

Time Trends and Geographical Variation in Prescribing of Antibiotics in England 1998-2017

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**Time Trends and Geographical Variation in Prescribing of
Antibiotics in England 1998-2017**

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Short title: Antibiotic prescribing in England 1998-2017

Synopsis

Background: Reducing antibiotic overuse is a key NHS priority. The majority are prescribed in primary care.

Objectives: We describe antibiotic prescribing trends in NHS England primary care 1998-2017 using various measures. We investigate trends and variation between practices and geographic areas; out-of-hours prescribing; and seasonality.

Methods: We used publicly available prescribing datasets and calculated antibiotic prescribing rates per 1,000 age-sex adjusted population units; percentage broad-spectrum; and course length. We report national time trends 1998-2016, geographical variation across 2017, and variation trends 2010-2017. We calculated percentiles, ranges and plotted maps.

Results: The overall rate of antibiotic prescribing has reduced by 18% since 2010, with the steepest decline since 2013. The percentage broad-spectrum declined since 2006, from 18.0% to 8.4%. Between the best and worst clinical commissioning groups (CCGs) there was two-fold variation for total antibiotic prescribing, but seven-fold for cephalosporins. Variation across general practices has declined. The CCG to which a practice belongs accounted for 12.6% of current variation ($p < 0.0001$). Higher antibiotic prescribing was associated with greater practice size, proportion of patients over 65 or under 18, ruralness and deprivation. Seasonal increases have been declining for most antibiotics. If every practice prescribed antibiotics at the lowest decile rate in 2017, 10.8m fewer prescriptions could have been issued (34%). Compared to standard practices, out-of-hours practices prescribed a greater proportion of broad-spectrum antibiotics.

Conclusions: Despite a general trend towards more optimal antibiotic prescribing, considerable geographic variation persists across England's practices and CCGs.

Introduction

Antimicrobial resistance has been described as “one of the most significant threats to patients’ safety worldwide”,¹ and NHS England have supported various campaigns to reduce antibiotic prescribing.² Primary care prescribing accounts for the majority of healthcare antibiotics (86.3%).³ Between 8.8% and 23.1% of these prescriptions may be inappropriate,⁴ and higher antibiotic consumption is associated with higher incidence of resistant infections beyond the individual patient.⁵

In September 2013, the UK Department of Health published a five-year antimicrobial resistance strategy,⁶ outlining seven areas for action. These include optimising prescribing practice by reducing unnecessary prescribing; and ‘better access to and use of surveillance data’. In line with this, we run an openly accessible and publicly funded service (OpenPrescribing) that facilitates detailed exploration of NHS England prescribing data by practice and by month, with four measures of antibiotic prescribing written to reflect national guidelines⁷ including: the number of antibiotic items prescribed per STAR-PU (Specific Therapeutic group Age-sex Related Prescribing Units, population adjusted for likelihood of antibiotic prescribing by age group and gender); the proportion of antibiotic prescriptions that are broad-spectrum; and two measures on urinary tract infection (UTI) prescribing.

In this paper we set out to provide a detailed description of NHS antibiotic prescribing trends in primary care in England since 1998; current geographic variation in antibiotic prescribing in 2017; trends in variation between practices during the period 2010 to 2017; and patterns of seasonality. We also look at out-of-hours services, which are often the provider of primary care services outside of typical office hours.

Methods

Data Sources and Preparation

We used two sources of routinely collected NHS data: monthly practice-level prescribing data, October 2010 - December 2017; and annual Prescription Cost Analysis data, aggregated nationally, covering 1998-2016.

Annual national-level data

The annual Prescription Cost Analysis datasets contain one row for each treatment and dose, for all items dispensed in community settings in England, describing the number of prescriptions dispensed and the total cost. Data were processed as previously described.⁸ Briefly: data for each year between 1998 and 2016 were compiled; corrected for changes in drug names, spellings and classifications over time; and costs were corrected for inflation.⁹

Practice-level data

The monthly prescribing datasets published by NHS Digital contain one row for each treatment and dose, in each prescribing organisation in NHS primary care in England, describing the number of prescriptions issued and the total cost. We limited to institutions with setting code “4”: general practices,¹⁰ excluding all other organisations such as dentists, prisons and walk-in centres. Each English practice belongs to one of 207 Clinical Commissioning Groups (CCGs); we aggregated practice data for CCG-level analyses. For practice-level analysis we excluded practices for any month in which they had less than 1,000 registered patients. To explore prescribing at out-of-hours practices, we limited to organisations with setting code “2” and excluded practices for any month in which they prescribed fewer than 50 total antibacterial items: there are no registered population sizes for out-of-hours services and they often cover a wider area than standard practices.

STAR-PU

STAR-PU's for antibiotics are adjusted population denominators, normalised for likelihood of antibiotic prescribing in each age and sex group.¹¹ Multiplication factors for each sex and 5-year age band were obtained from NHS Digital¹² and applied to each quarterly practice population, and to annual population data for national figures.¹³ CCG-level STAR-PU's were summed from practice-level values. For the latest 12 months, STAR-PU's were averaged across all months.

Extraction and classification of Antibiotic data

We extracted data for all drugs in BNF section 5.1 (Antibacterials). We used number of items which represents the number of prescriptions, and actual cost which represents the cost to the NHS, including excess costs and discounts. BNF codes used for individual antibiotic items and measures are listed in Table S1.

Analysis

We calculated number of items prescribed or cost per 1,000 STAR-PU (all antibiotics) or per 1,000 patients (individual antibiotics). We also include total items/cost. We calculated the proportion of selected items prescribed as broad-spectrum as per national performance metrics (Table S1).² Course length (days) was calculated as number of average daily quantities per item for selected UTI antibiotics (Table S1).

Trends and geographical variation

We produced long-term trend charts for overall prescribing (broken down by BNF paragraph), the most-prescribed paragraph (by chemical substance) and the proportion broad-spectrum. We created maps of antibiotic prescribing rates by all CCGs, aggregated for the latest available 12 months (Jan-Dec 2017). To examine practice-level prescribing trends, for each measure we calculated deciles (10-90th percentiles) and also extreme percentiles for standard practices (1-9th, 91-99th) for each month and plotted time trend charts. Where indicated, percentiles were

smoothed to remove seasonal trends using a non-parametric regression method: locally weighted scatterplot smoothing.

Seasonality

We examined seasonality using time series decomposition to calculate and plot the mean versus actual monthly change in overall antibiotic prescribing rate. For each standard practice (>1,000 patients) we also calculated the change in mean monthly antibiotic prescribing rate between each winter (Dec-Feb) and its preceding summer (Jun-Aug), then assigned practices into deciles based on their summer 'baseline' level. For each decile, we calculated the average percentage change compared to the mean summer prescribing level.

Factors associated with antibiotic prescribing rate

In order to measure what factors are associated with rate of total antibiotic prescribing we created a mixed effects linear regression model using publicly available practice data to define a number of fixed-effect variables, and CCG as a random effect. The variables were selected *a priori* using clinical judgement: proportion of patients over 65; proportion under 18; proportion with a long-term health condition; index of multiple deprivation; Quality Outcomes Framework score;¹⁴ single-handed practice (yes/no);¹⁵ rural/urbaness of practice postcode;¹⁶ and a composite measure of prescribing behaviour derived from the OpenPrescribing project (calculated as the mean percentile across 2017 for all measures on the site, as listed in Table S2). Continuous variables were categorised *a priori* into quintiles in order to allow for nonlinearity of effects and to enhance the intelligibility of results. The outcome used was: rate of total antibiotic prescribing per 1,000 patients in 2017. For each of the fixed effect variables, we determined the difference in rate with 95% confidence intervals, and to describe the degree of variance associated with CCG membership, we determined the R-squared value (and significance level).

146

147 *Data and Code*

148 Data were extracted using SQL in Google BigQuery. Further analyses were carried out in
149 Python, using ‘matplotlib.pyplot’, ‘seaborn’ and ‘geopandas’ modules; and the ‘stldecompose’
150 module for decomposition. Regression analysis was carried out using Stata v13.1. Complete
151 code and datasets are available online.^{17–19}

152

Results

Data Sources and Preparation

From the practice-level data between Oct 2010 and Dec 2017, 8,173 standard practices and all 207 CCGs were included. For practice-level analysis, we excluded standard practices for any months in which they had fewer than 1,000 registered patients (or less than 50 antibiotic items for out-of-hours services), leaving 8,052 standard and 260 out-of-hours services.

Long-Term Time Trends in Antibiotic Prescribing

Overall antibiotic prescribing rates per 1,000 STAR-PU declined slightly between 2013 and 2016, following a period of relative stability since 2000 (Figure 1a). In 2016, at 1,200 items per 1,000 STAR-PU, this represented approximately 38 million items in total; this cost £180 million, or £1,500 per 1,000 STAR-PU (Figure S1). Reductions are particularly apparent for penicillins, and cephalosporins and other beta-lactamases, but prescribing of items from the UTI paragraph increased. Within the penicillins, the reduction was largely in amoxicillin (Figure 1b). The proportion of items prescribed as broad-spectrum has declined since 2006, from 18.0% to 8.4% (Figure 1c). Up-to-date graphs for all individual antibiotics can be accessed online at OpenPrescribing.net.⁸

Variation in Prescribing Across Practices and CCGs in England

Maps indicate the geographic variation in prescribing behaviour across CCGs in England over the latest 12-month period (Figure 2). There was just over a two-fold difference between the lowest and highest-prescribing CCGs (600-1,200 items per 1,000 STAR-PU; Figure 2a). The proportion prescribed as broad-spectrum varied over three-fold, from approximately 4 to 14% (Figure 2b). There was more than a seven-fold difference in the prescribing rate for cephalosporins (Figure 2c). In some CCGs, course length for UTI antibiotics averaged seven days or above, with the best around five days (Figure 2d).

179

180 Figure 3 shows the range and time-course of variation in antibiotic prescribing behaviour across
181 England's standard **general** practices, **smoothed** over time. In all measures, there was a trend
182 towards more optimal prescribing and the range of values between the highest and lowest
183 percentiles has decreased. **However,** some subgroups of antibiotics have seen an increasing
184 prescribing trend and widening range across percentiles, e.g. UTI antibiotics, and **some other**
185 **antibacterials** (Figure S3).

186

187 *Factors associated with antibiotic prescribing rate*

188 We modelled the practice factors associated with total antibiotic prescribing **rates** (Table 1). The
189 **overall** mean **rate** was 535 **items per year per 1,000 patients**. Practices with a higher proportion
190 of **patients over 65** prescribed more antibiotics than those with a lower proportion (multivariable
191 change for lowest versus highest: 148 more items per year per 1,000 patients, 95% CI 127-
192 170). **Other factors associated with higher antibiotic prescribing were:** higher proportion of
193 patients under 18 (**58 more items**, 95% CI 41-74), higher proportion of patients with long-term
194 **conditions** (**43 more items**, 95% CI 28-57), ruralness (multivariable change **between least and**
195 **most rural**: 58, 95% CI 34-82) **and deprivation** (multivariable change **between least and most**
196 **deprived**: 108, 95% CI 89-126). Singlehandedness and practice **Quality Outcomes Framework**
197 score were not associated with antibiotic prescribing rate, with **no effect in the** multivariable
198 analysis. Practices with a lower (better) composite prescribing score had **lower** antibiotic
199 prescribing (multivariable change for lowest versus highest: 118, 95% CI 103-132). The CCG to
200 which a practice belongs (as a random effect) was significantly associated with prescribing rate
201 ($p < 0.0001$) and accounted for 12.6% of the variation **between practices**.

202

203 *Opportunity Modelling*

If every practice in the country prescribed antibiotics at the same rate as the lowest decile over the latest year (636 total items per 1,000 STAR-PU, 53.0 per month), overall 10.8m fewer prescriptions could have been issued, out of a total of 31.5m prescriptions (34%).

Seasonal variation

Overall antibiotic prescribing exhibited seasonality with winter peaks particularly pronounced in 2014/15, but since declining (Figure 4a): in December 2017, an extra 5 items/1,000 were prescribed above the trend line, compared to 17 in 2014 (Figure 4b). Practices with higher overall prescribing rates in summer months (Jun-Aug) tended to have a lower relative increase in winter (Dec-Feb) (Figure S4). Winter peaks are clear for some antibiotic subgroups (Figure S3), and although declining for cephalosporins, co-amoxiclav, and macrolides, seasonality appears to be persisting for penicillins and tetracyclines.

Prescribing in out-of-hours settings

Analysis of antibiotic prescribing in out-of-hours settings can be found in the Supplementary Material under the above title and Figure S5.

Discussion

Summary

There has been a general trend towards lower antibiotic prescribing in England since at least 2013 across all measures, with the percentage of items prescribed as broad-spectrum declining since 2006. There is strong geographic variation in antibiotic prescribing behaviour across CCGs, with a two-fold difference in overall prescribing rate and seven-fold for cephalosporins. The variation across practices in most antibiotic prescribing measures has been declining. Higher overall antibiotic prescribing rates were associated with practices having a greater

proportion of patients over 65 or under 18, larger size, poorer prescribing on other measures of prescribing quality, and greater ruralness and deprivation. The CCG to which a practice belongs accounted for 12.6% of the variation. Seasonality in overall prescribing rate reduced since 2014. Compared to standard practices, out-of-hours practices tended to prescribe a greater percentage of broad-spectrum antibiotics but shorter courses for UTIs.

Strengths and Weaknesses

This work includes all practices in England, not a sample. Our data includes all items written in standard primary care practices which were dispensed (including delayed prescriptions and those from extended opening hours²⁰), and excludes those not dispensed (hence not contributing to antimicrobial resistance). Primary care accounts for the majority of antibiotic prescribing³ and out-of-hours services prescribe the most out of the other community settings.³

It is important to carry out antibiotic prescribing analyses in datasets covering identifiable organisations, because clinician and setting are important focuses for behaviour change initiatives.

Using individual patient data could allow separation of different indications for each prescription: however in previous such analyses, around a third of antibiotics could not be linked to a documented diagnostic code^{4,21}. Furthermore, our data covers the whole country, which no patient level dataset achieves. We used items as a measure of prescribing in order to analyse individual decisions to prescribe courses of antibiotics rather than total volumes.

All choices of population denominator have strengths and weaknesses. For total antibiotics, we used STAR-PU as a population denominator in order to adjust for age and sex distribution. There are no appropriate population denominators for out-of-hours services; additionally the data for such services may omit any prescription items given directly to patients. Some

differences in prescribing between standard practices and out-of-hours services may be explained by differences in patients presenting to these services.

Findings in Context of Other Research

Our findings on change in prescribing over time are consistent with, but more detailed than, prior work on public datasets. A report (ESPAUR) issued annually on behalf of PHE includes primary and secondary care prescribing, but with little information on geographical variation, no exploration of factors associated with antibiotic prescribing, only annual data (with no seasonal trends), and time-course limited to five years.³ The PHE interactive online service Fingertips²² shows a limited range of antibiotic prescribing measures, over limited time periods, and with a long time delay for updates. The 2017 ESPAUR report found a 13.4% reduction in antibiotic prescribing rate per 1,000 between 2012 and 2016,³ consistent with our data for this narrow date range.

The proportional usage of cephalosporins and quinolones was recently reported as decreasing between 2004 and 2014 for older adults with UTI,²³ consistent with our findings on broad-spectrum antibiotics for this date range. In September 2014, half of the practices in the highest 20% for antibiotic prescribing were sent a letter from the chief medical officer (CMO) of NHS England.²⁴ However, our data indicate that the sharpest decline among the highest prescribing percentiles appeared to precede this intervention by more than a year. Substantial practice-level variation still exists, particularly in broad-spectrum prescribing.

We found significant associations between total antibiotic prescribing rate and practice characteristics, particularly with higher proportions of older patients, deprivation and the OpenPrescribing composite prescribing score. Associations with age and deprivation were expected from previous work.^{25–27} We found weaker associations with single-handedness and

ruralness, consistent with previous findings.^{28,29} The CCG to which a practice belongs accounted for 12.6% of practice variation; this may be driven by local guidelines or formularies, which we explore in another paper on UTIs.³⁰

We found that seasonality is generally decreasing, and that higher baseline prescribing rates in summer predicted lower proportional increases in winter prescribing. Greater levels of ampicillin/amoxicillin prescribing during winter months were previously associated with increased resistance.²⁹ However, it is difficult to assess to what extent the seasonal increase is warranted.

We found out-of-hours services prescribed a higher proportion of broad-spectrum antibiotics than standard practices, but exhibited similar trends towards improvement. Our precise figures differ from some previous work³¹ largely because we included all CCGs, and calculated our broad-spectrum measure as per national performance metrics.² Nonetheless, our results were consistent in showing a small increase in out-of-hours antibiotic prescribing between 2010 and 2014.³¹

Previous work suggests that much antibiotic prescribing is avoidable. A previous study found prescribing levels of antibiotics for coughs and colds well above recommended levels (1994-2011), with wide variation amongst practices, indicative of substantial opportunity for improvement.³² A later study also found potential for reduction in inappropriate prescribing across most practices.³³

Policy Implications

Reductions in antibiotic prescribing are broadly desirable. Small increases in antibiotic prescribing at practice level have been linked to a reduction in the number of bacterial infections

in the practice population which are susceptible to those antibiotics.²⁹ Similarly, practices reducing total antibiotic prescribing across a seven-year period had a measurable reduction in ampicillin resistance.³⁴ We found a reduction in antibiotic prescribing rate of approximately 18%, 2010-2017. In Australia, following introduction of ongoing national interventions to reduce inappropriate prescribing, a 14% reduction in the monthly prescribing rate was seen between 2009 and 2015,³⁵ indicating that the campaigns in the UK are making a comparable impact. It is encouraging that antibiotic prescribing rates have declined despite overall demand for primary care services increasing.³⁶ Exposure to data feedback has been shown to be associated with a modest improvement in clinical practice.³⁷ Our OpenPrescribing tool gives easy open access to current antibiotic prescribing data and measures, and to email alerts automatically notifying any subscriber when their selected CCG/practice falls behind national trends. We suggest that better access to, and use of, audit data is likely to improve clinical care and antibiotic use.

Conclusions

There has been a general trend towards reduced antibiotic prescribing across all measures since at least 2013. There is geographic variation in antibiotic prescribing behaviour across England's practices and CCGs, which has declined, but remains substantial for some measures.

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Transparency Declarations

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450

TABLES

Table 1.

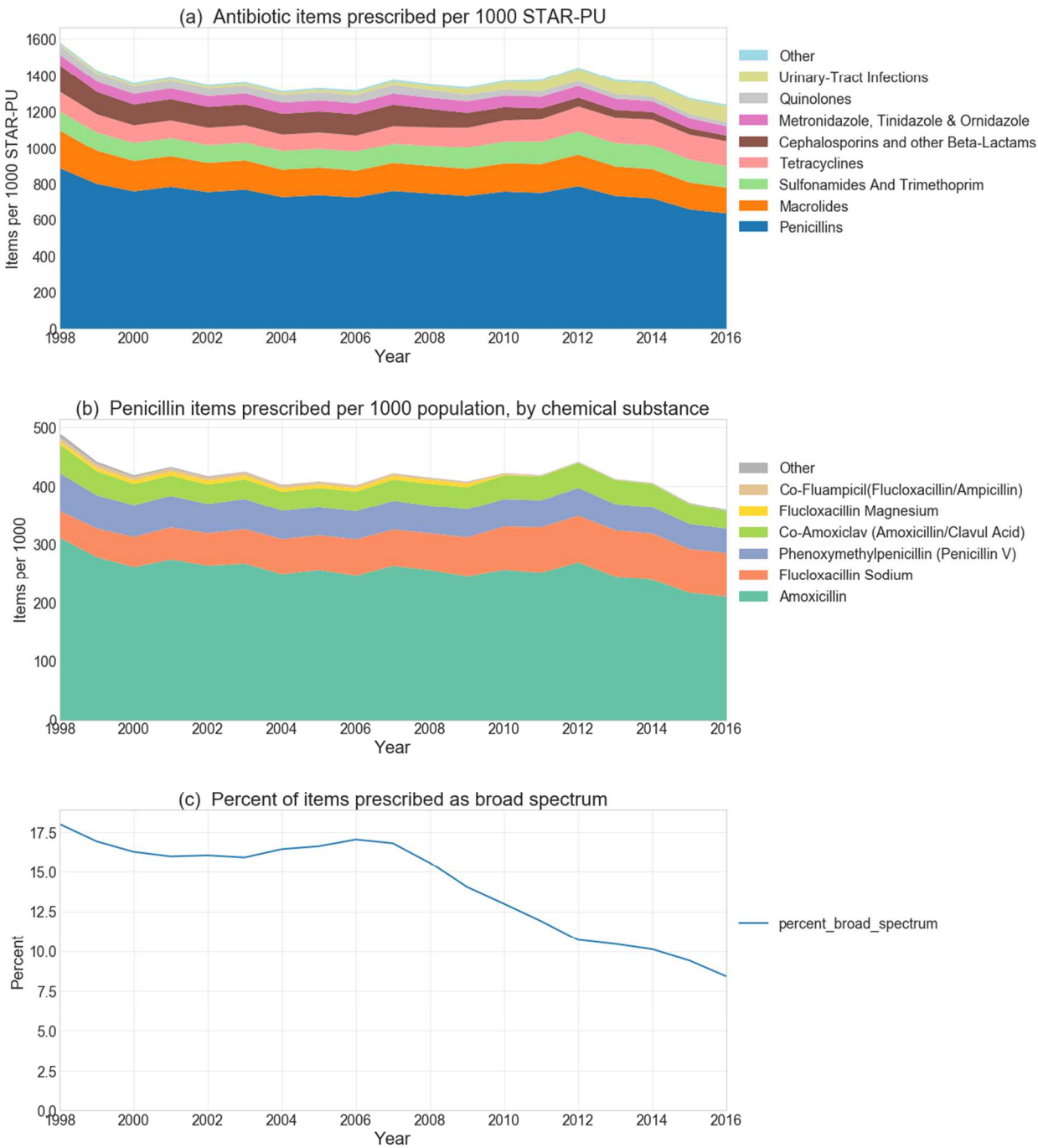
Variable	Category boundaries	Mean antibiotic prescribing per 1000 patients	Univariable linear regression		Multivariable linear regression		
			Change	95% CI	Change	95% CI	
% of patients over 65	0-10.9	399	Ref		Ref		
	10.9-15.5	504	65	52 78	25	11 39	
	15.5-18.9	553	113	99 126	64	48 81	
	18.9-22.5	578	143	129 156	105	87 124	
	22.5-92.2						
% of patients under 18		607	171	157 184	148	127 170	
	0-17.8	548	Ref		Ref		
	17.8-19.6	560	24	10 38	11	-2 24	
	19.6-21.2	554	20	5 34	32	18 46	
	21.2-23.6	538	5	-9 19	48	33 63	
% with a long term health condition	23.6-53.6						
		492	-16	-30 -2	58	41 74	
	16.5-47.0	437	Ref		Ref		
	47.0-51.5	518	76	63 90	24	12 37	
	51.5-55.3	549	104	90 117	26	13 39	
Single handed practice	55.3-59.7	570	126	112 139	29	16 43	
	59.7-96.0						
		606	157	143 171	43	28 57	
	No	541	Ref		Ref		
	Yes						
Urban/rural		515	-25	-43 -7	-14	-30 1	
	Urban with major conurbation	488	Ref		Ref		
	Urban with minor conurbation	548	55	32 78	38	-1 78	
	Urban with city and town	544	49	37 60	41	22 59	
	Urban with significant rural	566	76	61 91	39	18 61	
Index of multiple deprivation	Largely rural	602	109	93 124	68	45 91	
	Mainly rural						
		596	103	86 120	58	34 82	
	Least deprived	538	Ref		Ref		
		554	13	-1 27	23	10 36	
Quality Outcomes Framework score		546	1	-13 15	44	30 59	
		526	-13	-28 1	58	42 74	
	Most deprived						
		530	14	0 29	108	89 126	
	14-523	513	Ref		Ref		
Composite prescribing score (lower is better)	523-541	535	16	2 30	6	-7 19	
	541-550	536	9	-5 23	-10	-22 3	
	550-557	551	31	17 46	9	-4 22	
	557-559						
		555	38	24 53	2	-11 15	
	<38.7	463	Ref		Ref		
	38.7-43.5	510	52	38 66	42	30 55	
	43.5-47.8	540	75	61 89	61	48 74	
	47.8-52.4	558	98	84 112	84	70 98	
	>52.4	603	144	130 158	118	103 132	

454 Linear regression to describe factors associated with overall antibiotic prescribing rate (per
455 1,000 patients) in English general practices over the latest 12-month period (Jan-Dec 2017).
456

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FIGURES

Figure 1.

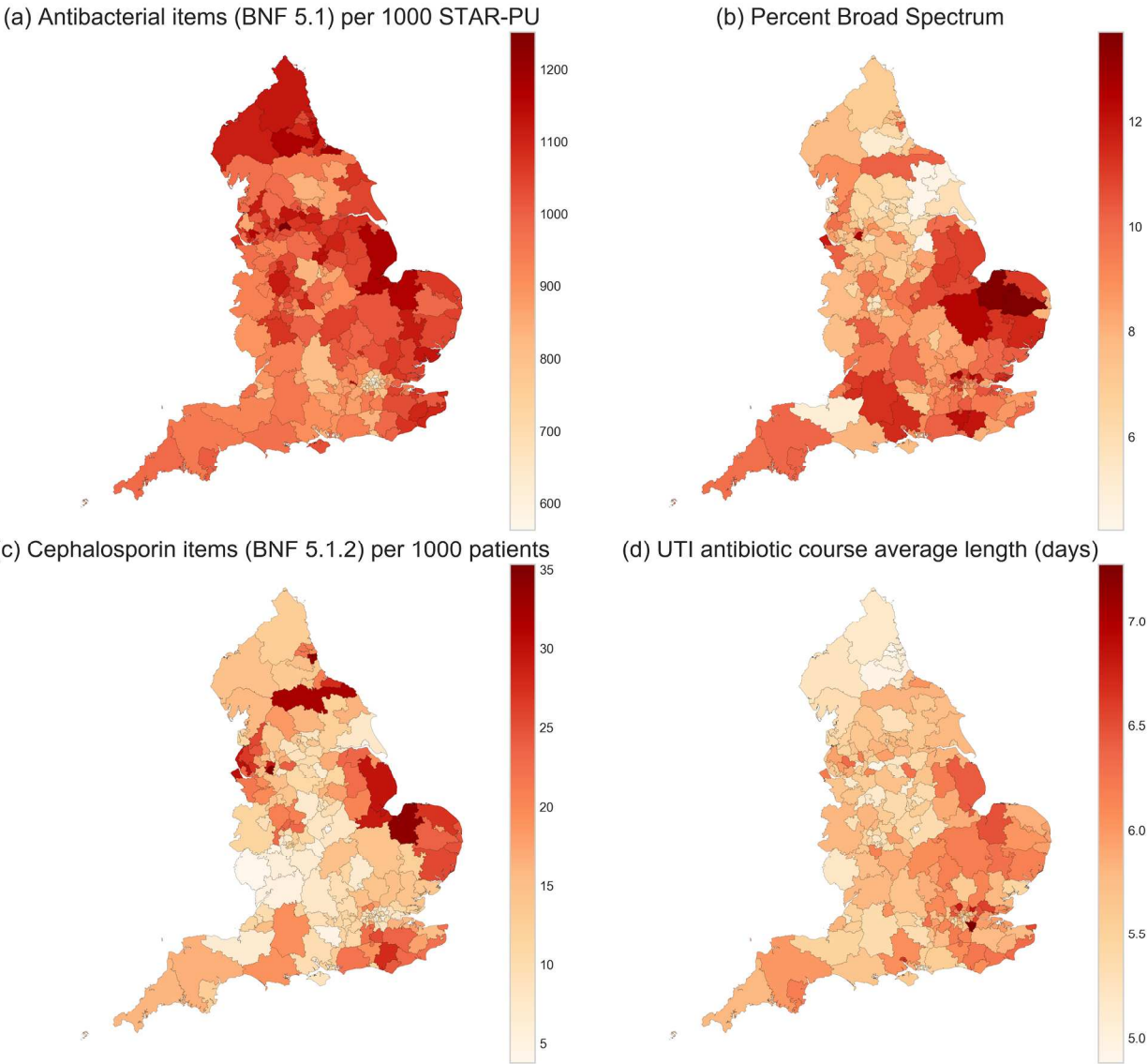


Trends in antibiotic prescribing in community settings in England, 1998-2016. (a) Items per 1,000 STAR-PU for all antibiotics (BNF 6.1, Antibacterials), broken down by BNF paragraph. (b) Items per 1,000 population for penicillins (BNF 6.1.1), broken down by BNF chemical

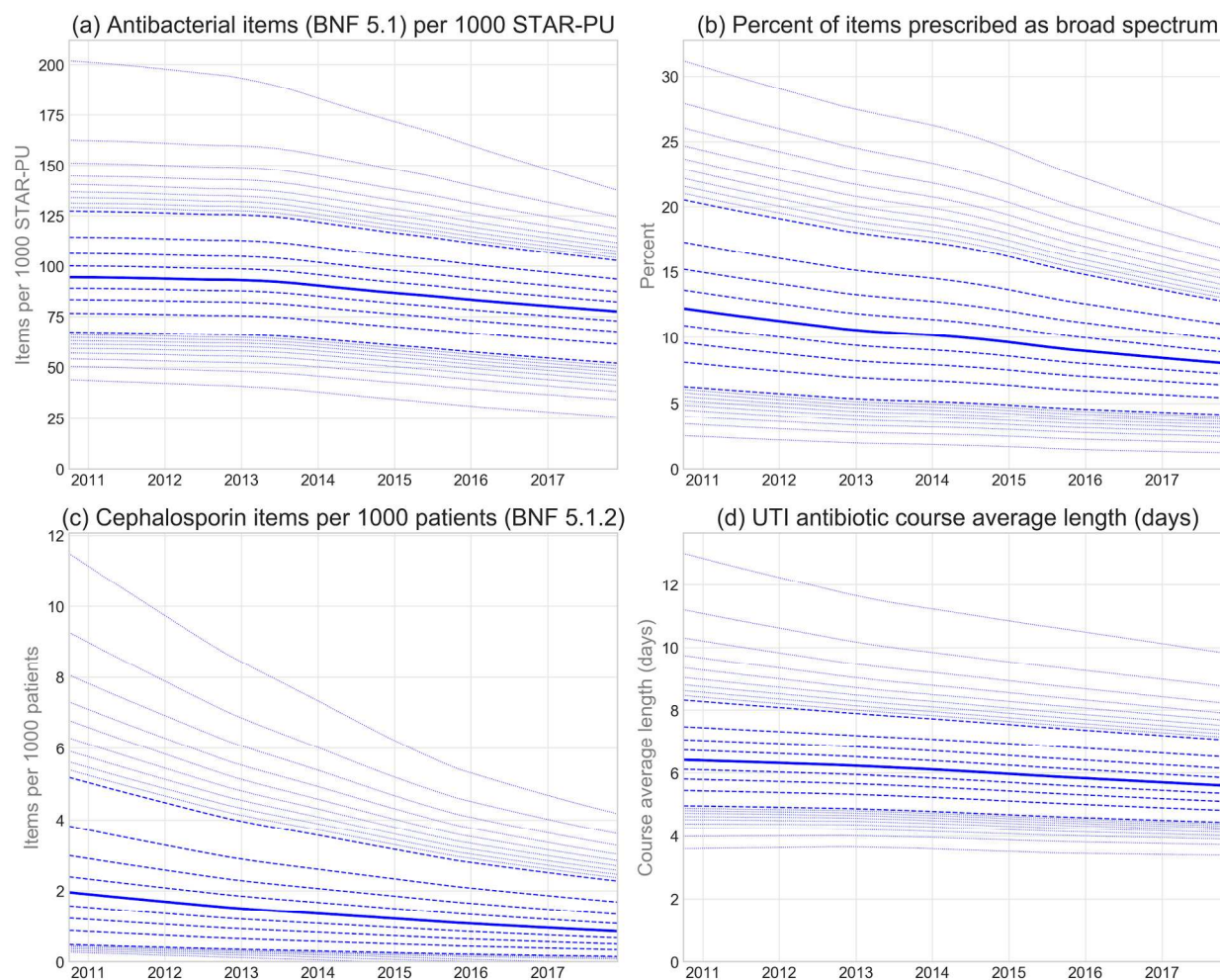
substance. (c) Percentage of selected common antibiotics prescribed as broad-spectrum.

Summary data are presented in Table S3. This figure appears in colour in the online version of JAC and in black and white in the printed version of JAC.

Figure 2.

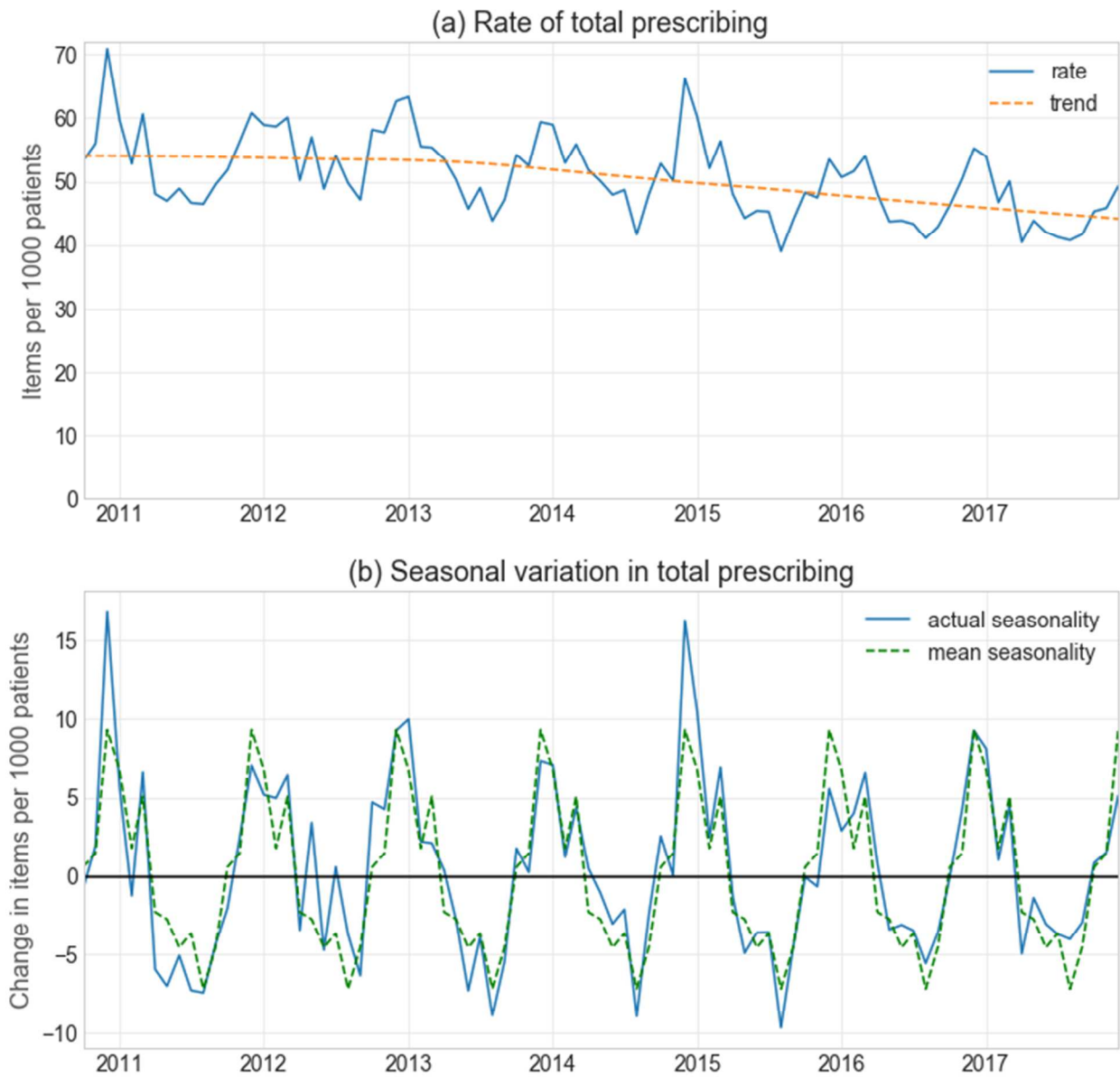


Variation in antibiotic prescribing by England's CCGs, Jan-Dec 2017. (a) Total items per 1,000 STAR-PU for all antibiotics (BNF 5.1, Antibacterials). (b) Broad spectrum items as a percentage of selected common antibiotic items. (c) Cephalosporin & other beta-lactamase (BNF 5.1.2) items per 1,000 patients (other individual classes of antibiotics are shown in appendix Figure S3). (d) Average course length for selected UTI antibiotics (days). This figure appears in colour in the online version of JAC and in black and white in the printed version of JAC.

Figure 3.

Smoothed trends over time in antibiotic prescribing by England's practices, Oct 2010 - Dec 2017. Solid line shows median, heavy dashed lines are deciles (10-90) and light dotted lines are extreme percentiles (1-9, 91-99). (a) Total antibacterial items (BNF 5.1) per 1,000 STAR-PU. (b) Broad spectrum items as a percentage of selected common antibiotic items. (c) Cephalosporin and other beta-lactamase (BNF 5.1.2) items prescribed per STAR-PU. (d) Average course length for selected UTI antibiotics (days). Unsmoothed versions of these charts are shown in Figure S2.

Figure 4.



Seasonality of overall antibiotic prescribing for all standard practices included in England. (a) Actual (solid line) and smoothed (dashed) trend in total items prescribed per 1,000 patients. (b) Actual (solid line) and mean (dashed) seasonality with trend line values set to zero. This figure appears in colour in the online version of JAC and in black and white in the printed version of JAC.

Time Trends and Geographical Variation in Prescribing of Antibiotics in England 1998-2017

SUPPLEMENTARY MATERIAL

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Figure S2. Unsmoothed version of Figure 3. Trends over time in antibiotic prescribing by England's practices, Oct 2010 - Dec 2017.

Figure S3. Trends in antibiotic prescribing by England's standard practices, Oct 2010 - Dec 2017 for subsets of antibiotics, per 1,000 registered patients.

Figure S4. Seasonal prescribing across practices. Mean increase in prescribing rate between summer (Jun-Aug) and winter (Dec-Feb) across practices ranked into deciles (0-9) based on their prescribing rate in summer.

Prescribing in out-of-hours settings

Figure S5. Monthly prescribing trends in out-of-hours services, Oct 2010 - Dec 2017.

Table S1. BNF codes used for antibiotic sub-groups and measures. BNF codes represent the beginning of each code, except for Selected UTI antibiotics where they represent the whole code.

Antibiotic/Measure		BNF codes
BNF Paragraph	UTI	050113
BNF Paragraph	tetracyclines	050103
BNF Paragraph	sulphonamides & trimethoprim	050108
BNF Chemical	coamoxiclav	0501013K0
BNF Paragraph	cephalosporins & other beta-lactamases	050102
BNF Paragraph	quinolones	050112
BNF Paragraph	macrolides	050105
BNF Paragraph	metronidazole, tinidazole & ornidazole	050111
BNF Paragraph	penicillins	050101
BNF Paragraph	antileprotic	050110
BNF Paragraph	antituberculosis	050109
BNF Paragraph	some other antibacterials	050107
BNF Paragraph	aminoglycosides	050104
BNF Chemical group	amoxicillin	0501013B0, 0501013C0, 0501013E0, 0501013F0
Measure	Selected UTI antibiotics†	0501130R0%AG, 0501130R0%AA, 0501130R0%AD, 0501015P0%AB, 0501080W0%AE
Measure	Broad spectrum	0501013K0, 0501021, 050112
Measure	Denominator for % broad spectrum measure	050101, 0501021, 050103, 050105, 050108, 050111, 050112, 050113

† % indicates any four characters

Table S2. OpenPrescribing measures used in composite prescribing outcome. Note: measures of overall antibiotic prescribing rate, direct acting oral anticoagulants and pregabalin measures were excluded.

Antibiotic stewardship: co-amoxiclav, cephalosporins & quinolones (KTT9)
Antibiotic stewardship: three-day courses for uncomplicated UTIs
Ciclosporin and tacrolimus oral preparations prescribed generically
Co-proxamol
Desogestrel prescribed as a branded product
Diltiazem preparations (>60mg) prescribed generically
Extended-release quetiapine
Glaucoma eye drops prescribed by brand
High-cost ACE inhibitors
High-cost ARBs
High-cost drugs for erectile dysfunction
High-cost PPIs
High-cost statins
High dose inhaled corticosteroids
High dose opioids as percentage regular opioids
High dose opioids per 1000 patients
Higher dose Proton Pump Inhibitors (PPIs)
Keppra vs. levetiracetam
Long-acting insulin analogues (KTT12)
Low and medium intensity statins
Methotrexate 10 mg tablets
Nebivolol 2.5mg tablets
NHS England Low Priority Treatment - All Low Priority Treatments
Non-preferred NSAIDs and COX-2 inhibitors (KTT13)
Other lipid-modifying drugs (KTT3)
Pregabalin prescribed as Lyrica
Prescribing of dipyridamole
Prescribing of high cost tramadol preparations
Prescribing of opioids (total oral morphine equivalence)
Prescribing of trimethoprim vs nitrofurantoin
Short acting beta agonist inhalers
Silver dressings
Soluble/effervescent forms of paracetamol and co-codamol
Topical treatment of fungal nail infections
Vitamin B complex

Table S3. Summary data for long term trends as shown in Figure 1 and Figure S1.

year	Items per 1,000 STAR-PU	Total Items (millions)	Cost per 1,000 STAR-PU	Total Cost (2016 equivalent £ millions)	Percent broad- spectrum
1998	1,583.4	42.6	2,064.2	230.1	18.0
1999	1,430.0	38.6	2,206.9	247.0	16.9
2000	1,359.3	36.9	2,119.2	238.1	16.3
2001	1,391.4	37.9	1,969.4	222.4	16.0
2002	1,348.9	36.9	1,952.7	221.7	16.0
2003	1,364.8	37.6	1,967.6	224.8	15.9
2004	1,315.6	36.5	1,953.8	224.6	16.4
2005	1,332.1	37.2	1,798.4	208.5	16.6
2006	1,319.3	37.2	1,839.9	215.0	17.0
2007	1,377.2	39.2	1,808.1	213.3	16.8
2008	1,352.9	38.9	1,564.4	186.4	15.5
2009	1,336.0	38.7	1,400.2	168.3	14.0
2010	1,372.8	40.2	1,576.1	191.4	13.0
2011	1,378.4	40.8	1,495.4	183.5	11.9
2012	1,445.7	43.3	1,649.8	204.7	10.7
2013	1,377.6	41.6	1,567.5	196.3	10.4
2014	1,365.4	41.7	1,572.3	199.0	10.1
2015	1,277.5	39.4	1,704.8	217.8	9.4
2016	1,240.5	38.6	1,497.4	193.1	8.4

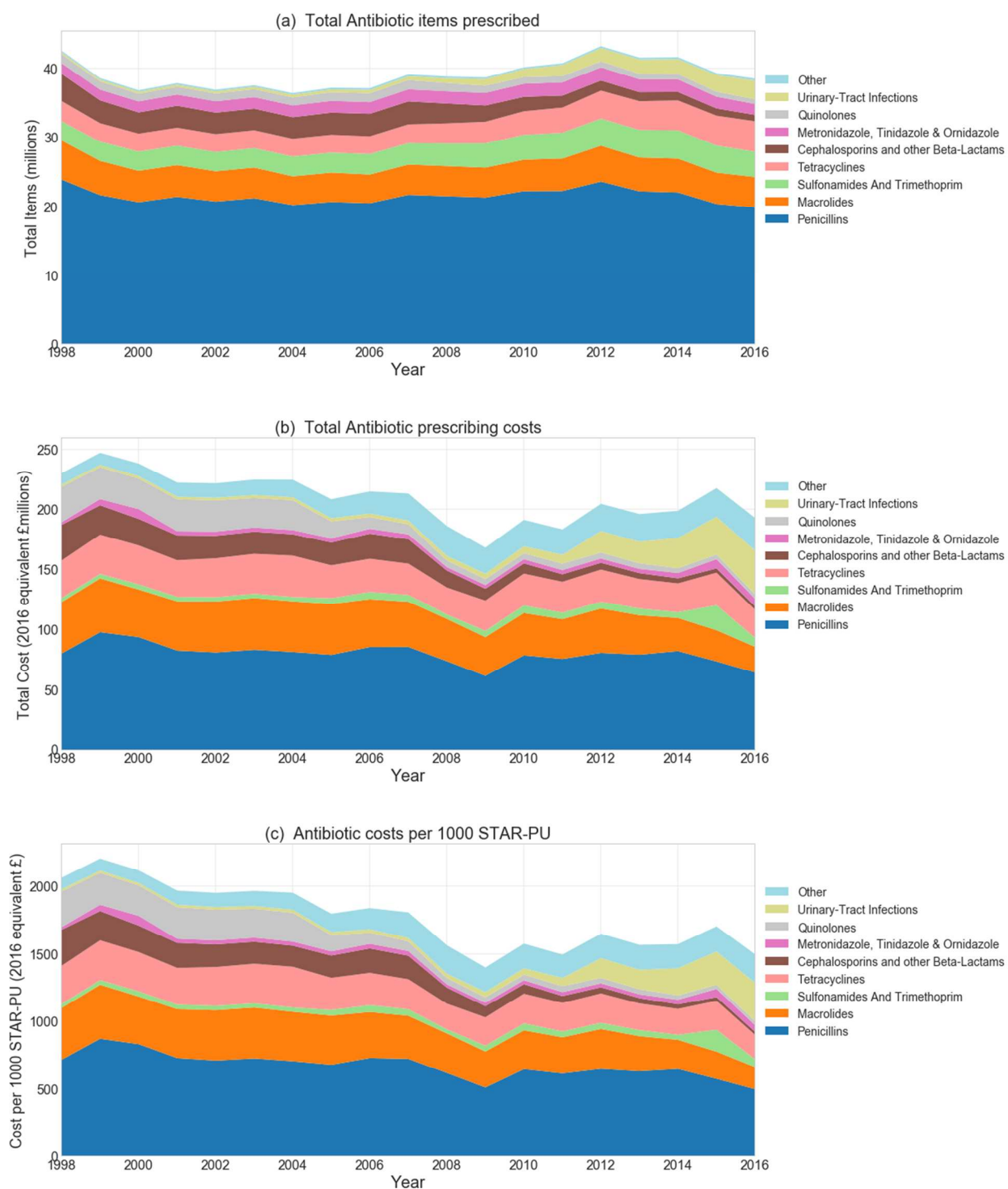


Figure S1. Trends in antibiotic prescribing in community settings in England for all antibiotics (BNF 6.1, Antibacterials), 1998-2016. (a) Total items. (b) Total cost per 1,000 STAR-PU (2016 equivalent GBP, millions) (c) Cost per 1,000 STAR-PU (2016 equivalent GBP).

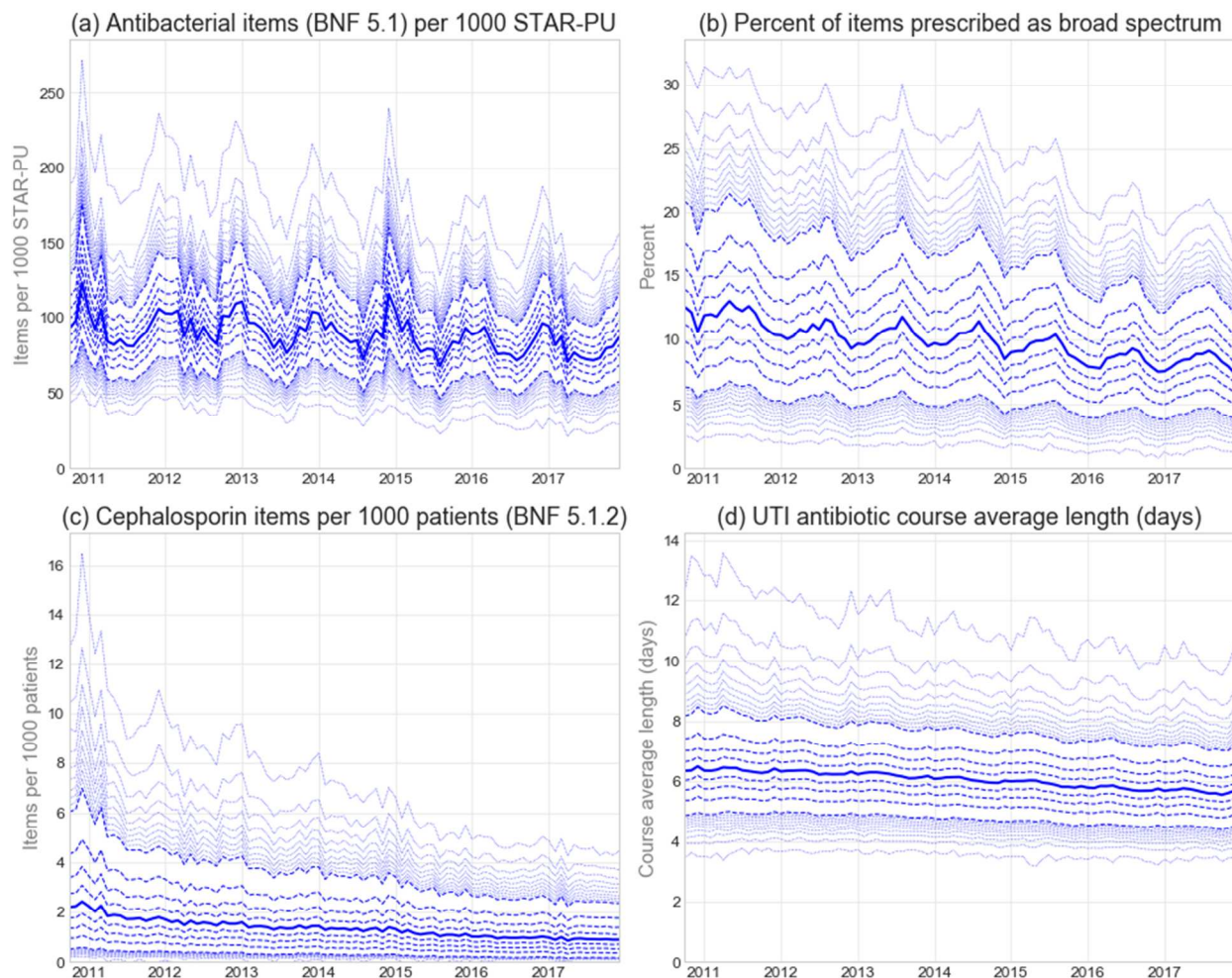


Figure S2. Unsmoothed version of Figure 3. Trends over time in antibiotic prescribing by England's practices, Oct 2010 - Dec 2017. Solid line shows median, heavy dashed lines are deciles (10-90) and light dotted lines are extreme percentiles (1-9, 91-99). (a) Total antibacterial items (BNF 5.1) per STAR-PU. (b) Proportion prescribed as broad-spectrum. (c) Cephalosporin items prescribed per STAR-PU. (d) Course length for selected antibiotics used for UTIs.

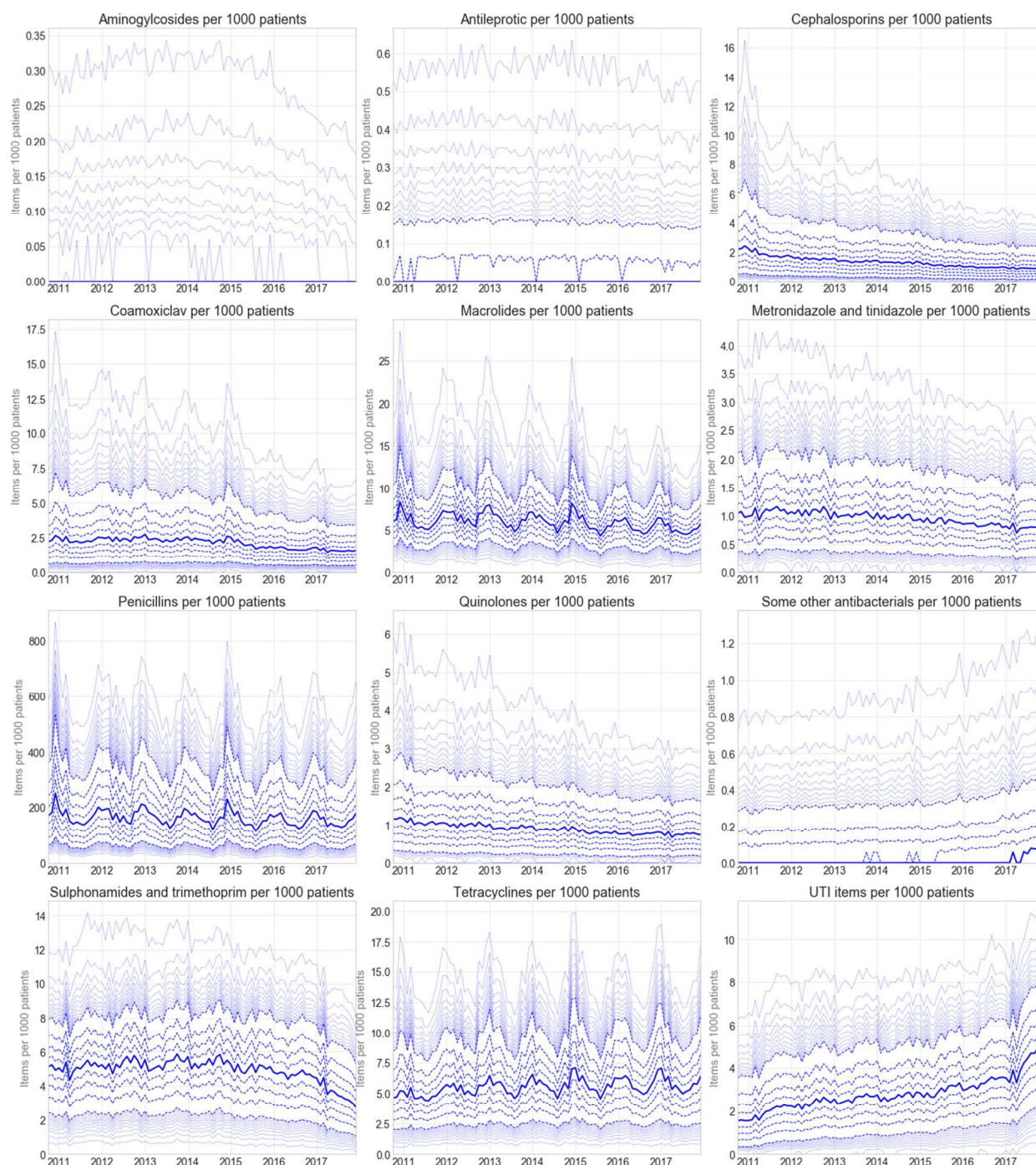


Figure S3. Trends in antibiotic prescribing by England's standard practices, Oct 2010 - Dec 2017 for subsets of antibiotics, per 1,000 registered patients. Solid line shows median, heavy dashed lines are deciles (10-90) and light dotted lines are extreme percentiles (1-9, 91-99).

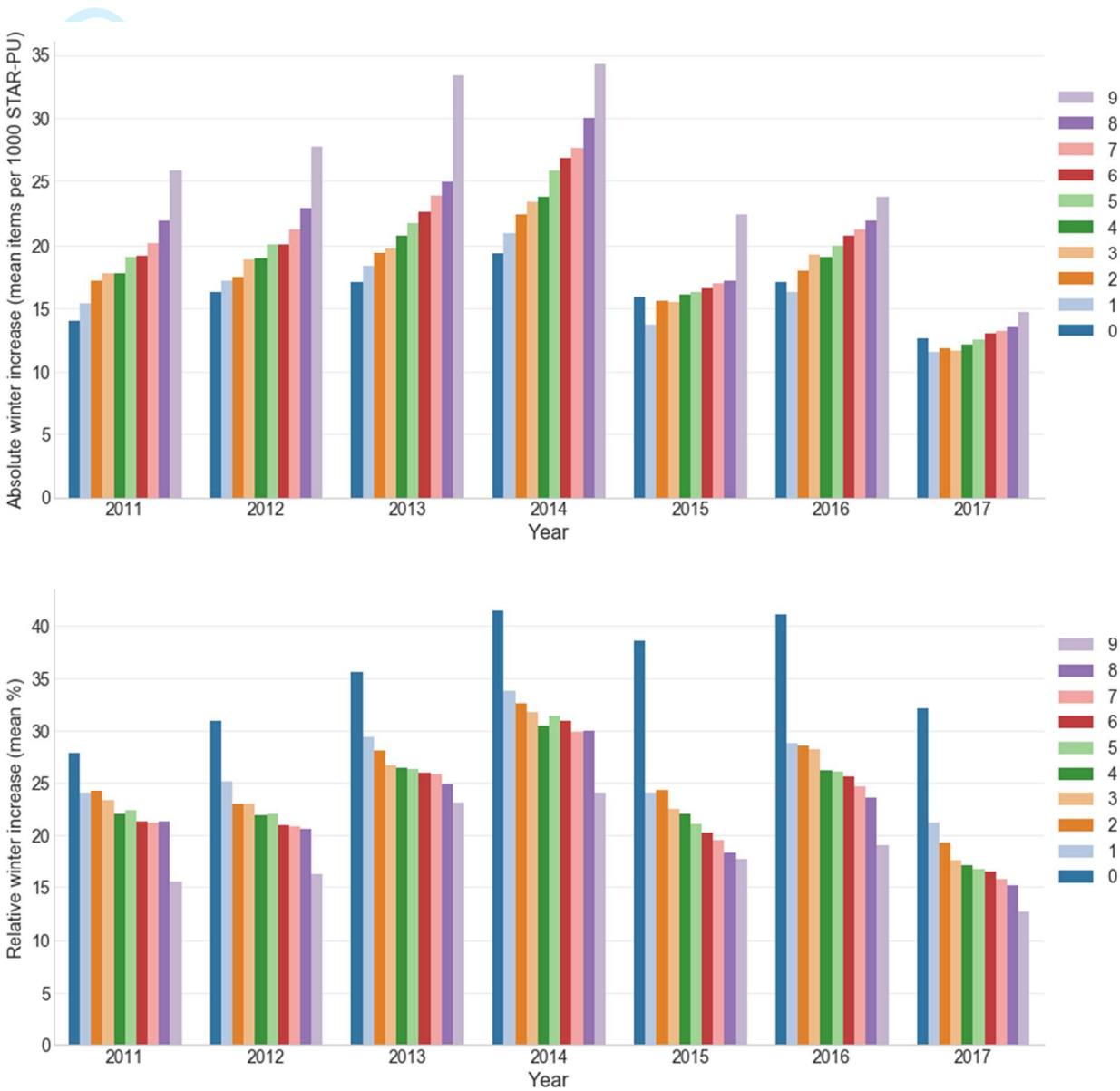


Figure S4. Seasonal prescribing across practices. Mean increase in prescribing rate between summer (Jun-Aug) and winter (Dec-Feb) across practices ranked into deciles (0-9) based on their prescribing rate in summer. Values are shown in items per 1,000 STAR-PU (top) and as percentages (bottom).

Prescribing in out-of-hours settings

The total antibiotic items prescribed in out-of-hours services made up 3.3% of the total in all standard and out-of-hours practices in 2017, and has declined by 9.0% since 2013, from 94,000 to 85,000 average items per month (Figure S5a). Standard practices declined by 12.9% over the same period. The proportion prescribed as broad spectrum has declined (median 16.5% to 9.8%), but remained higher than standard practices (Figure S5b). Total cephalosporin items prescribed have declined dramatically (-63.6%, Figure S5c; standard practices -49.2%). The length of courses for UTIs has been consistently lower than standard practices, with median declining from 5.5 to 5 days (Figure S5d).

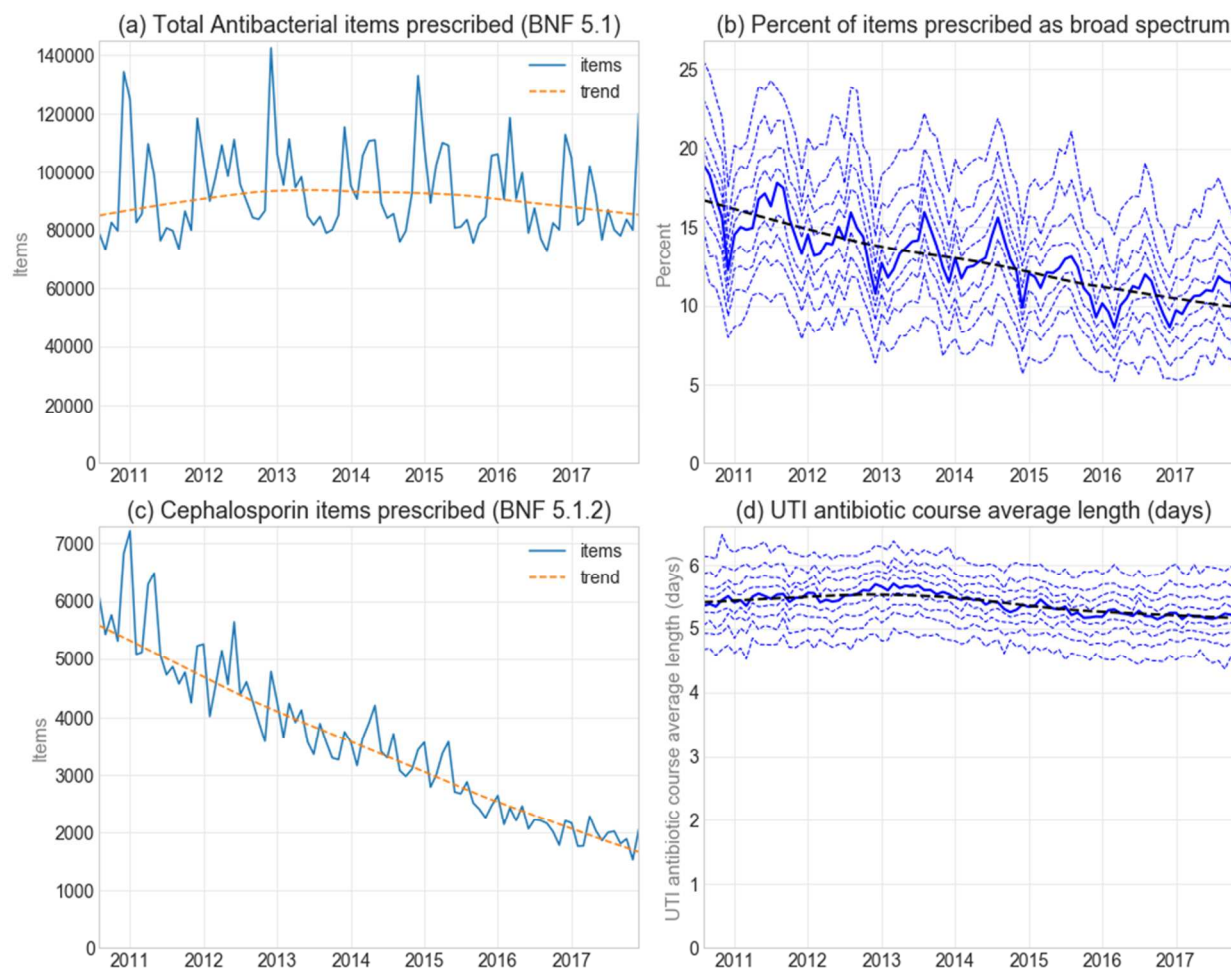


Figure S5. Monthly prescribing trends in out-of-hours services, Oct 2010 - Dec 2017. For (b) and (d), solid line shows median, heavy dashed line shows median trend line, thin dashed lines are deciles (10-90). (a) Total antibacterial items. (b) Broad spectrum items as a percentage of selected common antibiotic items. (c) Total cephalosporin items prescribed. (d) Average course length for selected antibiotics used for UTIs (days).