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Antibiotics in primary care in England: which antibiotics are prescribed and for which conditions?

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Objectives: To analyse antibiotic prescribing behaviour in English primary care with particular regard to which antibiotics are prescribed and for which conditions.

Methods: Primary care data from 2013–15 recorded in The Health Improvement Network (THIN) database were analysed. Records with a prescription for systemic antibiotics were extracted and linked to co-occurring diagnostic codes, which were used to attribute prescriptions to clinical conditions. We further assessed which antibiotic classes were prescribed and which conditions resulted in the greatest share of prescribing.

Results: The prescribing rate varied considerably among participating practices, with a median of 626 prescriptions/1000 patients (IQR 543–699). In total, 69% of antibiotic prescriptions ($n = 3156507$) could be linked to a body system and/or clinical condition. Of these prescriptions, 46% were linked to conditions of the respiratory tract, including ear, nose and throat (RT/ENT); leading conditions within this group were cough symptoms (22.7%), lower respiratory tract infection (RTI) (17.9%), sore throat (16.7%) and upper RTI (14.5%). After RT/ENT infections, infections of the urogenital tract (22.7% of prescriptions linked to a condition) and skin/wounds (16.4%) accounted for the greatest share of prescribing. Penicillins accounted for 50% of all prescriptions, followed by macrolides (13%), tetracyclines (12%) and trimethoprim (11%).

Conclusions: The majority of antibiotic prescriptions in English primary care were for infections of the respiratory and urinary tracts. However, in almost one-third of all prescriptions no clinical justification was documented. Antibiotic prescribing rates varied substantially between practices, suggesting that there is potential to reduce prescribing in at least some practices.

Introduction

Antimicrobial resistance (AMR) compromises the effective treatment of bacterial infections and represents a global threat to public health.[1,2] Antibiotic consumption is a key driver of the development and spread of AMR, and prudent antibiotic prescribing has been identified as an important strategy to curb this problem.[3] Prudent prescribing includes avoiding unnecessary prescriptions, delaying prescriptions when possible, favouring narrow-spectrum over broad-spectrum antibiotics and optimizing treatment duration.[4] Antimicrobial stewardship interventions can facilitate more-prudent antibiotic prescribing, but identifying specific challenges and goals for prescribing improvement in any given setting requires a thorough understanding of prescribing behaviour.

In 2016 the UK government set a target to halve inappropriate antibiotic prescribing by 2020.[5] Primary care is a natural target for antimicrobial stewardship interventions, in part because outpatients are frequently prescribed antibiotics for self-limiting and/or non-bacterial infections,[6] and because primary care accounts for approximately three-quarters of human antibiotic prescriptions in the UK.[2] However, an up-to-date inventory of antibiotic prescribing in English primary care is lacking, yet is a prerequisite to identify and quantify potentials for improving prescribing in line with government ambitions. Although antibiotic prescribing in English primary care has been studied extensively (including the main indications for antibiotic prescribing and the specific drugs used to treat them[6–10]), most of the studies were conducted some years ago, and it is unclear how prescribing has shifted as a consequence of changing prescribing guidelines and various initiatives to reduce the unnecessary use of antibiotics.

The aim of this article is to provide thorough insight into the current use of antibiotics in English primary care. Here, we detail antibiotic prescribing by: (i) age; (ii) antibiotic class; (iii) body system and condition; and (iv) acute versus overall use.

Methods

Ethics

The Health Improvement Network (THIN) data were used for this work. The data collection scheme for THIN is approved by the UK Multicentre Research Ethics Committee (reference number 07H1102103). In accordance with this approval, the study protocol was reviewed and approved by an independent Scientific Review Committee (reference numbers 16THIN071 and 16THIN071-A1).

Database

Antibiotic prescribing events were extracted from THIN, a primary care electronic database that contains anonymized patient, prescribing practice, and consultation data. The database is representative (∼7% coverage) of the general UK population and rates of consultation and prescribing are similar to national estimates.[11,12] We included data from English general practices that participated in THIN and provided data for at least one full calendar year between 1 January 2013 and 31 December 2015. Prescribing data were collected for a 3 year period to more accurately assess average annual prescribing rates. Patients of all ages were included in this study, provided that each individual patient's record contained valid data on birthdate and practice registration. Patients were split into three age groups: children (aged <19 years), adults (19–64 years) and the elderly (≥65 years).

Selection and grouping of antibacterial drugs

We restricted our analyses to systemic antibiotics listed in the British National Formulary (BNF),[13] chapter 5.1, excluding topical antibiotics as well as antituberculosis and antileprosy drugs. We used the Anatomical Therapeutic Chemical (ATC) classification system[14] to group antibiotics, which facilitates international comparisons.[12]

Selection and grouping of diagnostic codes

To facilitate analysis of the vast number of different Read codes (the standard clinical diagnostic codes used in UK general practice) in the data, Read codes were organized using two different hierarchical groups. First, as in the BNF, Read codes were mapped to body systems (e.g. gastrointestinal, skin, cardiovascular, etc.). Second, within each body system, Read codes were mapped to 'conditions': concrete diagnoses or, if not possible, other broad diagnostic categories such as 'symptoms' and 'examinations' (for details see Supplementary data Figures S1–S4, available at *JAC* Online). Using this system, in the absence of a diagnosis, vague yet clinically informative Read codes (e.g. 'miscellaneous urinary symptoms') could still be mapped to conditions. However, some Read codes were clinically uninformative (e.g. 'had a chat with patient') and were not mapped to body systems or conditions.

Linking prescriptions to diagnostic codes

Antibiotic prescriptions are not automatically linked to Read codes in THIN, and so two linking algorithms were developed. The first algorithm (used for all analyses presented here) linked all prescriptions of systemic antibiotics: (i) to Read codes entered on the same day as the prescription for the respective patients; and/or (ii) with the same consultation identifier, given that the Read codes were entered on or before the date of the prescription. A second, more comprehensive algorithm was developed to capture additional prescriptions that could not be linked to a condition using the baseline algorithm. This second algorithm used consultation and prescribing data in three ways in the following order: (i) if a prescription was part of a sequence of repeat prescriptions, it was linked to Read codes with the same date as the first antibiotic prescribed in the sequence; (ii) if not, Read codes coinciding with the same antibiotic prescribed within the previous 30 days were used; (iii) and lastly, if no Read code could be found in the previous steps, any codes dated <8 days before the prescription were used to capture delayed prescribing. For all analyses, except where noted in the detailed subdivision of antibiotics and conditions, we assumed that nitrofurantoin prescriptions with or without a diagnostic code were attributed to urinary tract infection (UTI), since nitrofurantoin is exclusively prescribed for management of UTI.

Multiple Read codes are often entered for the same patient and the same consultation. If a code describing a diagnosis co-occurred with a code describing symptoms or examinations within the same body system (e.g. 'acute otitis media' co-occurring with 'ear pain'), precedence was given to the diagnosis. However, Read codes can coincide without being causally linked, such as when a patient consults a prescriber for multiple reasons during the same consultation (e.g. if a patient consulted with depression and UTI, both the depression and UTI codes would be documented for that consultation). To minimize false associations between antibiotic prescriptions and unrelated codes, we extracted for analysis only Read codes that were potentially related to antibiotic prescribing. However, some prescriptions were still linked to multiple Read codes from different body systems that could potentially underlie antibiotic prescribing, and so a 'multiple body system' group was created to identify when a specific body system could not be determined.

Analyses

The annual prescribing rate for each practice was determined by dividing the total number of antibiotic prescriptions by the number of registered patients at 1 July. Proportions of the total number of prescriptions were established for (i) antibiotic class, (ii) condition and (iii) age group. These analyses were performed separately for (i) all prescriptions and (ii) only acute prescriptions. Acute prescriptions were isolated by excluding prescriptions: (i) explicitly coded as a repeat prescription; (ii) that were part of a prescribing sequence where the same antibiotic was prescribed every month for at least 6 months; or (iii) that covered >162 exposure days over a period of 180 days; and (iv) that were preceded by an antibiotic prescription in the 30 days before, unless that prescription was made for another body system.

Results

Between 2013 and 2015, 4.57 million antibiotic prescriptions were issued in 349 practices in 2013, 285 practices in 2014 and 191 practices in 2015. Overall prescribing rates were 659, 654 and 607 per 1000 registered patients for 2013, 2014 and 2015, respectively. On average 30.3% of registered patients received at least one antibiotic prescription per year.

The median prescribing rate among participating practices was 626 prescriptions/1000 patients (IQR 543–699). The mean age of patients receiving antibiotics was 47 years and 62.6% of the antibiotics were prescribed to female patients. Antibiotic prescribing rates were highest in the elderly (aged ≥65 years), but approximately half of all antibiotics were prescribed to adults aged 19–64 years (Table 1).

Practices that discontinued contribution to the database were comparable to practices with continuing contribution. Practices that participated in THIN for the whole period ($n = 191$) had, in 2013, a median of 7956 registered patients and a median prescribing rate of

661/1000 patients; practices that discontinued participation during this period ($n = 158$) had a median of 7831 patients and a median prescribing rate of 648 prescriptions/1000 patients.

Antibiotic prescriptions by antibiotic class

The distribution of antibiotic prescriptions by antibiotic class is shown in Tables 2 and 3. About half of all antibiotics prescribed were penicillins (50.3% in 2013 and 48.8% in 2015; Table 2), of which ~55% was amoxicillin (Table 3). The proportion of penicillins was even higher in acute prescriptions (59.2% of all prescriptions in 2013 and 58.4% in 2015). The proportion of prescriptions for nitrofurantoin increased year on year.

The distribution of prescribed antibiotics varied substantially by age group (Tables 4 and 5). Penicillins were the most prescribed antibiotics in all age groups, but accounted for 66.7% of prescriptions in children, compared with 48.7% in adults and 41.9% in the elderly. After penicillins, the most prescribed antibiotics were macrolides in children (15.3%), tetracyclines in adults (14.0%) and trimethoprim in the elderly (15.8%).

Antibiotic prescriptions by body system and condition

Of all antibiotic prescriptions, 69.0% were linked to one or more clinical conditions (i.e. were linked to a Read code that was mapped to a body system and a diagnosis, symptom, etc. using the hierarchical grouping of Read codes), 18.0% were linked to clinically uninformative codes (e.g. 'telephone consultation') and 13.0% could not be linked to any Read code whatsoever (Table 6). Using the second linking algorithm, an additional 6% of prescriptions (total 75%) were linked to a clinically informative Read code, but this did not have a substantial impact on the distribution of antibiotics across body systems (Table S1). Among prescriptions linked to an informative Read code, most were linked to conditions of the respiratory tract including ear, nose and throat (RT/ENT; 46.0%), the urogenital tract (22.7%) and the skin (including wounds) (16.3%). Among specific conditions, antibiotics were prescribed most often for UTI (20.6%), cough (10.4%) and lower respiratory tract infection (RTI) (8.2%) (Table 7).

Table 8 shows how antibiotics grouped by antibiotic class were prescribed for different body systems, including selected conditions of the respiratory tract, urogenital tract and skin. The majority (81.6%) of all linked amoxicillin (in J01CA) prescriptions were prescribed for respiratory tract conditions, and 75.4% of all linked phenoxymethylpenicillin (in J01CE) prescriptions were for sore throat. Large differences between antibiotic classes were observed in the percentage of prescriptions not linked to a useful Read code, and less common or 'other' antibiotics were documented particularly poorly. As expected, nitrofurantoin was mainly prescribed for UTI (77.0% of linked prescriptions), with just 3% of prescriptions linked only to a clear non-urogenital condition.

Table 9 shows the distribution of different antibiotics that were prescribed to treat a selection of different conditions. RT/ENT conditions were treated with amoxicillin more often than any other antibiotic, except for sore throat, where 61.7% of all prescriptions were for phenoxymethylpenicillin. The distribution of antibiotic prescriptions linked to multiple body systems was markedly similar to the overall distribution of prescriptions. Conversely, the distribution of prescriptions that could not be mapped to a condition [i.e. no (informative) Read code] was substantially different from the overall distribution of prescriptions.

It was found that frequently used first-line antibiotics, in particular penicillins, were comparatively well documented. For instance, among extended-spectrum penicillins, which are

Table 1. Yearly antibiotic prescribing rates (number of prescriptions per 1000 mid-year registered patient population) by age group

	No. prescriptions/1000 registered patients in indicated age groups		
Year	<19 years	19–64 years	≥65 years
2013	580	542	1138
2014	568	533	1145
2015	497	491	1113
Total (%) 2013–15	849539 (18.6)	2241664 (49.0)	1483170 (32.4)

Table 2. Prescriptions by year and antibiotic class, comparing acute prescriptions (no repeat prescriptions, no other antibiotic prescriptions 30 days earlier and no long-term/prophylactic prescriptions) and all prescriptions

		Antibiotic prescriptions in indicated year (%)					
		acute			all		
Antibiotic class	ATC code	2013	2014	2015	2013	2014	2015
Penicillins[a]	J01C	59.2	59.4	58.4	50.3	49.9	48.8
Macrolides, lincosamides and streptogramins	J01F (99% macrolide)	12.0	11.9	11.8	13.4	13.5	13.4
Sulphonamides and trimethoprim	J01E (97% trimethoprim)	10.6	10.9	10.8	11.0	11.3	11.2
Tetracyclines	J01A	7.6	7.4	8.0	11.7	11.7	12.4
Nitrofurantoin	J01XE01	4.5	4.8	5.4	5.9	6.2	6.8
Other β-lactam antibacterials	J01D (91% cefalexin)	2.0	1.7	1.6	3.1	2.9	2.8
Quinolones	J01M (93% ciprofloxacin)	1.7	1.6	1.7	2.2	2.2	2.2
Others		2.4	2.3	2.3	2.4	2.3	2.4

[a]The breakdown by class of penicillin is shown in Table 3.

Table 3. Penicillin prescriptions by year and class, comparing acute prescriptions (no repeat prescriptions, no other antibiotic prescriptions 30 days earlier and no long-term/prophylactic prescriptions) and all prescriptions

		Penicillin prescriptions in indicated year (%)					
		acute			all		
Penicillin class	ATC code	2013	2014	2015	2013	2014	2015
Extended-spectrum penicillins	J01CA (99% amoxicillin)	58.4	58.5	58.0	55.1	55.3	55.0
β-Lactamase-sensitive penicillins	J01CE (99% phenoxymethylpenicillin)	11.0	11.0	11.1	12.0	12.0	12.2
β-Lactamase-resistant penicillins	J01CF (100% flucloxacillin)	22.4	22.7	23.2	22.2	22.3	22.8
Penicillin combinations[a]	J01CR (99% co-amoxiclav)	8.2	7.8	7.7	10.7	10.4	10.0

[a]Including β-lactamase inhibitors.

Table 4. Antibiotic prescriptions in patients of different age groups by antibiotic class, comparing acute (no repeat prescriptions, no other antibiotic prescriptions 30 days earlier and no long-term/prophylactic prescriptions) and all prescriptions

		Antibiotic prescriptions in indicated year age groups (%)							
		acute				all			
Antibiotic class	ATC code	<19	19–65	≥65	all	<19	19–65	≥65	all
Penicillins[a]	J01C	75.2	56.4	51.7	59.1	66.7	48.7	41.9	49.8
Macrolides, lincosamides and streptogramins	J01F (99% macrolide)	13.1	12.1	10.7	11.9	15.3	13.6	12.2	13.4
Sulphonamides and trimethoprim	J01E (97% trimethoprim)	5.9	10.3	15.5	10.7	6.4	9.9	15.8	11.1
Tetracyclines	J01A	3.4	9.0	8.3	7.6	7.9	14.0	10.9	11.9
Nitrofurantoin	J01XE01	0.8	5.1	7.4	4.8	1.0	5.8	9.8	6.2
Other β-lactam antibacterials	J01D (91% cefalexin)	0.8	1.8	2.5	1.8	1.5	2.5	4.6	3.0
Quinolones	J01M (93% ciprofloxacin)	0.2	1.9	2.2	1.6	0.4	2.3	3.0	2.2
Others	–	0.6	3.4	1.7	2.5	0.8	3.2	1.8	2.4

[a]The breakdown by class of penicillin is shown in Table 5.

Table 5. Prescriptions for penicillins in patients of different age groups by antibiotic class, comparing acute (no repeat prescriptions, no other antibiotic prescriptions 30 days earlier and no long-term/prophylactic prescriptions) and all prescriptions

		Antibiotic prescriptions in indicated year age groups (%)							
		acute				all			
Penicillin class	ATC code	<19	19–65	≥65	all	<19	19–65	≥65	all
Extended-spectrum penicillins	J01CA (99% amoxicillin)	63.4	54.4	60.8	58.3	60.8	56.4	51.6	55.2
β-Lactamase-sensitive penicillins	J01CE (99% phenoxymethylpenicillin)	17.8	11.4	2.3	11.0	18.5	5.4	12.5	12.0
β-Lactamase-resistant penicillins	J01CF (100% flucloxacillin)	14.2	25.3	26.8	22.7	14.6	24.7	25.0	22.3
Penicillin combinations[a]	J01CR (99% co-amoxiclav)	4.6	8.9	10.1	8.0	6.1	13.5	10.9	10.5

[a]Including β-lactamase inhibitors.

dominated by amoxicillin, only 22.3% of prescriptions could not be linked to a diagnostic code (Table 8). Further, amoxicillin was dominant among linked prescriptions, accounting for 32.2% of all prescriptions, but only 17.8% among unlinked prescriptions. First-line antibiotics to treat UTI, i.e. nitrofurantoin and trimethoprim, were less well documented: 44.7% and 37.4% of prescriptions were unlinked to a diagnostic code, respectively. Infrequently used antibiotics were documented particularly poorly; for example, 70.5% of oxytetracycline prescriptions lacked an informative diagnostic code. Of the prescriptions that were linked to one or more diagnostic codes, 80.3% were for acute conditions. By contrast, just 43.0% of prescriptions without a diagnostic code were for acute conditions.

Discussion

Between 2013 and 2015, ∼4.6 million antibiotic prescriptions were registered in the THIN database. Most antibiotics were prescribed for infections of the respiratory and urinary tracts, although almost one-third (31%) of prescriptions could not be mapped to any clinical condition. Amoxicillin was the most commonly prescribed antibiotic in all age groups, but the distribution of prescribed antibiotics varied substantially between children, adults and the elderly. The overall prescribing rate decreased slightly and the overall distribution of prescribed antibiotics remained relatively stable over the 3 years included here.

This study represents an up-to-date assessment of antibiotic prescribing in England and is consistent with findings from previous work. A recent study by Shallcross *et al.*[15] analysed data from THIN from 2011–13 and found a similar antibiotic prescribing rate (0.67 prescriptions per person year) as was found in this study (on average 0.66 prescriptions per patient per year for 2013, the only year with overlap). They also found that, on average, 30.1% of patients were prescribed at least one antibiotic per year, consistent with the 30.3% reported here.

In the current study, a slight increase in the use of nitrofurantoin was observed between 2013 and 2015. This is in line with recent changes in treatment guidelines, which now recommend the use of nitrofurantoin as first-line therapy to treat UTI.[16] However, despite this increase in nitrofurantoin use, no decline was observed for trimethoprim (which is another standard treatment option for UTI). Furthermore, among all antibiotic prescriptions linked to a code for UTI (i.e. when not automatically assuming that all nitrofurantoin prescriptions are for UTI, as was done in other analyses), the proportions of prescriptions of trimethoprim (50.0%) and nitrofurantoin (26.3%) were similar to proportions reported by Hawker *et al.* from 2011 (53.5% and 24.0%, respectively, in England in women aged 16–74 years).[9]

Table 6. Prescriptions by body system for acute (no repeat prescriptions, no other antibiotic prescriptions 30 days earlier and no long-term/prophylactic prescriptions) and all prescriptions

System the prescription was linked to	Antibiotic prescriptions (%): acute, total	acute, with informative diagnostic code	all, total	all, with informative diagnostic code
Informative diagnostic code	80.6	–	69.0	–
respiratory tract (including ENT)	39.6	49.1	31.7	46.0
urogenital tract	15.8	19.6	15.7	22.7
skin and wounds	13.1	16.3	11.3	16.3
other body systems	8.1	10.0	7.1	10.3
multiple body systems	4.0	5.0	3.2	4.7
Uninformative diagnostic code	15.5	–	18.0	–
No diagnostic code	3.9	–	13.0	–
Total no. of prescriptions	3144367		4574373	

Table 7. Percentage of prescriptions for major conditions of the RT/ENT, urogenital tract and skin and wounds

Body system/condition	Prescriptions within body system (%)	All linked prescriptions (%)	Acute linked prescriptions (%)
RT/ENT			
cough	22.7	10.4	11.1
lower RTI	17.9	8.2	8.8
sore throat	16.7	7.7	8.6
upper RTI	14.5	6.7	7.5
ear-related diagnoses/symptoms	12.2	5.6	6.0
other diagnoses/symptoms	16.0	7.4	7.1
Total RT/ENT conditions	100.0	46.0	49.1
Urogenital tract			
urinary tract	90.6	20.6	17.3
genital tract	6.7	1.5	1.7
unspecific urogenital	2.7	0.6	0.6
Total urogenital tract conditions	100.0	22.7	19.6
Skin and wounds			
boil, cyst, abscess	13.9	2.3	2.4
unspecific	13.2	2.2	2.3
cellulitis	12.0	2.0	1.9
acne	9.2	1.5	1.3
ingrown/infected nail	7.4	1.2	1.2
bites	6.3	1.0	1.1
other diagnoses/symptoms	25.1	4.0	4.2
wounds	12.9	2.1	1.9
Total skin conditions and wounds	100.0	16.3	16.3

Using data from 1998-2001, Petersen *et al.*[10] found that the top five conditions for antibiotic prescriptions were RTI including productive cough (15%), upper RTI (14%), sore throat (11%), UTI including UTI symptoms (10%) and acute otitis media (8%). By comparison, here we found the leading condition to be UTI, accounting for 21% of prescriptions linked to a condition. This large difference may in part be explained by our assumption that all nitrofurantoin prescriptions were for UTI (Figure 1). Further, in contrast to Petersen *et al.*,[10] we defined a separate category for all cough-related codes (not only productive cough), which accounted for 10% of all linked prescriptions and may partially, together with the increase in UTI, explain the lower relative share of prescriptions for lower RTI (8%) found in our study. Overall, it is difficult to infer the degree to which these studies differ owing to different methodologies as opposed to true changes in prescribing over time. In both studies, amoxicillin was the most frequently prescribed antibiotic (26.4% of all prescriptions then, 26.8% of all prescriptions in 2015), but our findings suggest that erythromycin (the second most prescribed drug in 1998–2001 with 9.5% of all antibiotic prescriptions, now 4.9%) has been

Table 8. Within antibiotic classes, the percentage of all antibiotic prescriptions by linked condition

		Percentage of total prescriptions per antibiotic class																
		RT/ENT							Skin and wounds		Urogenital tract			Other and unknown body system				
Antibiotic or class	ATC code	GI tract	LRTI	URTI excl. sore throat	sore throat	cough	ear	other RTI	skin excl. acne	acne	urinary tract	genital tract	unspecific urogenital[a]	other body systems[b]	misc. codes	multiple body systems	no (informative) diagnostic code	Total no. prescriptions
Doxycycline	J01AA02	0.3	12.6	10.5	0.7	10.1	0.8	9.1	3.7	1.7	0.6	1.3	0.8	2.0	4.3	3.4	38.1	302879
Oxytetracycline	J01AA06	0.3	2.0	1.1	0.3	1.9	0.3	1.4	7.0	9.3	0.3	0.2	0.1	0.6	2.4	2.3	70.5	75754
Other tetracyclines	other J01AA	0.2	0.2	0.2	0.1	0.2	0.2	0.6	6.4	16.7	0.2	0.3	0.1	0.4	2.2	2.7	69.3	163972
Extended-spectrum penicillins	J01CA	0.7	14.5	10.4	3.3	17.3	9.8	8.2	1.3	0.0	2.3	0.2	0.2	1.5	4.3	3.7	22.3	1257935
β-Lactamase-sensitive penicillins	J01CE	0.2	0.1	2.4	54.7	0.8	0.4	1.6	4.3	0.0	0.2	0.2	0.1	0.5	4.0	3.0	27.5	274197
β-Lactamase-resistant penicillins	J01CF	0.1	0.1	0.1	0.1	0.1	1.9	0.6	56.6	0.2	0.3	0.8	0.2	2.7	7.7	3.7	24.8	509259
Combinations of penicillins	J01CR	1.3	5.6	2.8	1.5	4.1	4.5	4.0	14.0	0.0	9.3	2.0	1.2	2.8	8.9	3.9	34.1	238295
Cephalosporins (1st generation)	J01DB	1.2	1.9	1.1	1.0	2.0	1.0	1.4	2.7	0.0	22.3	0.9	2.1	0.7	6.1	3.0	52.6	130279
Trimethoprim and derivatives	J01EA	0.3	0.2	0.1	0.1	0.2	0.2	0.3	0.6	0.2	46.1	0.5	5.3	0.3	4.2	4.0	37.4	496114
Erythromycin	J01FA01	0.7	5. 2	5.3	9.9	8.1	5.6	3.7	15.0	2.4	0.4	0.6	0.2	1.5	5.0	3.1	33.3	225027
Clarithromycin	J01FA09	2.0	12.6	5.5	6.1	12.9	3.9	8.0	11.4	0.1	0.3	0.3	0.1	1.1	4.9	3.6	27.2	320462
Other macrolides	other J01FA	0.4	2.6	0.9	0.7	2.3	0.8	3.8	1.3	0.0	0.5	3.5	0.5	0.7	3.7	1.2	77.1	62317
Fluoroquinolones	J01MA	4.1	2.7	0.6	0.2	1.9	2.4	2.2	3.2	0.0	18.9	3.5	5.9	0.9	7.3	3.2	43.0	100323
Imidazole derivatives	J01XD	9.3	0.1	0.2	0.5	0.2	0.4	0.5	8.0	0.1	1.5	19.8	2.0	4.8	10.7	3.6	38.3	93786
Nitrofurantoin[c]	J01XE01	0.3	0.1	0.0	0.0	0.1	0.1	0.3	0.5	0.0	42.4	0.3	4.1	0.3	3.7	3.1	44.7	284264
Others	others	1.0	1.3	0.5	0.4	1.3	0.7	1.8	7.0	0.0	2.4	0.5	0.3	0.7	5.4	1.1	75.6	39510
	Total	0.9	6.5	4.6	5.3	7.2	3.9	4.2	10.3	1.0	10.0	1.1	1.3	1.4	5.1	3.5	33.7	4574373

GI, gastrointestinal; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.
[a]Unspecific urogenital: conditions where urinary tract and genital tract could not be distinguished.
[b]Other body systems: includes but is not limited to cardiovascular, dental and prophylactic use.
[c]Unlike in other analyses, nitrofurantoin prescriptions were here not automatically assumed to be for UTI.

Table 9. Within diagnoses, the percentage of all antibiotic prescriptions by antibiotic class

	Percentage of total prescriptions by body system/condition																
		RT/ENT						Skin and wounds		Urogenital tract			Other and unknown body system				
ATC code[c]	GI tract	LRTI	URTI excl. sore throat	sore throat	cough	ear	other RTI	skin excl. acne	acne	urinary tract	genital tract	unspecific urogenital[a]	other body systems[b]	misc. codes	multiple body systems	no (informative) read code	Overall
J01AA02	2.3	12.8	15.1	0.9	9.3	1.3	14.2	2.4	10.7	0.4	8.4	4.1	9.5	5.6	6.5	7.5	6.6
J01AA06	0.5	0.5	0.4	0.1	0.4	0.1	0.6	1.1	14.9	0.0	0.3	0.1	0.8	0.8	1.1	3.5	1.7
Other J01AA	1.0	0.1	0.1	0.1	0.1	0.2	0.5	2.2	57.8	0.1	1.0	0.2	1.1	1.5	2.8	7.4	3.6
J01CA	22.7	61.4	62.1	17.1	66.0	69.0	53.3	3.6	0.2	6.4	6.2	5.3	29.4	23.3	29.4	18.0	27.5
J01CE	1.3	0.1	3.1	61.7	0.7	0.5	2.2	2.5	0.1	0.1	1.4	0.3	2.1	4.8	5.1	4.9	6.0
J01CF	1.9	0.1	0.3	0.1	0.1	5.5	1.6	61.4	1.9	0.3	8.8	1.7	21.9	17.0	12.0	8.2	11.1
J01CR	7.9	4.5	3.1	1.5	3.0	6.0	4.9	7.1	0.2	4.9	10.0	4.8	10.4	9.1	5.8	5.2	5.2
J01DB	4.0	0.8	0.7	0.6	0.8	0.7	1.0	0.8	0.0	6.3	2.3	4.7	1.3	3.4	2.4	4.4	2.8
J01EA	4.1	0.3	0.2	0.1	0.3	0.5	0.9	0.6	1.9	50.0	4.8	44.2	2.0	9.0	12.5	12.0	10.8
J01FA01	3.8	3.9	5.7	9.2	5.6	7.0	4.3	7.2	11.4	0.2	2.7	0.6	5.1	4.8	4.4	4.9	4.9
J01FA09	15.5	13.6	8.4	8.1	12.5	7.0	13.2	7.8	0.6	0.2	2.0	0.6	5.6	6.8	7.3	5.6	7.0
Other J01FA	0.6	0.6	0.3	0.2	0.4	0.3	1.2	0.2	0.0	0.1	4.6	0.5	0.7	1.0	0.5	3.1	1.4
J01MA	10.1	0.9	0.3	0.1	0.6	1.3	1.1	0.7	0.0	4.1	7.2	10.0	1.3	3.2	2.0	2.8	2.2
J01XD	21.6	0.0	0.1	0.2	0.0	0.2	0.2	1.6	0.1	0.3	38.5	3.2	7.1	4.3	2.1	2.3	2.1
J01XE01[d]	2.0	0.1	0.1	0.0	0.1	0.1	0.4	0.3	0.0	26.3	1.5	19.5	1.4	4.5	5.6	8.3	6.2
Others	0.7	0.3	0.0	0.0	0.1	0.3	0.4	0.5	0.2	0.3	0.3	0.2	0.3	0.9	0.5	1.9	0.9
Total no. prescriptions	40510	297246	211025	242932	329443	177875	193775	469437	47250	457852	48339	59082	63896	231805	158497	1545409	4574373

GI tract, gastrointestinal tract; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.
[a]Unspecific urogenital: conditions where urinary and genital tract could not be distinguished.
[b]Other body systems: includes but is not limited to cardiovascular, dental and prophylactic use.
[c]J01AA02, doxycycline; J01AA06: oxytetracycline; other J01AA, other tetracyclines; J01CA, extended-spectrum penicillins; J01CE, β-lactamase-sensitive penicillins; J01CF, β-lactamase-resistant penicillins; J01CR, combinations of penicillins; J01DB, cephalosporins (1st generation); J01EA, trimethoprim and derivatives; J01FA01, erythromycin; J01FA09, clarithromycin; other J01FA, other macrolides; J01MA, fluoroquinolones; J01XD, imidazole derivatives; J01XE01, nitrofurantoin.
[d]Unlike in other analyses, nitrofurantoin prescriptions were here not automatically assumed to be for UTI.

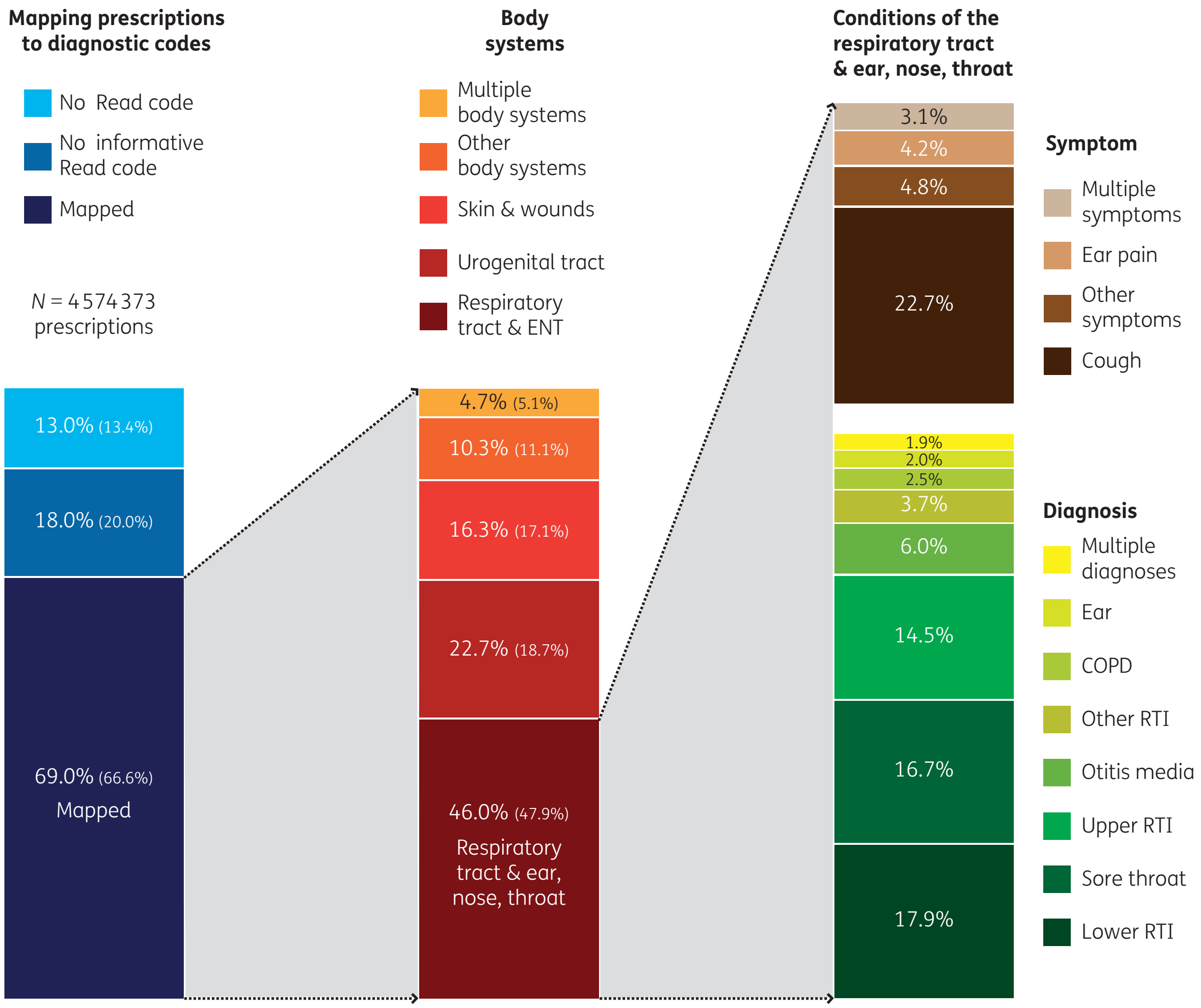

Figure 1. Mapping prescriptions to Read codes using a hierarchical system that mapped each Read code to (i) a body system and (ii) a condition (with varying specificity, e.g. a specific diagnosis or a general symptom). All columns add up to 100%. Percentage values with large font size assume that nitrofurantoin prescriptions without a linked Read code were used to treat UTI; values in parentheses with smaller font do not make this assumption.

partially replaced by clarithromycin (then 1.9%, now 7.0%). Between 1998–2001 and 2013–15, the most substantial shifts in antibiotic choice seem to have happened for UTI: nitrofurantoin use increased from 5.1% to 26.3%, first-generation cephalosporin use decreased from 19.9% to 6.3%, and slight decreases were also observed in use of trimethoprim (56.1% to 50.0%) and fluoroquinolones (5.9% to 4.1%).

Strengths and limitations

A major strength of this study is the use of recent individual patient data recorded in THIN, a large primary care database that is representative of the UK patient population.[12] The extensive mapping of Read codes to body systems and clinical conditions allowed us to provide a more complete overview of prescribing behaviour in English primary care than has been done in previous studies. However, despite this extensive approach, 31% of antibiotic prescriptions could still not be linked to clinically informative information owing to missing or unspecific diagnostic codes (or 25% using our most sensitive algorithm).

Further, it appears that poor documentation of antibiotic prescribing is non-random, because the distribution of antibiotics unlinked to a clinical condition differed substantially from the overall distribution of prescribed antibiotics. Penicillin prescriptions were more likely than any other antibiotic class to be linked to a diagnostic code. Comparatively, prescriptions for first-line UTI treatment (nitrofurantoin, trimethoprim) were less well documented. Prescriptions for rarely used antibiotics and prescriptions issued to complex patients on long-term or repeated treatment were documented particularly poorly. One could speculate that, for some prescribers, an antibiotic with only one (primary) indication can supplant the need for a diagnostic code (e.g. nitrofurantoin or trimethoprim prescription signifying UTI). The lack of diagnostic codes in complex patients could potentially be explained by prescribers storing all relevant information in free text (unavailable to us) instead of using diagnostic codes. Another explanation could be that they prescribed on the advice of hospital clinicians and did not additionally document the indications.

We tried to minimize the risk of including clinical conditions that do not have a causal link to the prescription by prioritizing diagnostic Read codes for specific conditions over more general Read codes or Read codes corresponding to symptoms, and by excluding Read codes for conditions unrelated to antibiotic prescribing (e.g. depression). Despite these efforts, it cannot be ruled out that some prescriptions have been falsely mapped to certain conditions, since our algorithms could not account for every caveat and exception. An illustration of this can be found in Table 8, where 3.0% of nitrofurantoin prescriptions (with diagnostic code) were only linked to non-urogenital diagnoses (more than expected, given that nitrofurantoin is only indicated for use in UTI). Another limitation is the decline in the number of practices participating in THIN from 2013 to 2015. Although the annual variation in prescribing seems low, 2013 may be overrepresented in some results. However, we also showed that practices that withdrew did not differ markedly in their overall prescribing behaviour.

Conclusions

In English primary care, we found that antibiotics were most commonly prescribed to treat RTI (including cough) and UTI, although no clinical justification for prescribing could be determined in 31% of all antibiotic prescriptions. The most commonly prescribed antibiotics were amoxicillin, flucloxacillin and trimethoprim, and the majority of all prescriptions (69%) were for acute conditions. Results from this study can be used to support national and international policy on the reduction of inappropriate antibiotic prescribing, possibly by defining target indications for prescribing reductions. More efforts are needed to explain practice variation in the prescribing of antibiotics.

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Transparency declarations

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Supplementary data

Figures S1 to S4 and Table S1 are available as Supplementary data at *JAC* Online.

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