Duration of antibiotic treatment for common infections in English primary care: cross sectional analysis and comparison with guidelines

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Antibiotic therapy duration for common infections in English primary care: a cross-sectional analysis and comparison with guidelines.

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Section 1: What is already known on this topic

- There is a clear causal link between antibiotic exposure and antibiotic resistance
- Strategies to reduce antibiotic use in primary care focus on decisions to start treatment
- It is not known to what extent excessive treatment duration contributes to antibiotic overuse in primary care.

Section 2: What this study adds

- For many common infections treated in primary care, a substantial proportion of antibiotic prescriptions (>50%) have durations which exceed those recommended in guidelines
- Rates of treatment duration beyond guidelines are highest for respiratory tract infections and are similar among patients with and without comorbidities.
- Substantial reductions in antibiotic use in primary care could be achieved by closer compliance with recommended treatment durations.

Abstract

Objectives To evaluate antibiotic therapy durations for common infections in English primary care and to compare this with guidelines.

Design Cross-sectional study.

Setting General practices contributing to The Health Improvement Network database, 2013-2015.

Participants 931,015 consultations that resulted in an antibiotic prescription for one of the following indications: acute sinusitis, acute sore throat, acute cough and bronchitis, pneumonia, acute exacerbation of chronic obstructive pulmonary disease (COPD), acute otitis media, acute cystitis, prostatitis, pyelonephritis, cellulitis, impetigo, scarlet fever and gastroenteritis.

Main outcome measures The main outcomes were the percentage of antibiotic prescriptions with a duration exceeding the guideline recommendation and the total number of days beyond the recommended duration for each indication.

Results The most common reasons for the prescriptions were patients consulting with acute bronchitis and cough (386,972), acute sore throat (239,231), acute otitis media (83,054), and acute sinusitis (76,683). Antibiotic treatments for upper respiratory indications and acute bronchitis accounted for more than two thirds of the total prescriptions considered, and ≥80% of these treatment courses exceeded guideline recommendations. Notable exceptions were acute sinusitis, where only 9.6% (95% CI 9.4 to 9.9%) of prescriptions exceeded 7 days and acute sore throat where only 2.1% (95% CI 2.0 to 2.1) exceed 10 days (recent guidance recommends 5 days). More than half of antibiotic prescriptions were longer than guidelines recommend for acute cystitis among females (54.6%, 95% CI 54.1 to 55.0%). The percentage of antibiotic prescriptions exceeding the recommended duration was lower for most non-respiratory infections. For the 931,015 included consultations resulting in antibiotic prescriptions, approximately 1.3 million days were beyond the durations recommended by the guidelines.

Conclusion For most common infections treated in primary care, a substantial proportion of antibiotic prescriptions have durations exceeding those recommended in guidelines. Substantial reductions in antibiotic exposure can be accomplished by aligning antibiotic prescription durations with guidelines.

Print abstract:

Study question: Are general practitioners prescribing longer antibiotic courses than recommended in the guidelines?

Methods: Antibiotic prescribing and consultation data were extracted from The Health Improvement Network (THIN) primary care database between 2013 and 2015. The duration of antibiotic prescriptions for the following indications were evaluated: acute sinusitis, acute sore throat, acute cough and bronchitis, pneumonia, acute exacerbation of chronic obstructive pulmonary disease (COPD), acute otitis media, acute cystitis, prostatitis, pyelonephritis, cellulitis, impetigo, scarlet fever and gastroenteritis. The main outcomes were the percentage of antibiotic prescriptions with a duration exceeding the guideline recommendation and the total number of days beyond the recommended duration of each indication.

Study answer and limitations: Overall, substantial reductions in antibiotic exposure can be accomplished by aligning antibiotic prescription durations with guidelines. Although we excluded complicated, recurrent infections that may require longer treatment, we were not able to account fully for patient factors which might underlie decisions to prolong therapy.

What this study adds: For many common infections treated in primary care, a substantial proportion of antibiotic prescriptions have durations which exceed those recommended in guidelines.

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Introduction

Many countries, including the United Kingdom, are trying to reduce antibiotic resistance by reducing unnecessary or inappropriate antibiotic prescribing.[1-3] The clear link between antibiotic prescribing and resistance at the individual[4,5] and population level[6] indicates that reducing antibiotic prescribing may decrease, or should at least stabilize, antibiotic resistance levels.[7-9] Previous work has reported substantial antibiotic over-prescribing in primary care in the UK[1,10,11] and elsewhere.[3,12] Reducing unnecessary antibiotic use can be achieved by not starting antibiotic treatments unless clearly indicated,[1,11] changing the choice of antibiotic for specific conditions,[6] or avoiding unnecessarily long antibiotic therapy durations.[13] Strategies to control antibiotic overuse in primary care focus on the initial prescribing decision (whether to treat and choice of agent) since reassessment of patients started on antibiotics is not routinely possible.[14] Little attention has been given to the possibility of reducing antibiotic overuse in primary care by reducing unnecessarily prolonged treatment.[15] Historically, general practitioners have been taught that antibiotic courses should be long enough to prevent the development of antibiotic resistance in the infection that is being treated, based on evidence of the emergence of resistance frequently related to sub-optimal dosing of penicillins in the treatment of *Streptococcus pneumoniae*.[16] However, current concerns primarily relate to the development of resistance in common commensal bacteria, rather than the ones causing the infections, where there is increasing evidence that the opposite is true – the longer the antibiotic exposure the greater the development of antibiotic resistance, which then leads to a greater risk of resistance in subsequent infections.[17,18] Overuse of antibiotics does not only contribute to increased antibiotic resistance levels, but also puts patients at risk of side-effects. Common side-effects include diarrhoea, rash and candidiasis.[19,20] Cumulative exposure to antibiotics has been identified as a major risk factor for *Clostridium difficile* infection, highlighting the need to reduce the duration of therapy where possible.[21,22] Although less common, other serious side effects are important reasons to minimise exposure to certain antibiotics. For example, macrolides are associated with an increased risk of serious ventricular arrhythmias and increased risk of sudden cardiac death.[23] Moreover, the Food and Drug Administration recently strengthened the current warning about fluoroquinolones potentially causing substantial decreases in blood sugar and mental health side effects.[24]

There is limited evidence about the contribution of excessive treatment duration to antibiotic overuse in primary care. A recent study from the US showed that more than two-thirds of antibiotic courses for acute sinusitis in adults were 10 days or longer, while the Infectious Disease Society of America recommends 5 to 7 days of therapy for uncomplicated cases.[25] A small study from the Manitoba region in Canada, focusing on urinary tract infection, pharyngitis, skin/soft tissue infections and pneumonia estimated that 15% of prescriptions with the appropriate antibiotic were longer than guideline-based recommendations.[26]

An up-to-date picture of prescribed antibiotic treatment durations for common infections in English primary care is lacking. Such an overview is especially relevant given the increasing evidence from randomized controlled trials and meta-analyses that shorter antibiotic courses clear infection as well as longer courses, while minimising selection, proliferation and spread of antibiotic resistant bacteria and the likelihood of side effects of the antibiotic.[18,27,28]

We therefore set out to assess to what extent antibiotic courses prescribed for common infections in English primary care are in line with relevant guidelines for duration of treatment. If substantial

proportions of antibiotic prescriptions are longer than recommended, this would indicate that there is potential to safely reduce total antibiotic use simply by better application of guidelines in clinical practice.

Methods

Data

Data were obtained from The Health Improvement Network (THIN), a primary care electronic database that contains anonymized patient, practice, and consultation data, and is representative of the general UK population, with consultation and prescribing rates similar to national data.[29] We used the same data extract that was previously used to evaluate which antibiotics are prescribed for different conditions in England.[29] This extract was limited to English practices that participated in THIN and provided data for at least one full calendar year between 1 January 2013 and 31 December 2015. The prescription-diagnosis linkage is described in detail elsewhere.[29] For the current analyses, we included only prescriptions for oral antibiotics linked to one of the following indications: acute sinusitis, acute sore throat, acute cough and bronchitis, pneumonia, acute exacerbation of chronic obstructive pulmonary disease (COPD), acute otitis media, acute cystitis, prostatitis, pyelonephritis, cellulitis, impetigo, scarlet fever or gastroenteritis. We excluded chronic and recurrent conditions, operationalized by excluding consultations explicitly coded as such and consultations where patients received antibiotics for a condition of the same body system (respiratory, urinary, gastrointestinal or skin) in the 30 days prior to the current antibiotic prescription. In addition, we excluded prescriptions that were i) explicitly coded as a repeat prescription; or ii) part of sequence of prescriptions where the same antibiotic was prescribed every month for at least 6 months or covered >162 exposure days over a period of 180 days.[29] Actual durations of antibiotic prescriptions for the 13 indications considered were compared with durations recommended in English guidance provided by Public Health England (PHE) – using the PHE 2013 guidance for the main analysis (Table 1 and Table S1): acute sinusitis,[30,31] acute sore throat,[31,32] acute cough and bronchitis,[31,33] pneumonia,[31,34] acute exacerbation of chronic obstructive pulmonary disease (COPD),[31,35] acute otitis media,[31,36] acute cystitis,[31,37] prostatitis,[31,38] pyelonephritis,[31,39] cellulitis,[31,40] impetigo,[31,41] scarlet fever[31,42] and gastroenteritis.[31,43]

Analysis

For each indication, we calculated the proportion of prescriptions longer than the recommended duration, separately for children (aged <16 years) and adults aged 16 years or over, and by antibiotic where guidelines recommended different durations for particular antibiotics. Because guidelines recommend prescribing longer antibiotic courses to treat cystitis in males compared to females,[31,37] we performed separate analyses for males and females for this condition. Acute prostatitis often has a different aetiology in young men (often sexually transmitted organisms)[44] as compared to older men (mostly Enterobacteriaceae) and prescribers might fear chronic prostatitis more in older men. Therefore, the following age-groups were evaluated for prostatitis: <35; 35-65 and >65 years old. In addition, for all conditions, we performed a secondary analysis restricting to healthy patients, defined as those without chronic kidney disease, COPD, asthma, coronary heart disease, immunosuppressive disease, use of immunosuppressive drugs, use of systemic corticosteroids, or use of inhaled corticosteroids.[11,45]

Multiple imputations via chained equations using sequential regression trees were used to impute duration data that was missing in 10-20% of the consultations (See supplementary file 2 for more details).[46] Confidence intervals were calculated using multiple imputation Wilson intervals, which have better properties than the usual multiple imputation confidence intervals, in particular always being bounded by zero and one.[47] In sensitivity analysis, we restricted the analysis to data with no missing values.

In addition, we calculated the total number of excess antibiotic days, defined as the total number of days beyond the recommended duration in the guidelines.

All analyses were performed using R version 3.4.3 (packages: "dplyr", "ggplot2", "mice", "nlme").

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. Results will be disseminated to relevant patient communities through news media.

Results

Between 2013 and 2015, 931,015 consultations for the 13 included indications led to antibiotic prescriptions. This subset – which focused on common conditions, but excluded chronic and recurrent cases, repeat prescriptions and antibiotic prophylaxis – covered approximately 20% of total antibiotics being prescribed (for any condition) during the study period. The most common indications were acute bronchitis and cough (386,972, 41.6% of the included consultations), acute sore throat (239,231, 25.7%), acute otitis media (83,054, 8.9%), acute sinusitis (76,683, 8.2%), cellulitis (54,610, 5.9%), and acute cystitis (53,010, 5.7%). Antibiotic treatment durations for the included indications showed poor guideline adherence for several indications (Fig 1 panel A-F, Fig S1-S8).

For all conditions grouped together, approximately 1.3 million days were beyond the durations recommended by guidelines (Table 2), which remained the same during 2013-2015.
The majority of excess days were due to respiratory indications (Table 2). Antibiotic treatments for respiratory indications, including otitis media, accounted for more than two thirds of the total prescriptions considered, and ≥80% of these treatment courses exceeded guideline recommendations (Table 2). A notable exception was acute sinusitis, for which only 9.6% (95% CI 9.4 to 9.9%) of prescriptions were longer than the 7 days recommended by the 2013 PHE guidance. For some indications, guidelines recommend longer durations for more unwell patients, such as patients with pneumonia and a CRB65 (Confusion, Respiratory rate, Blood pressure, 65 years of age and older) score between 1 and 2, or a range of appropriate durations (Table S1). A much smaller proportion of patients received antibiotic prescriptions exceeding these upper boundaries (Table 2, Table S3).

When restricting to antibiotic prescriptions beyond the recommended durations, the median number of days beyond the guideline recommendation was 2 (5th–95th percentile 2 to 3 days) for

acute cough & bronchitis, 2 days (5th-95th percentile 2 to 8 days) for acute otitis media, and 3 days (5th-95th percentile 1 to 7 days) for acute sinusitis. This was 7 days (5th-95th percentile 3 to 8 days) for cellulitis (using 7 days as threshold), and for acute cystitis 4 days (5th-95th percentile 2 to 4 days) for females and 7 days (5th-95th percentile 3 to 32) for males. In general, there was a tendency to write prescriptions with a duration of 5 or 7 days or multiples thereof (Figure 1 and Figure S1-S8). However, the peak at 7 days tended to be higher than for 5 days, even for conditions where a duration of 5 days is recommended. For conditions where guidelines recommend longer durations, the percentage of prescriptions beyond the recommendation was substantially lower than for conditions where guidelines recommend relatively short duration.

For respiratory tract indications the total number of days of prescribed antibiotics beyond the recommended duration (approximately 1.1 million excess days in total) comprised a substantial proportion of the total number of days of antibiotic prescribed for these indications, e.g. 29.5% for acute bronchitis/cough (Table 2).

Fewer prescriptions exceeded recommended durations for non-respiratory tract indications, but still more than half of antibiotic prescriptions were longer than recommended for acute cystitis among females (54.6%, 95% CI 54.1 to 55.0%) (Table 2). Although guidelines recommend a shorter duration for fosfomycin,[31] this did not affect our comparisons because this antibiotic was only used in 2 acute cystitis cases. For prostatitis, the percentage of antibiotics prescribed for longer than the recommended duration was 12.5% (95% CI 11.1 to 14.2%) using the recommendation of 28 days treatment (Table 2). When antibiotics are indicated for gastroenteritis, guidelines recommend prescribing antibiotics for 5-7 days. Setting the threshold at 5 days, 53% (95% CI 50.8 to 55.8%) of prescriptions were longer than guideline recommendation, while this percentage was 6.3% (95% CI 5.2 to 7.7%) when using the 7 day threshold (Table 2).

The percentage of antibiotic prescriptions for which the actual duration was beyond the recommended duration was much lower for pyelonephritis (18.0%, 95% CI 16.3 to 19.9%), cystitis among males (4.2%, 95% CI 3.6 to 4.9%), impetigo (9.9%, 95% CI 9.4 to 10.4%), and cellulitis (13.9%, 95% CI 13.6 to 14.2%) but this still translated into 155,238 excess antibiotic days (Table 2).

For acute prostatitis and acute cystitis among males, there appeared to be substantial under treatment with a substantial amount of courses shorter than the guideline recommendations, with 52.3% below 28 days and 26% below 14 days for prostatitis and 31.8% below 7 days for acute cystitis among males (Fig 1, panel D-E). In addition, some under treatment was observed when using trimethoprim for pyelonephritis (Fig S5), antibiotics for impetigo (Fig S6), and penicillin V for scarlet fever (Fig S7).

There was no clear tendency to prescribe longer courses for children (<16 years of age) compared to adults (≥ 16 years of age) (Table S2). Nevertheless, the percentage of prescriptions that were longer than recommended was higher among younger patients for acute bronchitis/cough (89.0% versus 84.7%), acute otitis media (89.9% versus 78.6%), impetigo (12.1% versus 6.4%), pyelonephritis (27.2% versus 17.7%) and gastroenteritis (70.7% versus 51.0%).

Very similar results were obtained when restricting the analyses to patients without relevant comorbidities (Table 2-3). After excluding patients with comorbidities and prior use of immunosuppressive drugs, inhaled or systemic corticosteroids the percentage of prescriptions that were longer than recommended differed ≤2% with the estimates based on all patients.
When restricting the analyses to antibiotics only mentioned in the guidelines, results were generally similar to the analyses including all antibiotics (Table S3). A notable exception was acute gastroenteritis. The percentage of antibiotic prescriptions longer than guidelines recommended became lower for gastroenteritis when only considering antibiotics mentioned in the guidelines (40.0% versus 53.3%, using a threshold of 5 days). In addition, for sore throat, pyelonephritis and scarlet fever, longer prescriptions are recommended for specific antibiotics. In these cases, observed durations less frequently exceeded durations recommended in the guidelines compared to other antibiotics prescribed for the same condition (Table S3). For most conditions, ≥75% of the prescribed antibiotics were mentioned in the guidelines for treatment of that condition (Table S3). A notable exception was acute gastroenteritis where only 12.8% of the cases were treated with the recommended antibiotic.
Sensitivity analysis restricting the analysis to data with no missing values gave similar results as the main analysis (Table S4).

Discussion

Principal findings

For most common infections treated in primary care, a substantial proportion of antibiotic prescriptions have durations exceeding those recommended in guidelines. This is most marked for most respiratory indications and acute cystitis among females. If all patients receiving antibiotics for the included indications received durations recommended by guidelines over the study period (3 years in ~4.4% of the English population; included prescriptions captured ~20% of total antibiotic prescriptions in the included practices during the study period), this would equate to 1.1 million fewer days antibiotics for respiratory tract indications and 100,000 fewer days for acute cystitis among females. Our findings indicate substantial scope for reducing antibiotic prescribing through better adherence to recommended antibiotic durations. In contrast, the duration of antibiotic prescriptions for pyelonephritis, cystitis among men, impetigo and cellulitis generally did not exceed guideline recommendations, with only 4–18% of prescriptions exceeding them.

Comparison with other studies

This is the first study to assess to what extent the course lengths of antibiotic prescriptions, for a wide range of common infections, follow guidelines in English primary care. In contrast to a recent US study focusing on acute sinusitis only,[25] we were able to account for comorbidities and prior use of drugs that potentially influence prescription duration. We found very similar results restricting to healthy patients without comorbidities or prior use of immunosuppressive drugs or corticosteroids, suggesting that comorbidities do not play a major role in the decision process about the duration of the antibiotic prescribed. Similarly, we did not find large differences between antibiotic prescriptions for children and adults.. This provides further support for the argument that treatment durations are not increased because individual patient factors indicated a clinical need for prolonged therapy.

Of note, we only assessed whether the antibiotic prescription durations followed guidelines and not whether antibiotics should have been completely avoided. Previous work showed that a substantial proportion of prescriptions for acute bronchitis/cough, acute otitis media, acute sinusitis, acute sore throat and impetigo in primary care are unnecessary.[11] Hence, for these conditions, the total days of unnecessary antibiotic use will be higher than estimated here. For example, if 77% of antibiotic prescriptions for acute sinusitis were inappropriate,[11] the percentage of days of antibiotic treatment not following guidelines would increase from 7.1% to 81.1% for this indication. Antibiotics may also be unnecessary for community-acquired pneumonia, for which it has been estimated that up to 25% of cases are caused by viruses without a bacterial coinfection.[48] However, it can be difficult to distinguish between cases of community-acquired pneumonia requiring antibiotics and cases that can safely be treated without antibiotics in the primary care setting. Similarly, in suspected urinary tract infection significant bacteriuria (>10^3) colony-forming unit (CFU)/ml has been found in only 25-65% of patients under 65 years given antibiotic treatment. In older adults asymptomatic bacteriuria is extremely common and does not require antibiotic treatment.[11,49,50]

For two of the antibiotic indications we studied, treatment was frequently prescribed for shorter durations than recommended, both urinary tract infections in men: acute cystitis and prostatitis. This may arise because prescribers appreciate that recommendations for these conditions are based on expert opinion and historical precedent rather than evidence, and that treatment durations for urinary tract infections in women have declined markedly in recent years. There is a need to establish whether shorter treatment durations are effective for men with urinary tract infections, as

this is a small but important patient population in which there is risk of harm from under treatment. It is notable that conditions for which course durations tended to be less than recommended in the guidelines were those for which evidence supporting duration of treatment is weak (Fig S5-S7).
In general there seemed to be a preference for antibiotic prescriptions with durations of 5 or 7 days or multiples thereof, without a clear evidence base for this preference. The preference for such durations has been observed previously in other settings and depended more on local practice and subspecialty than clinical features such as fever, comorbidities and severity.[51-53] In addition, it is noticeable that for conditions where guidelines recommend longer durations, the percentage of prescriptions beyond the recommendation is substantially lower than for conditions where guidelines recommend relatively short duration.

Limitations

One important limitation is that some antibiotic prescriptions may have been falsely linked to certain conditions in our study, because there is no automatic link between prescriptions and diagnoses in THIN.[29] However, results were very similar when restricting the analyses to only antibiotics mentioned in the guidelines for each specific condition, which increases the chance that the antibiotic was being used for the condition of interest. Although we excluded complicated, recurrent infections that may require longer treatment, we were not able to account fully for patient factors which might underlie decisions to prolong therapy. We were also not able to explore clinician-factors which may underlie deviation from recommended antibiotic treatment durations. For some patients in some cases longer durations would be appropriate, however there is no clear evidence about the percentage of patients that should legitimately receive longer prescriptions. Moreover, for some infections, such as acute sinusitis, recent evidence indicates that antibiotic therapy duration should actually be shorter instead of longer than the recommended durations in the 2013 PHE guidance (5 vs 7 days respectively).[30]
We are not able to account for the possibility that treatment durations for some patients are influenced by pack sizes, which may include more than the prescriber would like dispensed, or by protocolised durations set in electronic prescribing decisions. The former could result in unintended antibiotic overuse, while the later might be expected to guide prescribers to recommended durations. However both are system factors which could be addressed to help prescribers make more patient-tailored decisions about minimum effective treatment duration.
The evidence base for optimal durations of therapy for respiratory tract infections in primary care is relatively small;[27,28,54] while there is increasing evidence that antibiotic course lengths can safely be reduced for several conditions in primary care,[18,27] clinicians may lack confidence in guidelines around antibiotic treatment duration.[55,56] We were only able to measure prescribed antibiotics and cannot determine how often patients did not take or complete their prescribed course, previously estimated to be between 1 in 10 and 1 in 4 patients.[57,58] Of note, we did not exclude or separately analyse acute cystitis among pregnant women, for whom guidelines recommend 7 rather than 3 days.[31] However, because women are pregnant during a minority of their lifespan, only a small proportion of the total number of cases of acute cystitis occur among pregnant women, thereby limiting the impact on the overall estimates.

Conclusion and implications

While previous work has shown that antibiotic use can potentially be substantially reduced by not prescribing antibiotics when they are unnecessary,[1,11] this study shows that unnecessary exposure to

antibiotics may also be substantially reduced by aligning the course length more with guidelines and best available evidence. Highlighting the magnitude of this issue is only a first step. We need a better understanding of why clinicians have a tendency to prescribe antibiotic courses that are longer than guideline recommendations, especially for respiratory tract infections. Poor guideline adherence may result from several factors, including lack of awareness and/or scepticism of specific guideline recommendations.[55,56] Moreover, the idea that shorter courses increase the risk of antibiotic resistance for common bacterial infections is not evidence based, but may – together with concerns about treatment failure due to undertreatment - make primary care physicians hesitant to prescribe shorter antibiotic courses in line with guidance. Understanding the reasons would enable the development of interventions and/or support tools that could increase adherence to the guidelines and reduce unnecessary exposure to antibiotics.

Overall, substantial reductions in antibiotic exposure can be accomplished by aligning antibiotic prescription durations with guidelines.

Contributors: KBP designed the study, cleaned and analysed the data, and drafted and revised the manuscript. He is the guarantor. SH and MJL contributed to the interpretation of data and revised the draft manuscript. ASW contributed the statistical analysis plan and revised the draft manuscript. CAMM and JVR contributed to the design of the study and revised the draft manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethical approval: 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, 16THIN071-A1 and 16THIN071-A3).

Data sharing: THIN data were analysed under licence and are not available for sharing**.**

Transparency statement: The guarantor (KBP) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Fig 1 Durations of antibiotic prescriptions for various indications. The dark red portions of the bars are observed data, while the light blue portions are imputed data. The dark blue dotted vertical lines represent the durations recommended by 2013 PHE guidance.

Table 1 Antibiotic treatment durations for first-line antibiotics recommended by Public Health England (PHE) guidance during the period 2013-2015.

Indication	**PHE recommendation for antibiotic prescription duration of first-line antibiotics between 2013-2015**
Acute sinusitis	7 days
Acute sore throat	10 days
Acute bronchitis / cough	5 days
Community-acquired pneumonia & CRB65=0	7 days
Community-acquired pneumonia & CRB65=1	7-10 days
Acute exacerbation of COPD	5 days
Acute otitis media	5 days
Acute cystitis non-pregnant females	3 days
Acute cystitis males	7 days
Acute prostatitis	28 days
Pyelonephritis	7 days, except co-amoxiclav which is 14 days
Cellulitis	7 days, and continue for further 7 days if slow response
Impetigo	7 days
Scarlet fever[a]	10 days[a]
Gastroenteritis	5-7 days

[a]Not in 2013 PHE guidance; based on CKS guidance and PHE 2017 guidance.

Table 2 The percentage of antibiotics with a duration exceeding the guideline recommendations for all patients and antibiotics.

	Recommended treatment duration (days)	Antibiotic prescriptions with duration exceeding recommendations, n (%, 95% CI)	Excess days (% of total days)
Acute sinusitis (n=76,683)	7	7,384 (9.6%, 9.4 to 9.9%)	39,422 (7.1)
Acute sore throat (n=239,231)	5[a]	200,520 (83.8%, 83.7 to 84.0%)	640,381 (35.0)
	10[a]	4,972 (2.1%, 2.0 to 2.1%)	72,001 (3.9)
Acute bronchitis / cough (n=386,972)	5	331,257 (85.6%, 85.5 to 85.7%)	805,051 (29.5)
Community-acquired pneumonia (n=952)	7[b]	77 (8.1%, 6.4 to 10.1%)	744 (10.3)
	10[b]	32 (3.4%, 2.3 to 4.9%)	535 (7.4)
Acute COPD exacerbation (n=12,067)	5	10,742 (89.0%, 88.4 to 89.6%)	26,732 (30.8)
Acute otitis media (n=83,054)	5	71,750 (86.4%, 86.1 to 86.6%)	193,262 (31.9)
Acute cystitis females (n=48,734)	3	26,591 (54.6%, 54.1 to 55.0%)	99,321 (40.5)
Acute cystitis males (n=4,276)	7	181 (4.2%, 3.6 to 4.9%)	1541 (5.6)
Acute prostatitis (n=1,838)	28	231 (12.5%, 11.1 to 14.2%)	2,806 (7.3)
Pyelonephritis (n=1,948)	7[c]	351 (18.0%, 16.3 to 19.9%)	2,135 (14.1)
	14[c]	7 (0.3%, 0.1 to 0.9%)	269 (1.8)
Acute cellulitis (n=54,610)	7[d]	7,610 (13.9%, 13.6 to 14.2)	47,063 (11.2)
	14[d]	424 (0.8%, 0.7 to 0.9%)	6,719 (1.6)
Impetigo (n=16,599)	7	1,646 (9.9%, 9.4 to 10.4%)	13,948 (11.8)
Scarlet fever (n=2,350)	5[e]	1,887 (80.3%, 78.5 to 82.0%)	9,808 (45.7)
	10[e]	157 (6.7%, 5.7 to 7.9%)	1,493 (7.0)
Gastroenteritis (n=1,701)	5[f]	906 (53.3%, 50.8 to 55.8%)	3,071 (27.3)
	7[f]	108 (6.3%, 5.2 to 7.7%)	1,260 (11.2)

[a] When antibiotics are indicated, 2013 PHE guidance recommends 10 days when using penicillin V and 5 days when using clarithromycin for sore throat.

[b] 2013 PHE guidance recommends 7 days for patients with a CRB65 score of 0 and 7-10 days in patients with a CRB65 score of 1.

[c] 2013 PHE guidance recommends 7 days when treating pyelonephritis with ciprofloxacin and 14 days when using co-amoxiclav.

[d] For patients with cellulitis, the PHE guidance (2013) recommends starting with 7 days and in case of a slow response continuing for another 7 days. The CKS guidance (last revised in July 2015) recommends a treatment duration of 7 days, except for patients with known lymphoedema for whom antibiotics should be continued ≥14 days beyond first observation of clinical response.

[e] Scarlet fever was not included in the 2013 PHE guidance. 2017 PHE guidance and CKS guidance recommend 10 days of treatment when using penicillin V. The CKS guidance recommends treating children with 10 days of amoxicillin in case penicillin V is not deemed suitable. For other antibiotics (clarithromycin or azithromycin) guidelines recommend a treatment duration of 5 days.

[f] Where patients with gastroenteritis are systemically unwell and campylobacter infection is suspected, a duration of 5-7 days is recommend by 2013 PHE guidance.

Table 3 The percentage of antibiotics with a duration exceeding the guideline recommendations for patients without comorbidities or prior use of immunosuppressive drugs, inhaled corticosteroids or systemic corticosteroids.

	Recommended treatment duration when antibiotics indicated (days)	**Antibiotic prescriptions with duration exceeding recommendations n (%, 95% CI)**
Acute sinusitis (n=51,206)	7	4,701 (9.2%, 8.9 to 9.5%)
Acute sore throat (n=188,708)	5	156,722 (83.1%, 82.9 to 83.2%)
	10	4,114 (2.2%, 2.1 to 2.3%)
Acute bronchitis / cough (n=204,867)	5	175,193 (85.5%, 85.4 to 85.7%)
Community-acquired pneumonia (n=434)	7	30 (6.8%, 4.7% to 9.9%)
	10	11 (2.6%, 1.3% to 4.9%)
Acute COPD exacerbation[a] (n=5,737)	5	5,116 (89.2%, 88.3% to 90.0%)
Acute otitis media (n=69,217)	5	60,170 (86.9%, 86.7 to 87.2%)
Acute cystitis females (n=31,794)	3	17,008 (53.5%, 52.9 to 54.0%)
Acute prostatitis (n=1,240)	28	159 (12.8%, 11.0 to 14.8%)
Pyelonephritis (n=1,347)	7	254 (18.9%, 16.8 to 21.2%)
	14	3.1 (0.2%, 0.06 to 0.9%)
Acute cellulitis (n=26,041)	7	3,217 (12.4%, 12.0 to 12.8%)
	14	206 (0.8%, 0.7 to 0.9%)
Impetigo (n=13,457)	7	1,398 (10.4%, 9.9 to 10.9%)
Scarlet fever (n=2,081)	5	1,673 (80.4%, 78.5 to 82.2%)
	10	142 (6.8%, 5.8 to 8.1%)
Gastroenteritis (n=1,193)	5	628 (52.7%, 49.7 to 55.7%)
	7	78 (6.5%, 5.1 to 8.3%)

[a] Only considered other comorbidities than COPD and ignored corticosteroid use.