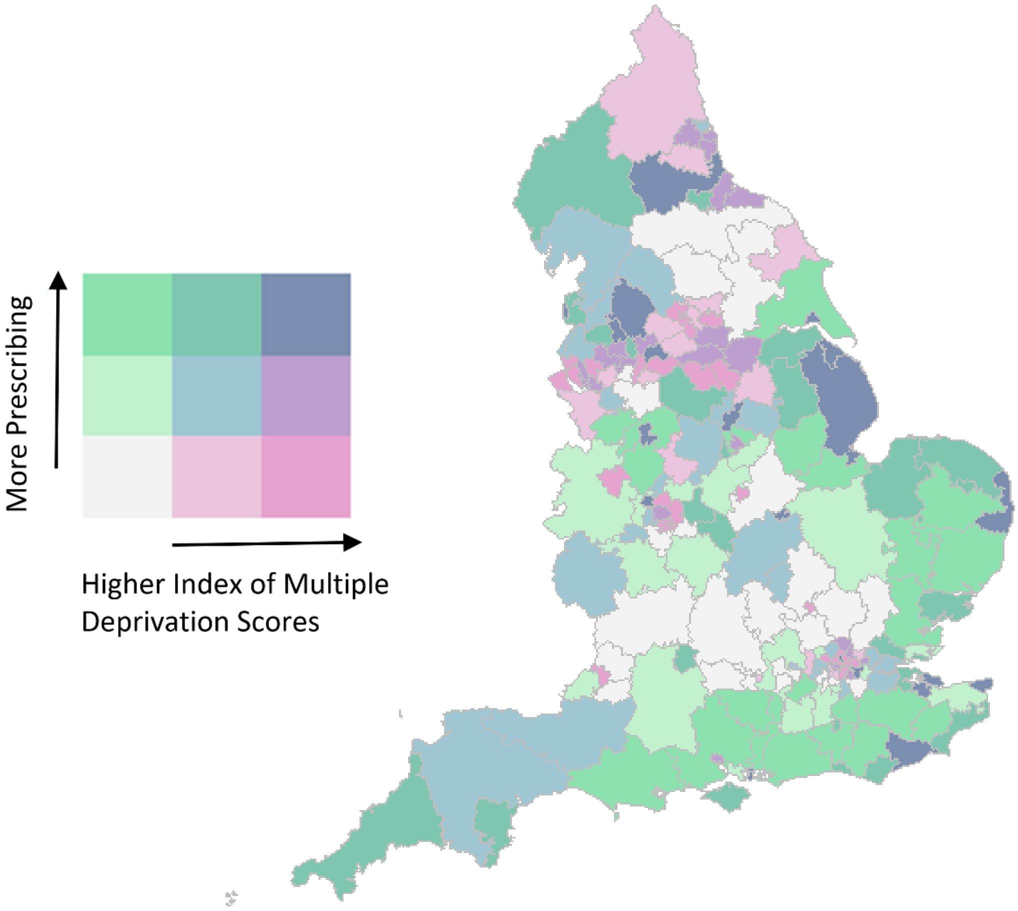
Clonazepam prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

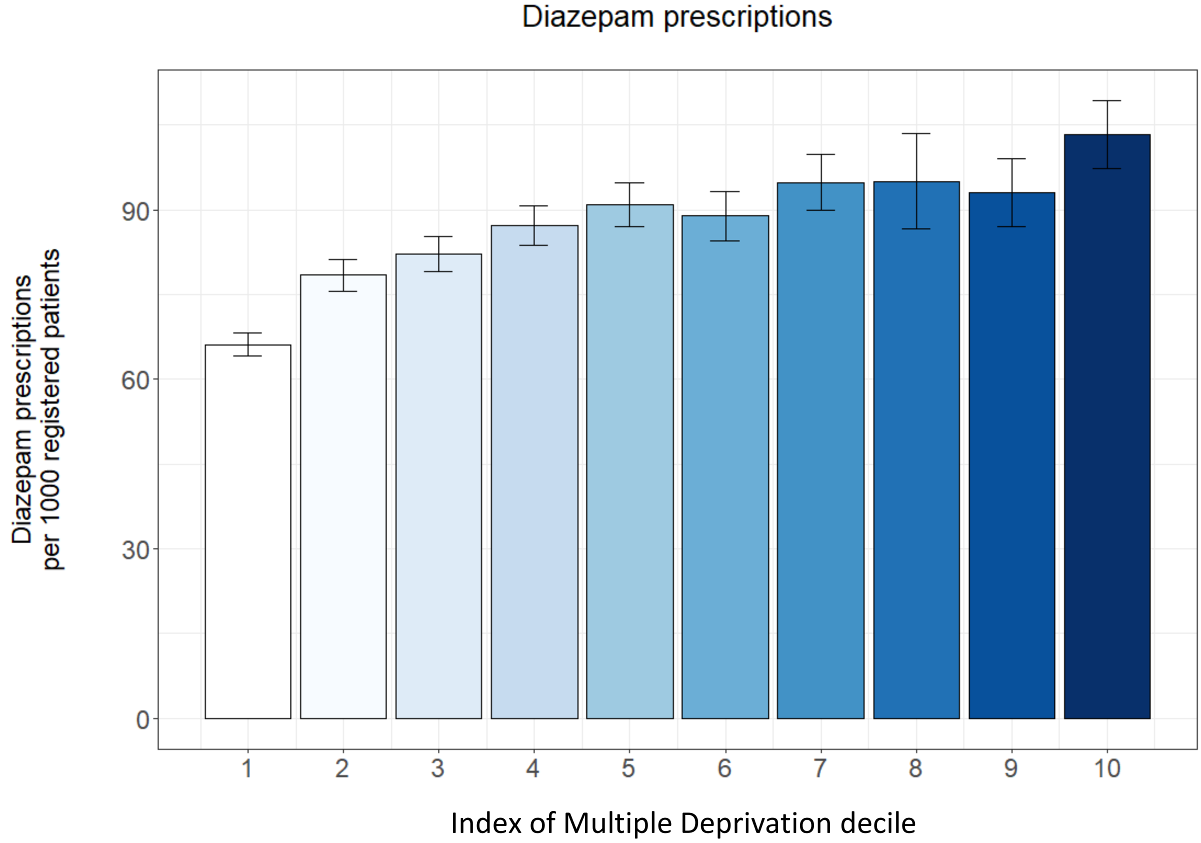


Clonazepam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

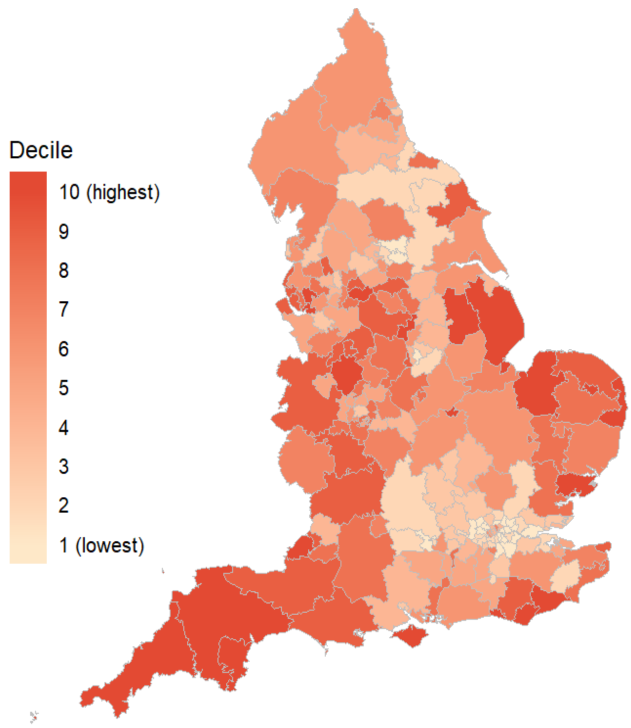


Diazepam

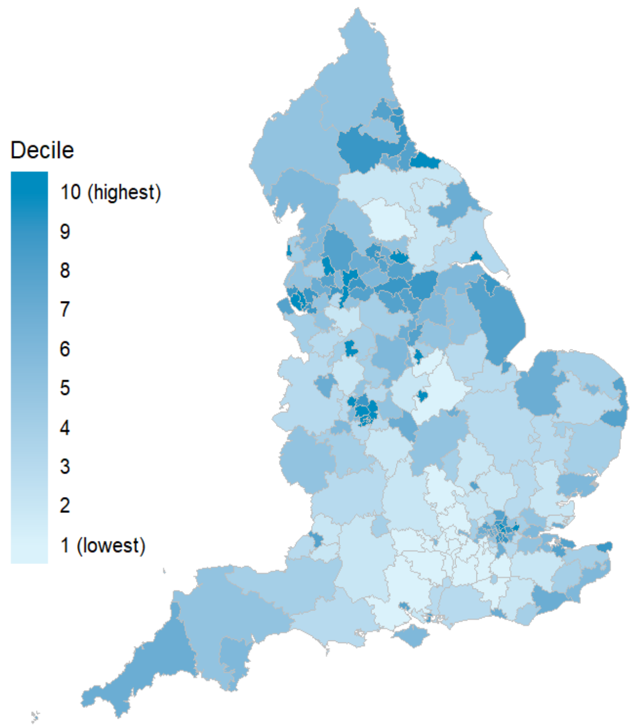
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



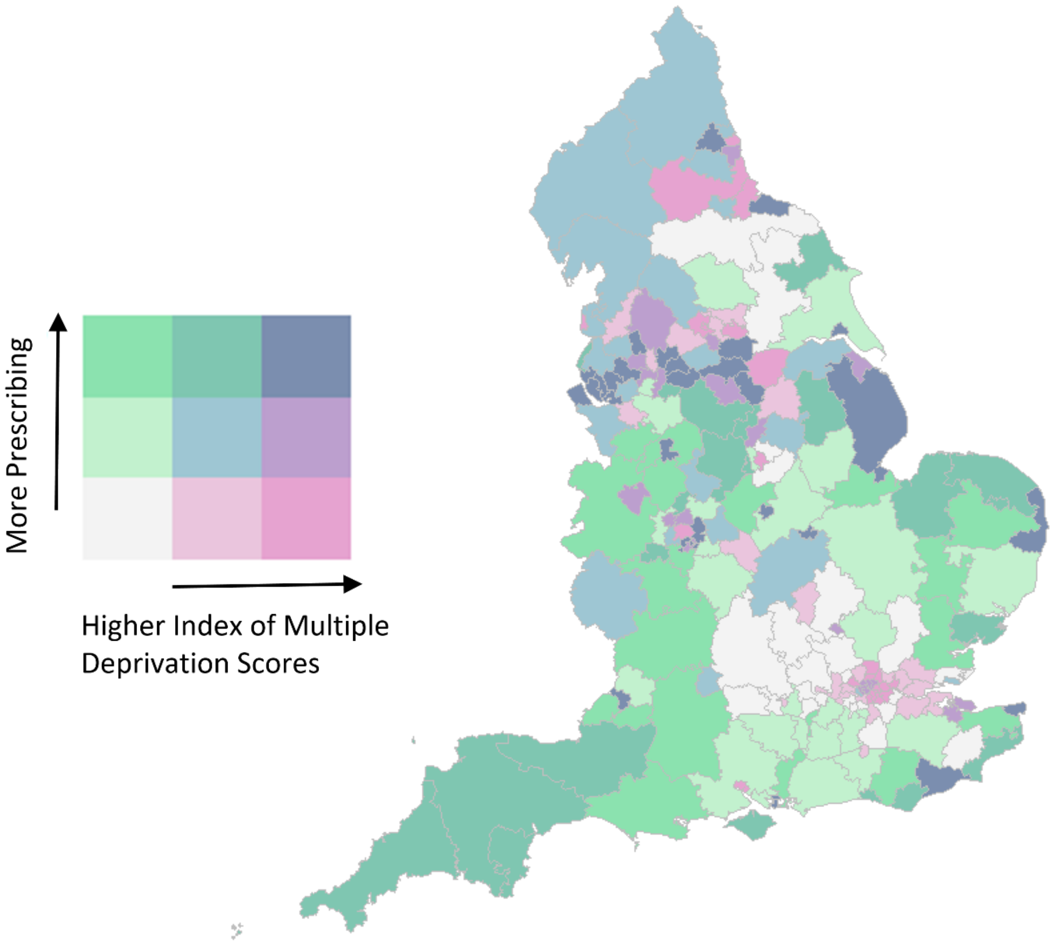
Diazepam prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

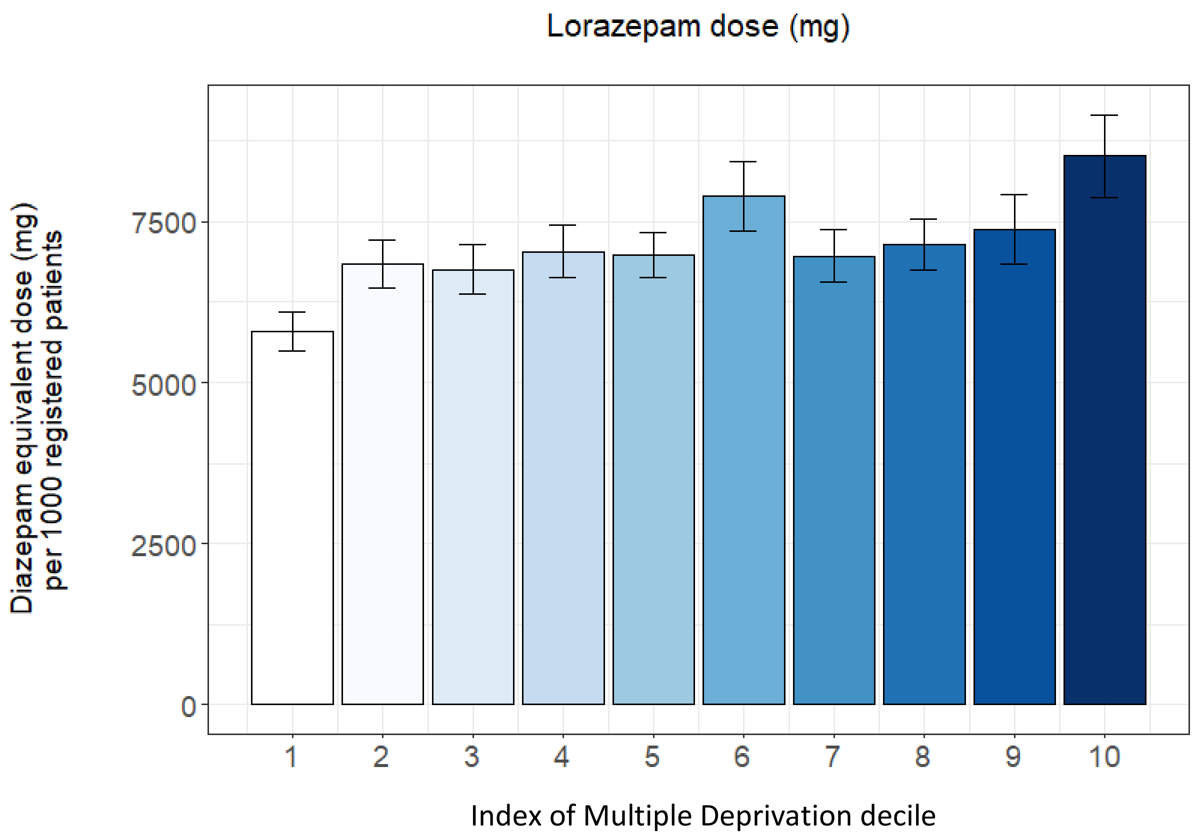


Diazepam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

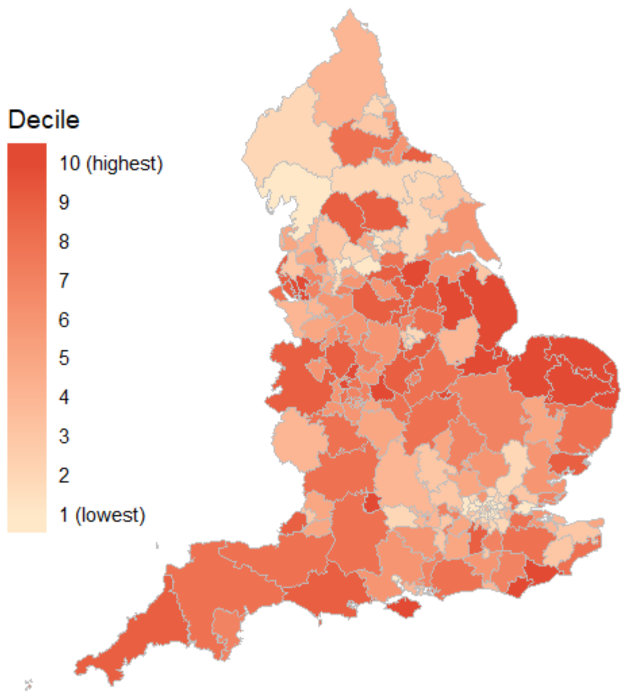


Lorazepam

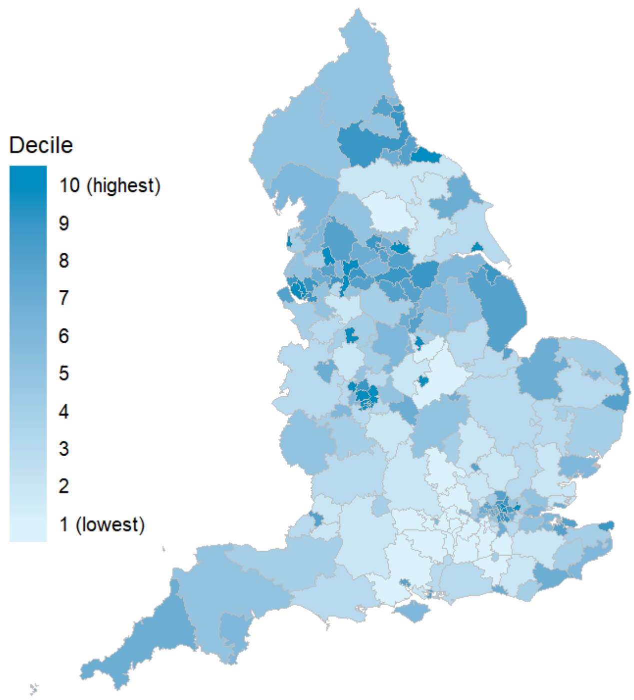
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



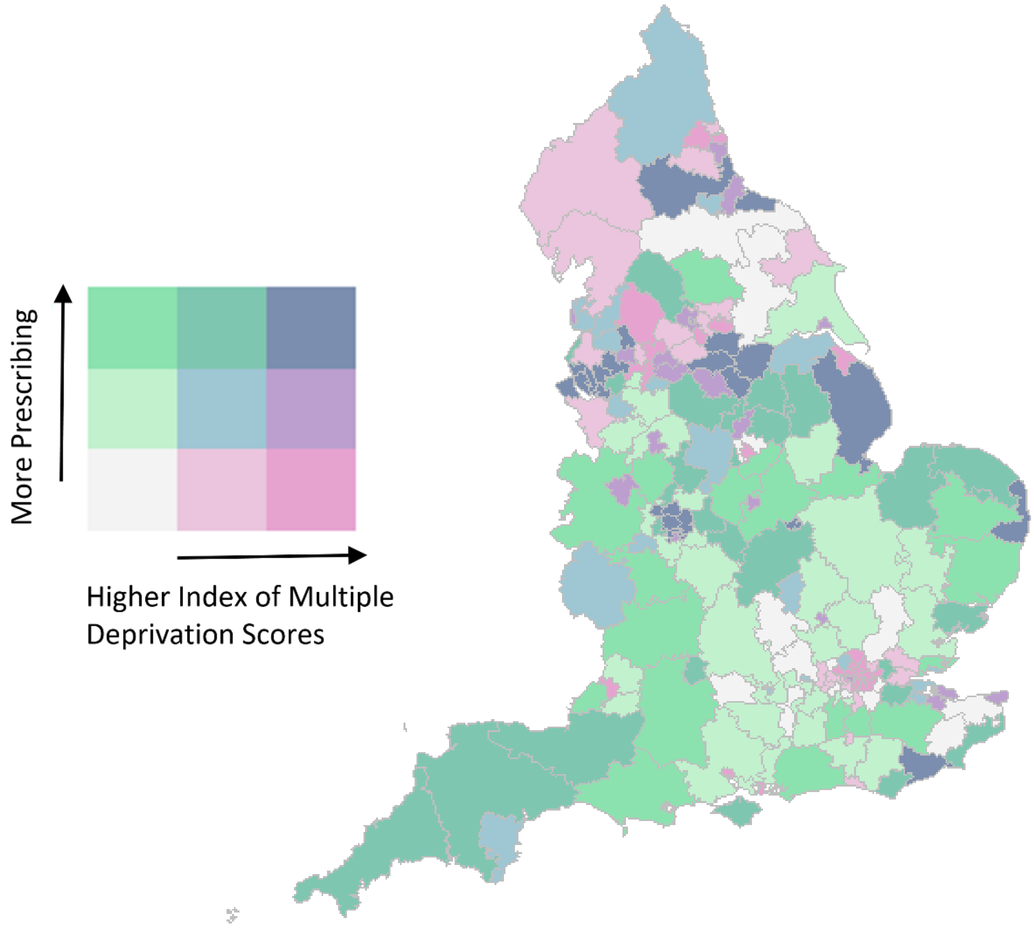
Lorazepam prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

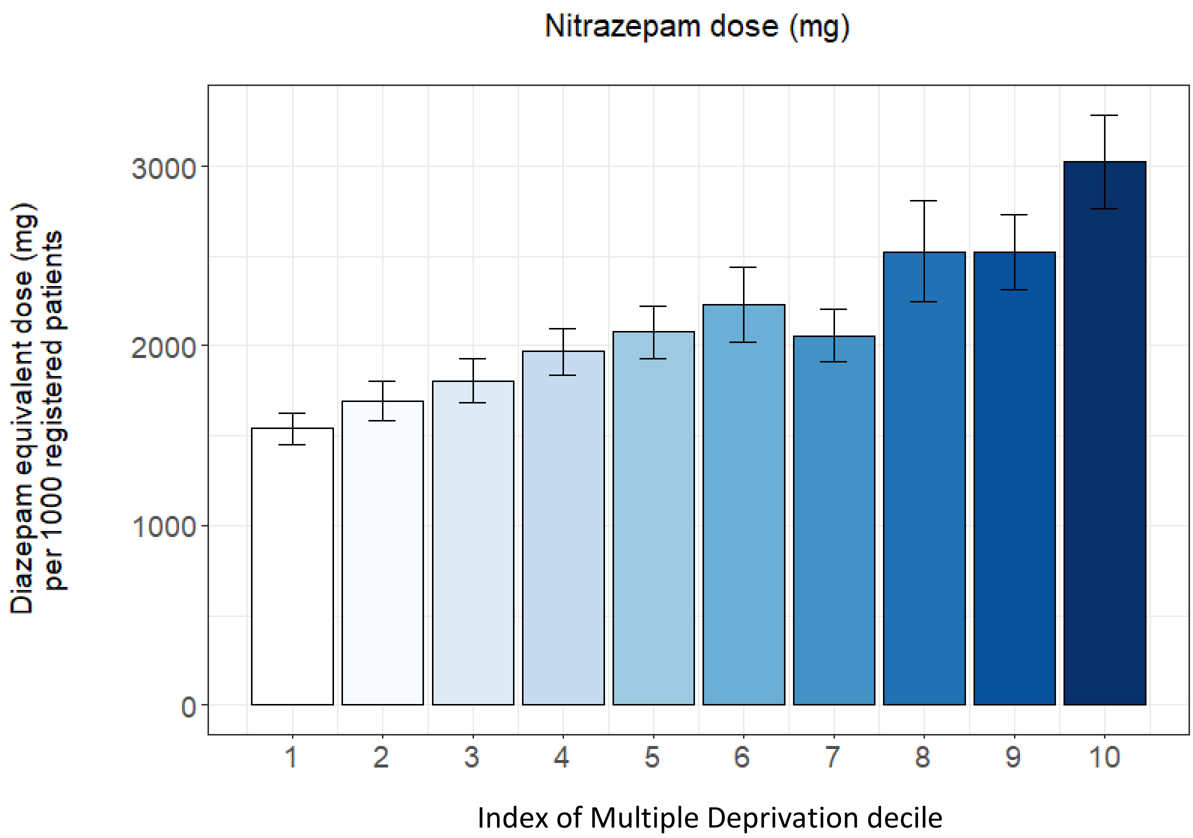


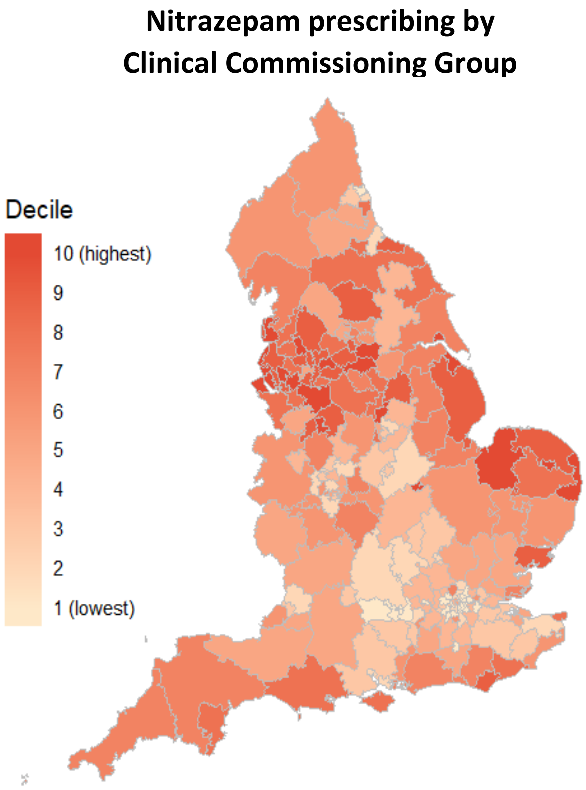
Lorazepam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

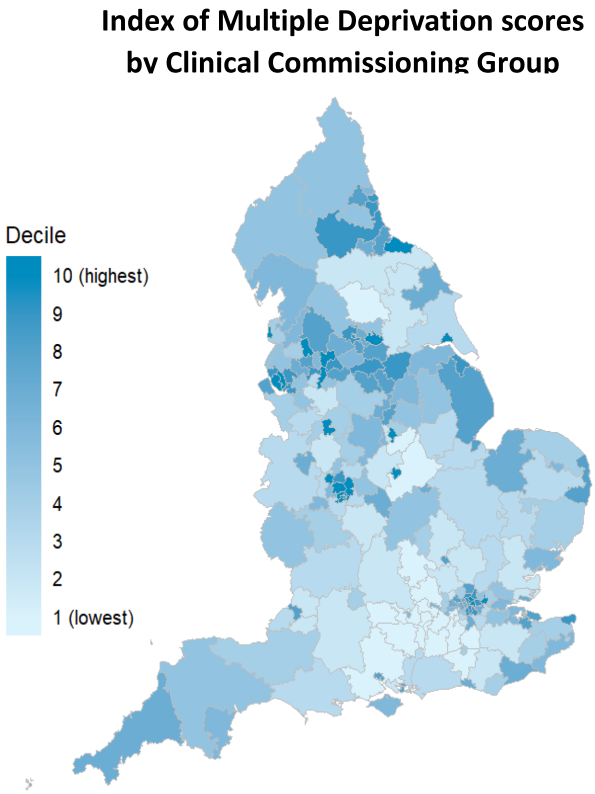


Nitrazepam

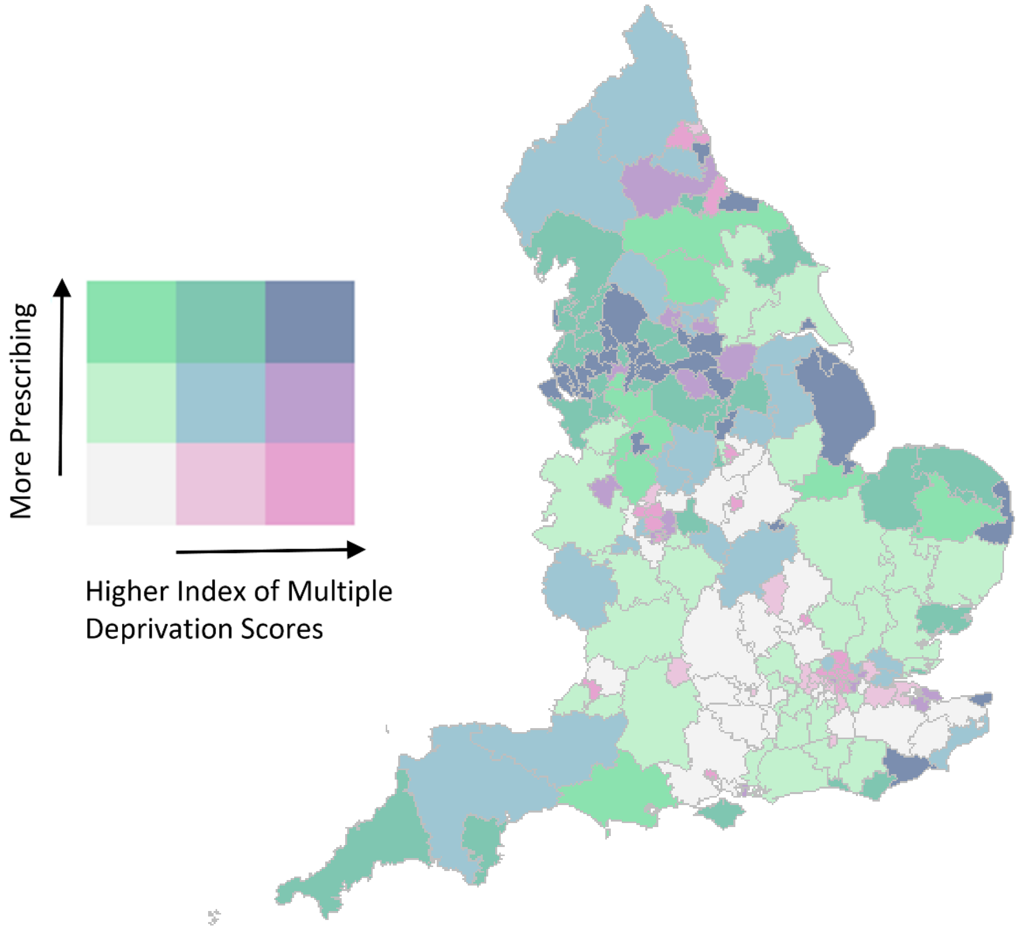
A Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):





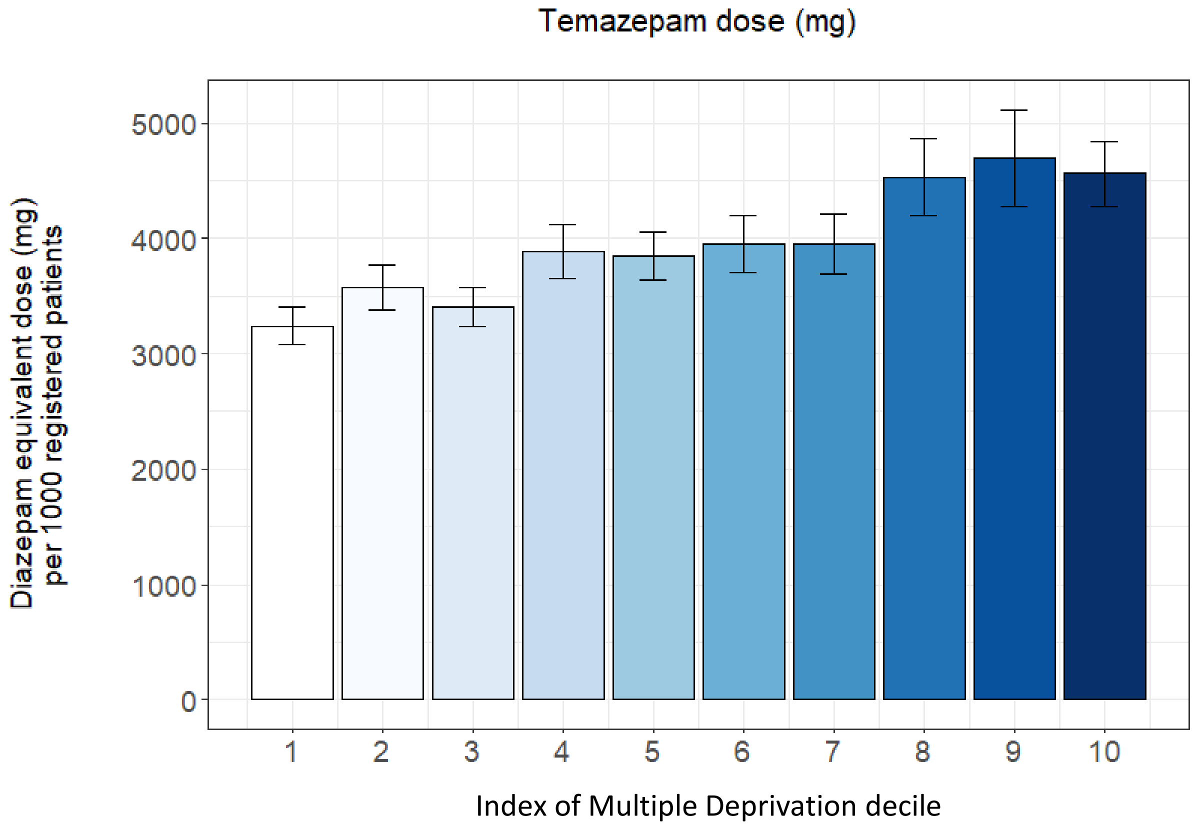


Nitrazepam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

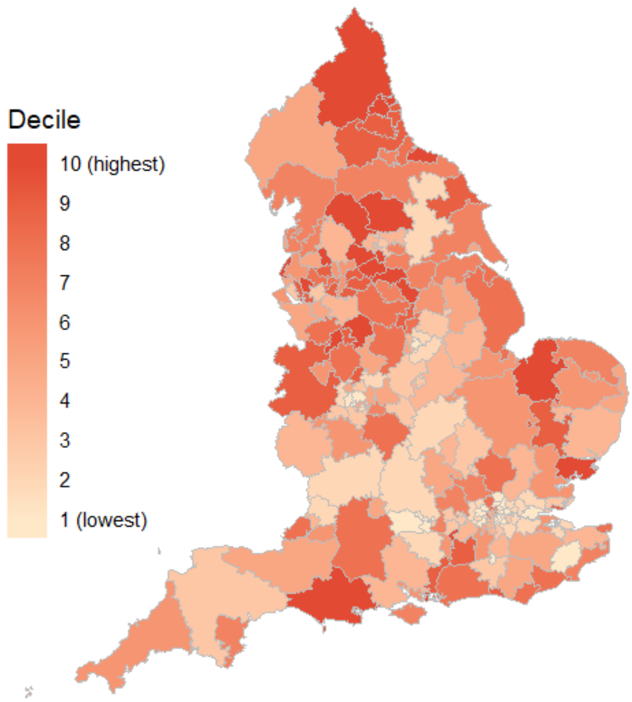


Temazepam

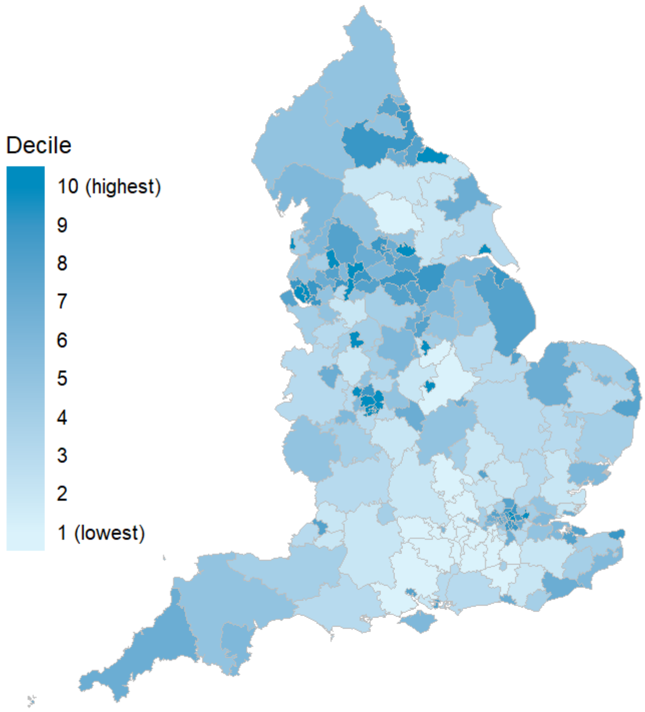
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



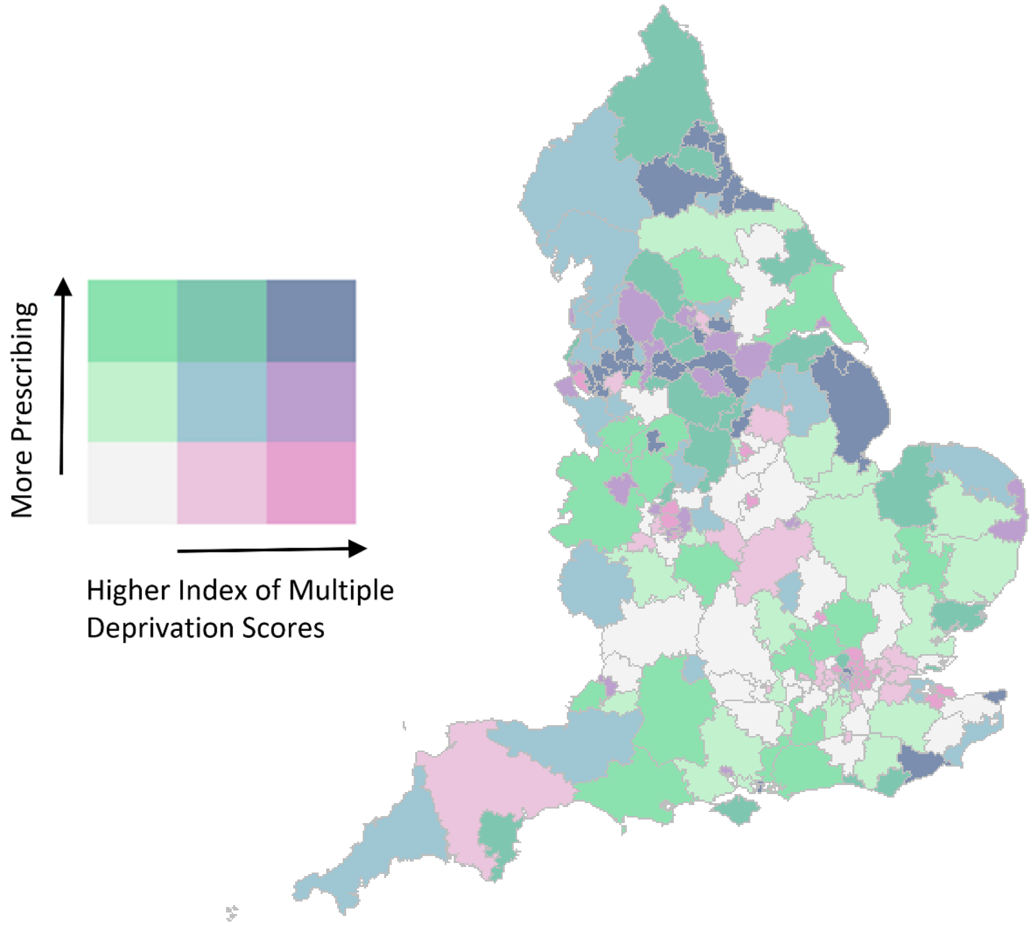
Temazepam prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group

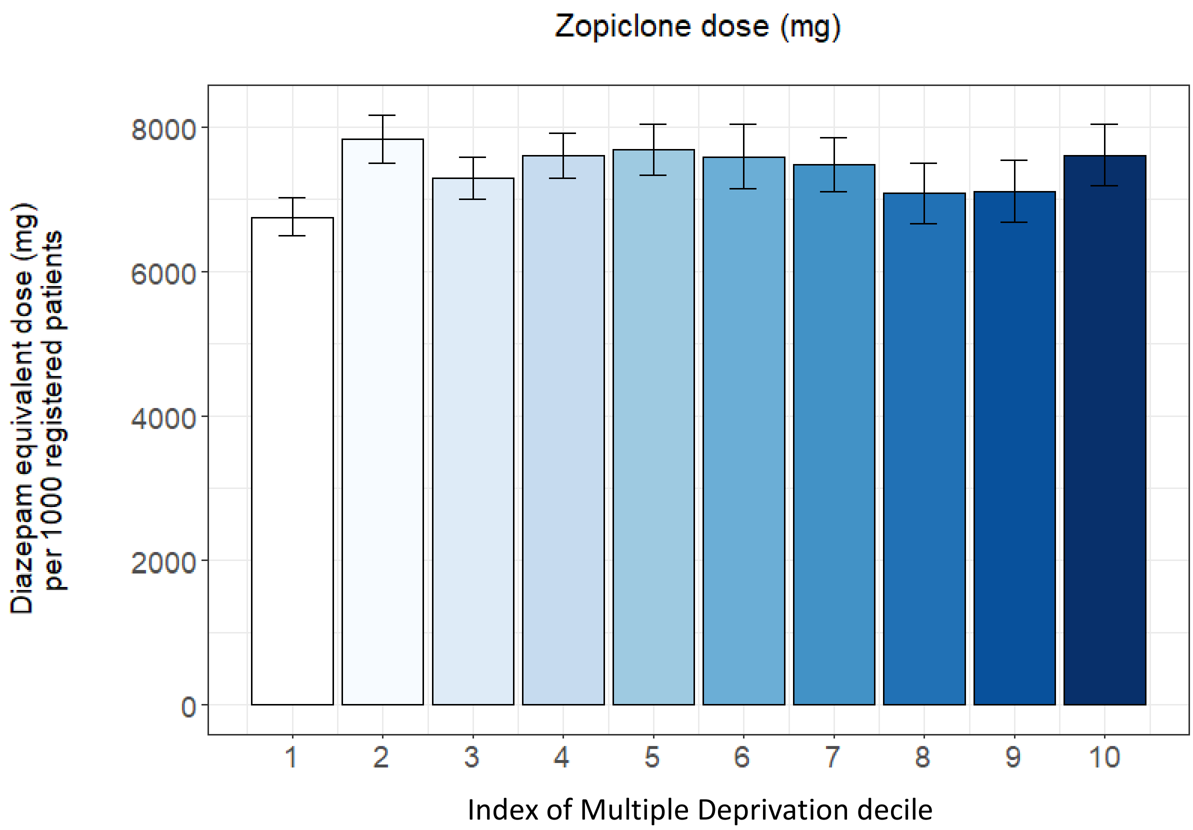


Temazepam prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group

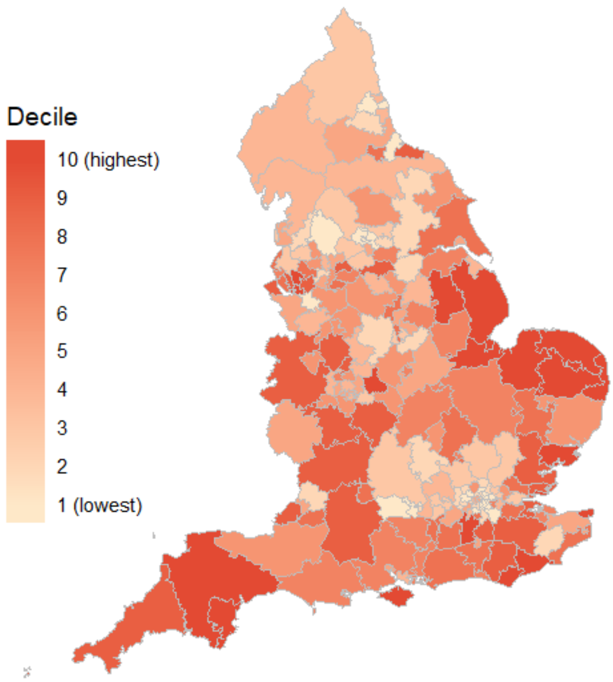


Zopiclone

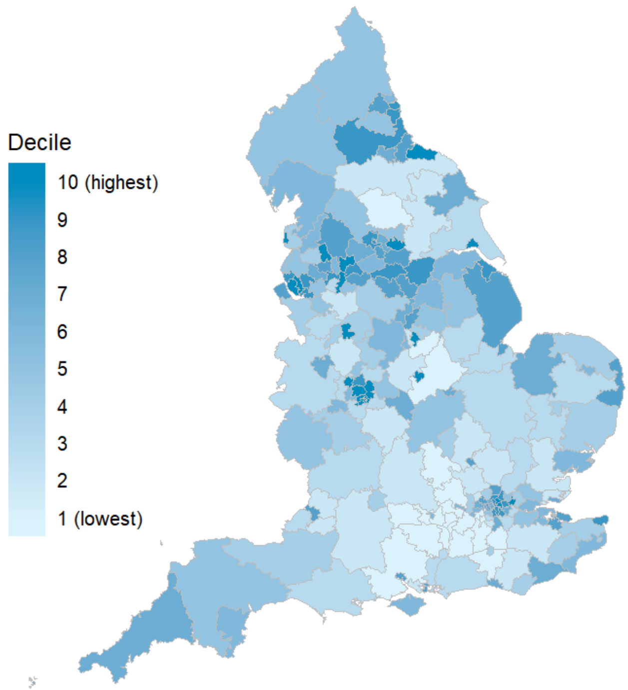
Average prescribing by practice Index of Multiple Deprivation (IMD) decile (England, 2017):



Zopiclone prescribing by Clinical Commissioning Group



Index of Multiple Deprivation scores by Clinical Commissioning Group



Zopiclone prescribing and Index of Multiple Deprivation score by Clinical Commissioning Group