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Within-episode repeat antibiotic prescriptions in patients with respiratory tract infections: A population-based cohort study

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SUMMARY

Background: Antimicrobial stewardship interventions mainly focus on initial antibiotic prescriptions, with few considering within-episode repeat prescriptions. We aimed to describe the magnitude, type and determinants of within-episode repeat antibiotic prescriptions in patients presenting to primary care with respiratory tract infections (RTIs).
Methods: We conducted a population-based cohort study among 530 sampled English general practices within the Clinical Practice Research Datalink (CPRD). All individuals with a primary care RTI consultation for which an antibiotic was prescribed between March 2018 and February 2022. Main outcome measurement was repeat antibiotic prescriptions within 28 days of a RTI visit stratified by age (children vs. adults) and RTI type (lower vs. upper RTI). Multivariable logistic regression and principal components analyses were used to identify risk factors and patient clusters at risk for within-episode repeat prescriptions.
Findings: 905,964 RTI episodes with at least one antibiotic prescription were identified. In adults, 19.9% (95% CI 19.3–20.5%) had at least one within-episode repeat prescription for a lower RTI, compared to 10.5% (95% CI 10.3–10.8%) for an upper RTI. In children, this was around 10% irrespective of RTI type. The majority of repeat prescriptions occurred a median of 10 days after the initial prescription and was the same antibiotic class in 48.3% of cases. Frequent RTI related GP visits and prior within-RTI-episode repeat antibiotic prescriptions were main factors associated with repeat prescriptions in both adults and children irrespective of RTI type. Young (<2 years) and older (65+) age were associated with repeat prescriptions. Among those aged 2–64 years, allergic rhinitis, COPD and oral corticosteroids were associated with repeat prescriptions.
Interpretations: Repeat within-episode antibiotic use accounts for a significant proportion of all antibiotics prescribed for RTIs, with same class antibiotics unlikely to confer clinical benefit and is therefore a prime target for future antimicrobial stewardship interventions.

Introduction

Antimicrobial resistance (AMR) poses a global threat to public health. Annual attributable mortality has been estimated at 700,000 deaths worldwide and is predicted to increase to 10 million by 2050 if no action is taken.[1,2] Tackling antibiotic overuse in primary care, where around 72% of all antibiotics are prescribed,[3] is a key strategy for addressing AMR.[4]

Since respiratory tract infections (RTIs) are considered typically viral in origin, current primary care guidelines advocate a no or delayed antibiotic prescribing strategy in the vast majority of patients.[5–8] Despite this, 54% of RTI consultations in UK primary care result in an antibiotic prescription, and RTIs account for 60% of

This study was approved by CPRD's Research Data Governance (RDG) Process (protocol 22_001775).

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antibiotic prescribing in primary care worldwide. As such, RTIs are one of the key drivers of AMR.[9]

Antibiotic stewardship campaigns mainly focus on the initial prescribing decision,[10–12] but rarely involve assessments of treatment duration[13] or within-episode repeat antibiotic prescribing. General practice observations suggest that a substantial number of patients who initially received antibiotics for RTIs are inclined to reconsult their general practitioner (GP) and receive a repeat prescription because of persisting symptoms, particularly for lower RTIs which typically last up to 28 days.[14,15] Data on repeat within-episode antibiotic prescriptions are however lacking.

Increased knowledge about repeat within-RTI episode antibiotic prescribing and factors associated with such routine could inform intervention development aimed at reducing this practice. We therefore aimed to (1) assess within-RTI episode repeat antibiotic prescription proportions, (2) describe the type and timing of repeat within-episode antibiotic prescriptions, and (3) to identify risk factors and patient clusters associated with within-RTI episode repeat antibiotic prescriptions among both children and adults.

Methods

Setting and design

A retrospective study within the Clinical Practice Research Datalink (CPRD) Aurum was conducted. CPRD Aurum covers data from 1483 general practices in UK. The current study included a sample of 530 general practices ensuring a sample size not exceeding normal data limits (i.e. > 1 million patients). Geographical area distribution of general practices was similar between the sampled and full CPRD Aurum set (Appendix 3).

Using methods successfully applied previously, all individuals with a CPRD SNOMED concept code for either RTI diagnosis or symptoms suggestive of RTI (Appendix 1)[16] between March 2018 and January 2022 were potentially eligible for inclusion in this study. Only those who received at least one RTI-related antibiotic prescription within one day before or during the RTI episode were included. Relevant antibiotic classes were based on NICE guidelines' and British National Formulary's main indications and included oral penicillins, macrolides, doxycycline, and tetracycline (Appendix 2A).[6–8] In addition, oral quinolones, co-trimoxazole and cephalosporins (Appendix 2B) were considered relevant when accompanied by a recorded history of chronic obstructive pulmonary disease (COPD) or bronchiectasis.

Outcomes

The primary outcome was the proportion of episodes in which within-RTI-episode repeat antibiotic prescriptions were issued. For this purpose, we first defined the period of an RTI episode as starting on the date of first RTI diagnosis (Appendix 4). The RTI episode was extended if another RTI consult occurred within 28 days, regardless of whether an antibiotic was re-prescribed. The episode was defined as ending 28 days after the last RTI consultation. For the outcome of interest, we looked at one or more additional antibiotic prescriptions at least one day after the initial antibiotic prescription at any time during the RTI episode. In sensitivity analyses, this maximum time between two consultations within an episode was defined as 14 and 21 days respectively. The primary outcome was pre-stratified by time (pre-pandemic defined as 1 March 2018 to 31 January 2020; and pandemic period as 1 March 2020 to 31 January 2022)[17]; age (< 18 years vs 18+ years), and type of RTI (lower or upper RTI).[16] Only in the absence of statistical interaction ($p > 0.05$), rates and risk factors were lumped.

Secondary outcomes included: (1) the type and timing of repeat within-episode antibiotic prescriptions, (2) the total number of repeat antibiotic prescriptions within the same RTI episode, (3) the corresponding cumulative expected duration of antibiotic use within RTI episodes, and (4) risk factors and patient clusters associated with repeat within-episode prescriptions.

Risk factors

Candidate risk factors for repeat within-episode prescriptions were based on the available literature, biological plausibility, and expert opinion. These included: age (< 2 years, 2–9 years, 10–17 years, 18–49 years, 50–64 years, 65+ years), gender, body mass index (< 20 kg/m^2, 20–24.9 kg/m^2, 25–29.9 kg/m^2, 30–34.9 kg/m^2, 35+ kg/m^2), smoking status (current, former, none, unknown), alcohol use (current, not now, unknown), ethnicity, index of multiple deprivation (IMD in quintiles), calendar time (1 March 2018 to 31 January 2020 versus 1 March 2020 to 31 January 2022), season (autumn, winter, spring versus summer), presence and number of RTIs in the preceding five years (A: without antibiotic use, B: with single antibiotic prescriptions, C: with within-episode repeat antibiotic prescriptions), annual number of GP consultations over the five previous years (for any reason), co-medication within the previous 12 months (systemic immunosuppressive agents, non-steroidal anti-inflammatory drugs, inhaled short/long acting beta agonists, antimuscarinic agents and corticosteroids), signs of active allergic rhinitis in the past 12 months (SNOMED concept code for allergic rhinitis or a GP prescription for oral antihistamines or cromoglicic acid), a history of comorbidities (COPD, asthma, pneumonia, acute myocardial infarction, stroke, congestive heart failure and diabetes mellitus), GP area (English region),[22] and presence of COVID-19-diagnosis within 7 days of the RTI diagnosis.[18]

Statistical analysis

A random effect for GP was used, as was done in previous studies to allow for repeated observations on physicians over years.[16] The proportion of RTI episodes in which within-episode repeat antibiotic prescriptions occurred was expressed as a percentage. The number of repeat antibiotic prescriptions, as well as the expected cumulative antibiotic duration (expressed as number of exposed days and cumulative daily defined dosage [DDD] exposure) within the same RTI episode were calculated for each individual, and expressed as medians for the entire study population.

For the predictor analyses, only first RTI episodes for each patient were included and results were stratified by type of RTI (lower versus upper) and age (adults versus children); i.e., each patient could only contribute once to this analysis. Using multivariable logistic regression, adjusted odds ratios (aORs) with accompanying 95% confidence intervals for risk factors across strata were calculated.

Funnel plots were constructed to visualise repeat prescription variability among individual GPs (confidence intervals for three-fold of the standard deviation),[19] and principal components analyses were used to identify patient clusters associated with having repeat antibiotic prescriptions. For this purpose, we included all potential risk factors and evaluated eigenvalues of its correlation matrix among individuals with a within-episode repeat antibiotic prescription. We then only selected components with an eigenvalue of at least 1.0 and clustered all individuals based on these components. For each individual, the predicted repeat prescription rate was calculated based on all available risk factors, and were visualised using jittered plots.

All analyses were done using SAS version 9.4 (PROC LOGISTIC, PROC IML and PROC FACTOR procedures). This study was approved by CPRD's Research Data Governance (RDG) Process (protocol 22_001775).

Table 1
Baseline characteristics of patients with a RTI primary care consultation and who were prescribed an antibiotic.

	Adults				Children			
	Lower RTI		Upper RTI		Lower RTI		Upper RTI	
	N = 217,788	(%)	N = 440,621	(%)	N = 25,114	(%)	N = 222,441	(%)
Age, years (median, SD)	62.0	(20.0)	37.0	(17.7)	3.5	(4.9)	5.6	(5.1)
Females	130,265	(59.8)	302,989	(68.8)	11,663	(46.4)	114,946	(51.7)
BMI, kg/m^2 (median, SD)	27.4	(6.8)	26.2	(6.8)	17.0	(7.5)	17.3	(8.0)
Smoking status								
Current	53,713	(24.7)	96,355	(21.9)	496	(2.0)	4355	(2.0)
Former	67,007	(30.8)	89,065	(20.2)	61	(0.2)	641	(0.3)
No	91,758	(42.1)	233,733	(53.0)	4816	(19.2)	41,328	(18.6)
Unknown	5310	(2.4)	21,468	(4.9)	19,741	(78.6)	176,117	(79.2)
Alcohol use								
Current	166,432	(76.4)	298,240	(67.7)	1039	(4.1)	10,232	(4.6)
No/former	22,361	(10.3)	37,795	(8.6)	350	(1.4)	3213	(1.4)
Unknown	28,995	(13.3)	104,586	(23.7)	23,725	(94.5)	208,996	(94.0)
No. of GP visits per year (median, SD)	12.8	(11.3)	9.5	(10.2)	8.3	(9.1)	6.4	(8.3)
Index of multiple deprivation								
Least deprived	41,289	(19.0)	88,861	(20.2)	4332	(17.2)	44,649	(20.1)
2	37,175	(17.1)	75,347	(17.1)	4338	(17.3)	37,958	(17.1)
3	38,226	(17.6)	79,889	(18.1)	4140	(16.5)	38,551	(17.3)
4	42,828	(19.7)	89,252	(20.3)	4565	(18.2)	43,786	(19.7)
Most deprived	41,880	(19.2)	68,546	(15.6)	5388	(21.5)	40,039	(18.0)
Prescribed antibiotic for index RTI episode								
Penicillins	142,967	(65.6)	337,722	(76.6)	22,684	(90.3)	200,349	(90.1)
Tetracyclines	48,698	(22.4)	48,033	(10.9)	149	(0.6)	775	(0.3)
Macrolides	25,071	(11.5)	54,547	(12.4)	2277	(9.1)	21,316	(9.6)
Other	1052	(0.5)	319	(0.1)	4	(0.0)	1	(0.0)
History of previous RTIs[a]								
No	95,979	(44.1)	303,068	(68.8)	11,694	(46.6)	86,733	(39.0)
Yes, without antibiotics	67,031	(30.8)	137,553	(31.2)	10,942	(43.6)	107,820	(48.5)
Yes + single antibiotic prescription	87,513	(40.2)	168,179	(38.2)	8366	(33.3)	89,847	(40.4)
Yes + repeat antibiotic prescriptions	34,153	(15.7)	46,876	(10.6)	2651	(10.6)	26,325	(11.8)
History of comorbidities (ever before, unless stated otherwise)								
Allergic rhinitis (last year)	28,652	(13.2)	50,886	(11.5)	3727	(14.8)	27,754	(12.5)
COVID-19 infection (last week)	3013	(1.4)	4246	(1.0)	123	(0.5)	858	(0.4)
COPD	41,441	(19.0)	23,023	(5.2)	520	(2.1)	2093	(0.9)
Asthma	65,270	(30.0)	97,815	(22.2)	3033	(12.1)	18,467	(8.3)
Pneumonia	25,736	(11.8)	14,911	(3.4)	750	(3.0)	2792	(1.3)
Acute myocardial infarction	10,387	(4.8)	4378	(1.0)	0	(0.0)	0	(0.0)
Stroke	15,079	(6.9)	6863	(1.6)	46	(0.2)	137	(0.1)
Heart failure	13,933	(6.4)	4759	(1.1)	33	(0.1)	100	(0.0)
Diabetes mellitus	43,821	(20.1)	41,741	(9.5)	312	(1.2)	2729	(1.2)
Drug use in previous year								
Systemic immunosuppressants	11,280	(5.2)	10,622	(2.4)	85	(0.3)	714	(0.3)
Systemic corticosteroids	61,705	(28.3)	38,487	(8.7)	3054	(12.2)	11,515	(5.2)
NSAIDs	27,926	(12.8)	60,240	(13.7)	1421	(5.7)	14,970	(6.7)
Inhaled beta-2 agonists	88,432	(40.6)	77,775	(17.7)	8348	(33.2)	34,619	(15.6)
Inhaled anticholinergics	59,246	(27.2)	54,368	(12.3)	3293	(13.1)	14,799	(6.7)
Inhaled corticosteroids	25,192	(11.6)	9565	(2.2)	492	(2.0)	1378	(0.6)

[a] Categories are not mutually exclusive, as an individual may have had multiple previous RTIs with (single/repeat) or without antibiotics and could therefore contribute to multiple categories.

Results

After exclusion of 298,775 RTI episodes (24.8%) with codes of low specificity (i.e., not specific enough to differentiate between lower and upper RTI), a total of 905,964 lower or upper RTI episodes with at least one antibiotic prescription were identified (Table 1). Almost half of all RTI episodes concerned adults consulting their GP for upper RTI (48.6%) and – in general – the main class of initial antibiotic prescription was an oral penicillin (66–90%). Among adults, individuals with lower RTI were older (median age 62 years) and more likely to have a history of comorbidities such as COPD, asthma and pneumonia, compared to those with upper RTI (median age 37 years). In children, 89.9% of episodes were related to upper RTI.

Within-episode antibiotic repeat prescription rates, stratified by age and RTI type, as well as rates per GP are illustrated in Fig. 1. The overall proportion of within-episode repeat prescriptions was 12.7% (95% CI 12.5–12.9%), but with considerable variability between individual GPs. Among adults, within-episode repeat rates were higher for lower RTI (19.9%, 95% CI 19.3–20.5%) than for upper RTI (10.5%, 95% CI 10.3–10.8%). In children, rates were similar for lower RTI (10.5%, 95% CI 9.4–11.5%) and upper RTI (10.0%, 95% CI 9.7–10.4%). Pre- and intra-pandemic within-episode prescription proportions did not change in most groups, except for upper RTIs in adults, which increased during the pandemic.

The majority of within-episode repeat events occurred more than 7 days after the initial antibiotic prescription (median time between first and second antibiotic prescription: 10 days, standard deviation 8.6 days), and in 48.3% the same antibiotic class was issued (Fig. 2 and Appendix 5). The majority of repeat prescriptions concerned a single repeat prescription, with 10% of those repeat cases having had at least two repeats within the same RTI episode. Results were similar in sensitivity analyses, in which we changed the RTI-related GP consultation free interval from 28 to 21 or 14.

Risk factors for within-episode repeat antibiotic prescriptions are presented in Fig. 3A (adults) and B (children). Consultation behaviour and prior within-RTI-episode repeat antibiotic prescriptions were main factors associated with within-episode repeat antibiotic prescriptions, in both adults and children. More frequent GP visits

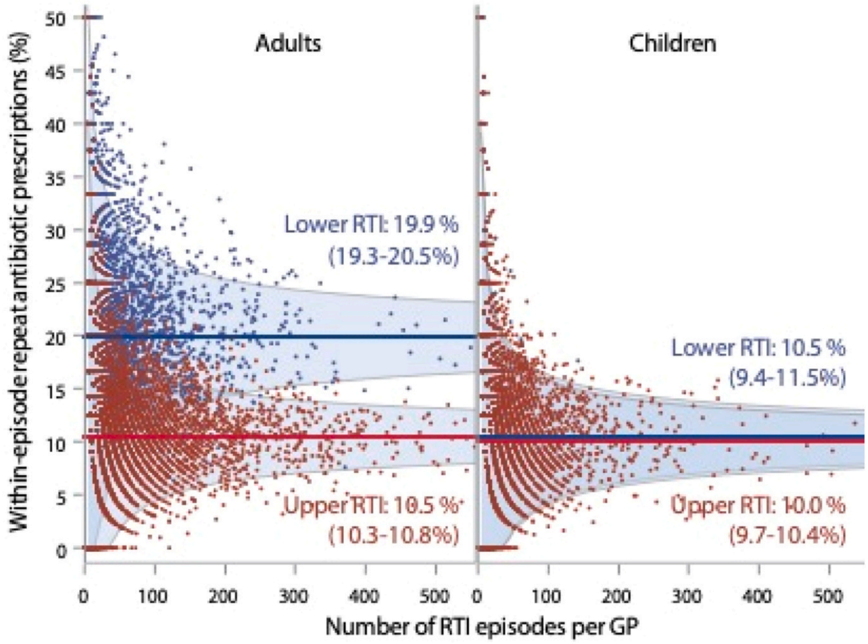


Fig. 1. Proportion of within-episode repeat antibiotic prescriptions per GP practice, stratified by type of RTI and age. Confidence band represents three standard deviations. The median number of RTIs per GP were among adults 15 for lower RTI and 30 for upper RTI, and in children were 3 and 17 for lower and upper RTI respectively.

were associated with a 47% (95% CI 38–57%) and 46% (95% CI 38–55%) increased risk in adults among lower and upper RTI episodes, respectively. These figures were 39% (95% CI 2–88%) and 54% (95% CI 38–71%) in children. Prior within-episode repeat antibiotic prescriptions resulted in a 57% (lower RTI) and 63% (upper RTI) increased risk in adults, and 55% and 64% respectively in children. Older age (65+) and young age (< 2 years) were associated with increased risk for within-episode repeat antibiotic prescriptions, but the latter was only statistically significant. Other risk factors in adults included allergic rhinitis, COPD, pneumonia, and recent systemic corticosteroids or inhaled anticholinergics use. Pandemic periods did not substantially change the direction of risk factors and were therefore not presented separately. Interestingly, among adults with a lower RTI, current smokers had a 10% lower risk of within-episode repeat antibiotic prescriptions (95% CI 6–13%), but this can only be considered as a hypothesis generating observation at best as we did not have an a priori hypothesis for a potential protective effect.

Principal components analyses suggested four patient clusters in which repeat prescriptions were more common, as shown in Fig. 4. Repeat prescriptions were most common in young individuals (< 2 years) with frequent GP visits and prior within-episode repeat prescriptions (32.9%, 95% CI 28.4–37.0%), followed by those aged 65+ years (30.9%, 95% CI 30.1–31.8%). Among those aged 2–64 years, individuals with both COPD and oral corticosteroid use yielded the highest risk (28.3%, 95% CI 27.5–29.1%), followed by those with allergic rhinitis and oral corticosteroid use (21.0%, 95% CI 20.4–21.7%).

Discussion

Summary of main results

In this large population-based cohort study of almost a million RTI episodes, we found an overall proportion of 10% for within-episode repeat antibiotic prescriptions across all types of RTIs among both adults and children. Nearly half of all within-episode prescriptions was the same antibiotic class. Increased prior GP consultations within-episode repeat prescriptions were main factors associated with within-episode repeat antibiotics, and increased proportions were most pronounced among older individuals (65+ years) and young children (< 2 years).

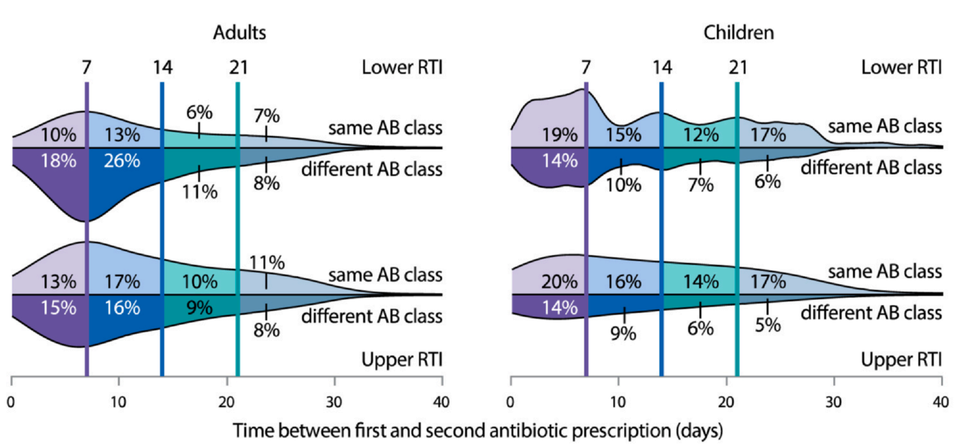


Fig. 2. Timing and type of within-episode repeat antibiotic prescriptions. Vertical lines represent 7, 14 and 21 days after the initial antibiotic prescription.

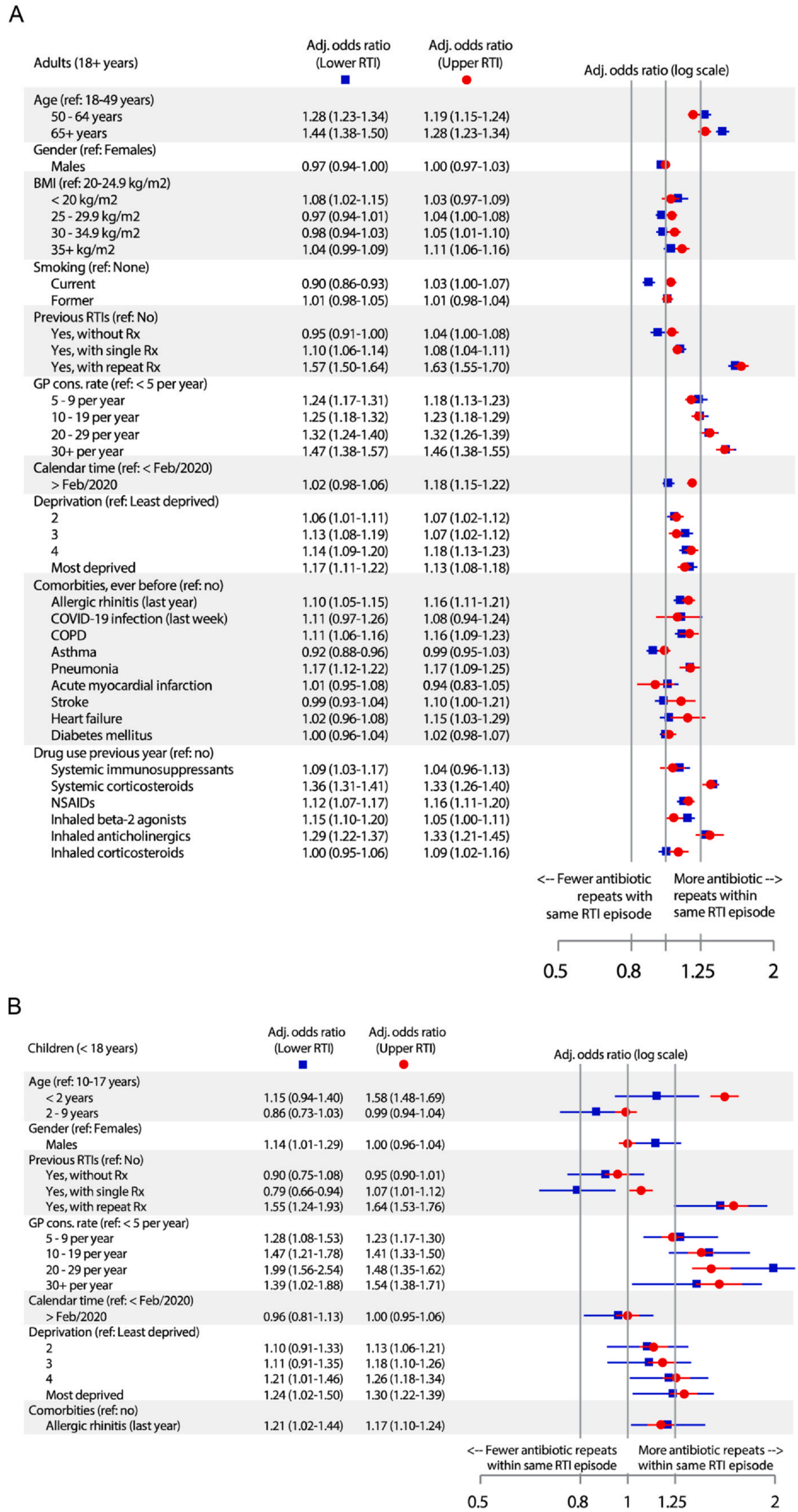


Fig. 3. A. Multivariate analysis of determinants for within-episode repeat antibiotic prescriptions in adults. B. Multivariate analysis of determinants for within-episode repeat antibiotic prescriptions in children.

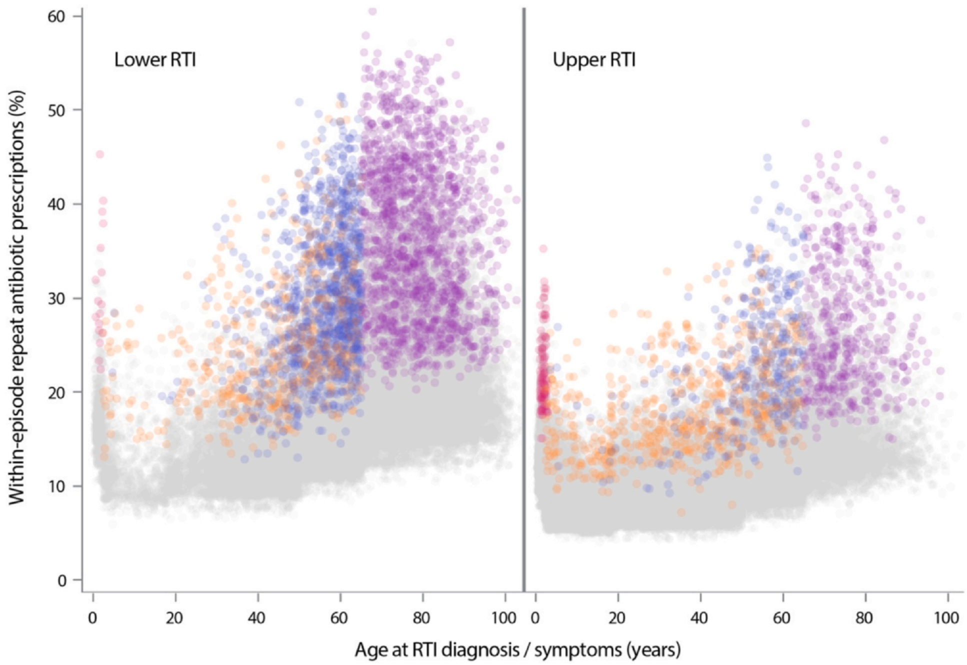


Fig. 4. Principal component analysis suggested patient clusters in relation to age and predicted within-episode repeat antibiotic prescription proportions. ● All individuals. ● < 2 years + frequent GP consults + prior within-episode antibiotic repeats. ● 2–64 years + allergic rhinitis + oral corticosteroids. ● 2–64 years + COPD + oral corticosteroids. ● 65+ years + frequent GP consults + prior within-episode antibiotic repeats.

Comparison with existing literature

To the best of our knowledge, this is the first study that assessed repeat antibiotic prescriptions within the same RTI episode. Prior studies have not distinguished between repeat antibiotics for the same RTI episode or a repeat prescription issued for a new consecutive episode. For example, a large British study assessed repeat antibiotic prescriptions within a time frame of three years and found that 57% had at least three prior antibiotic prescriptions during that period.[20] The study found no protective effect of frequent antibiotic use on the risk of infection-related hospital admissions, and authors therefore recommended reducing the practice of repeated, intermittent antibiotic use. A second British study used a different approach and assessed the prescription sequence variable available in CPRD (i.e., whether the prescription was part of a repeat schedule in the prescribing system) to estimate the proportion of repeat antibiotics.[16] In their analyses, repeat prescriptions only accounted for 1% of all antibiotics related to respiratory tract conditions. This may imply that the prescription sequence variable underestimates the antimicrobial burden, as we found that within-RTI-episode antibiotic prescriptions occurred in 13% of all RTI episodes in which an antibiotic was prescribed. Another population-based study analysed antibiotic prescriptions (for any underlying condition) in 1997 among a selected set of Danish children aged 0–5 years and found rates of repeat prescriptions of around 10% within 10 days of the initial course.[21]

Strengths and weaknesses

We included data of 530 English practices, covering 8% of the English population. CPRD Aurum has previously been demonstrated to be representative in terms of geographical spread, deprivation, age and gender,[22] and the high quality of antibiotic recordings was shown to be similar to CPRD GOLD.[23] Our results include both pre- and intra-pandemic periods, with prescriptions appearing to be stable in most groups, except for upper RTIs in adults, which increased during the pandemic, possibly as a result of changes in the use of diagnostic coding when most consultations were conducted remotely.

Despite the large sample size and completeness of data,[24] we can, however, not exclude the possibility of missed antibiotic prescriptions. For example, out-of-hours prescriptions are not well captured, hence, our results might have underestimated the true magnitude of within-episode repeat prescriptions. The same is true for antibiotic prescriptions that may have occurred in the hospital shortly after the initial GP diagnosis. The impact of the latter is however expected to be negligible since this only represent a small proportion of all RTI episodes.

Furthermore, we had no access to data on illness severity and causative pathogens. This would have helped us determine in whom re-prescribing (with the same or a different antibiotic) would have been appropriate. Indeed, some pathogens (including those associated with Brucellosis and Typhoid Fever) have been demonstrated to have a long incubation time with a severely delayed clearance rate and may sometimes be present as a lifelong infection.[25] In addition, chronic antimicrobial prophylaxis may be indicated in some conditions, such as COPD, recurrent cellulitis and urinary tract infections.[26] This effect seems to be negligible however, as the results from our sensitivity analysis were similar when we stratified repeat proportions by – for example – underlying COPD.

In addition, our RTI episode definition has not been validated. We assumed that re-consulting with RTI related symptoms within 28 days is likely to be related to the same RTI event, as normal course suggests an RTI duration of up to 28 days. Our sensitivity analysis, in which we tightened this gap to 14 or 21 days, showed very similar results, suggesting that the majority of re-consulting occurred relatively fast and our definition did not tend to falsely capture new RTI episodes.

We did not look at follow-up antibiotic prescribing behaviour after initial RTI visits at which an antibiotic was not prescribed. It may be speculated that risk factors might behave differently among these RTI episodes and our results may not be extrapolated to those cases.

Although our population-based design likely minimised the risk of selection bias, studies using routinely collected data can only estimate burden if coding is complete. A recent study investigating the appropriateness of antibiotic prescriptions in UK primary care found that 37% of antibiotics prescribed were not linked to a diagnostic code.[27,28] By thoroughly including codes for both RTI diagnosis, as well as symptoms suggestive of RTIs we have done all we could to minimise this phenomenon. The observed number of RTI episodes with an antibiotic prescription closely resembles earlier work,[11,23] but cannot rule out underestimation of the true burden of repeat antibiotic prescriptions. The impact is likely to be relatively low as we did not try to estimate the burden of RTI incidence itself, but rather looked at (repeat) antibiotic prescriptions among already recorded RTI episodes. Although we cannot entirely rule out selection bias (selecting unusual RTI episodes by exclusion of around 25% of all RTI episodes where we could not distinguish between upper and lower RTIs and lack of coding in current practice), this is not suggested by the number of visits, patients, physicians and practices, as well as the most frequently RTI codes represented in the data (see Appendix 6).

Finally, we used data on antibiotic prescriptions rather than dispensing. In some cases, prescribers may have opted for a delayed or deferred antibiotic prescribing strategy,[29] in which case, our results will overestimate antibiotic consumption. However, delayed prescribing is not frequently practised[30] and are more likely to have played a role in the decision for the initial antibiotic prescription, rather than the within-episode repeat.

Implications

Our finding of excessive within-episode repeat antibiotic use has two important clinical implications. First, where antibiotics are prescribed, clinicians should emphasise that a single treatment course is likely to be microbiologically adequate.[5–8] Clinicians should remind patients that the natural history of many RTIs is considerably longer than most antibiotic treatment courses, and that in the absence of deterioration, persisting symptoms are unlikely to require a treatment extension. This is closely in line with the “Shorter is Better” movement advocated by several authors, even for bacterial infections.[31–33] Second, future antimicrobial stewardship interventions should target within-episode repeat antibiotic use, particularly in adults with lower RTI.

Conclusions

Repeat within-episode antibiotic use accounts for a significant proportion of all antibiotics prescribed for RTIs, with same class antibiotics unlikely to confer clinical benefit and is therefore a prime target for future antimicrobial stewardship interventions.

Declaration of Competing Interest

No conflicts of interest to declare.

Appendix 1. SNOMED concept codes for diagnoses or symptoms suggestive of RTI

Term	Snomed_ConceptId	Type
Acute bronchitis	10509002	Lower
Acute membranous bronchitis	10509002	Lower
Acute bronchitis NOS	10509002	Lower
Acute bronchitis or bronchiolitis NOS	10509002	Lower
Acute bronchitis/bronchiolitis	10509002	Lower
Tracheobronchitis	13617004	Lower
Acute bronchiolitis with bronchospasm	15199004	Lower
Acute bronchitis and bronchiolitis	195712009	Lower
Acute bronchitis and/or bronchiolitis	195712009	Lower
Acute fibrinous bronchitis	195714005	Lower
Acute pseudomembranous bronchitis	195714005	Lower
Acute croupous bronchitis	195714005	Lower
Acute purulent bronchitis	195717003	Lower
Acute pneumococcal bronchitis	195719000	Lower
Acute streptococcal bronchitis	195720006	Lower
Acute haemophilus influenzae bronchitis	195721005	Lower
Acute Neisseria catarrhalis bronchitis	195722003	Lower
Acute Moraxella catarrhalis bronchitis	195722003	Lower
Acute bronchitis due to coxsackievirus	195725001	Lower
Acute bronchitis due to parainfluenza virus	195726000	Lower
Acute parainfluenza virus bronchitis	195726000	Lower
Acute bronchitis due to respiratory syncytial virus	195727009	Lower
Acute respiratory syncytial virus bronchitis	195727009	Lower
Acute bronchitis due to rhinovirus	195728004	Lower
Acute bronchitis due to echovirus	195729007	Lower
Acute exudative bronchiolitis	195737004	Lower
Acute bronchiolitis due to respiratory syncytial virus	195739001	Lower
Acute bacterial bronchitis	233598009	Lower
Acute bronchitis due to mycoplasma pneumoniae	233599001	Lower
Acute mycoplasmal bronchitis	233599001	Lower
Acute viral bronchitis	233601004	Lower
Acute bronchiolitis due to other specified organisms	233602006	Lower
Acute viral bronchiolitis	233602006	Lower
Acute wheezy bronchitis	275499005	Lower
Acute infective bronchitis	312371005	Lower
Bronchitis NOS	32398004	Lower
Chest infection - unspecified bronchitis	32398004	Lower
Bronchitis	32398004	Lower
Acute tracheobronchitis	35301006	Lower
Subacute bronchitis	36426008	Lower
Lower respiratory tract infection	50417007	Lower

Lower resp tract infection	50417007	Lower
Lower respiratory infection	50417007	Lower
LRTI - Lower respiratory tract infection	50417007	Lower
Acute bronchiolitis	5505005	Lower
Acute bronchiolitis NOS	5505005	Lower
[X]Acute bronchiolitis due to other specified organisms	5505005	Lower
Acute capillary bronchiolitis	5505005	Lower
Acute obliterating bronchiolitis	59903001	Lower
Laryngotracheobronchitis	85915003	Lower
LTB - Laryngotracheobronchitis	85915003	Lower
Ear infection	129127001	Upper
Infection of ear	129127001	Upper
Postmeasles otitis media	13420004	Upper
Post measles otitis media	13420004	Upper
Acute suppurative otitis media - tympanic membrane intact	14948001	Upper
Acute suppurative otitis media without spontaneous rupture of ear drum	14948001	Upper
Acute sinusitis	15805002	Upper
Other acute sinusitis	15805002	Upper
Other acute sinusitis NOS	15805002	Upper
Acute sinusitis NOS	15805002	Upper
[X]Other acute sinusitis	15805002	Upper
Acute inflammation of sinus	15805002	Upper
Acute infection of sinus	15805002	Upper
Earache symptom	162356005	Upper
Earache symptoms	162356005	Upper
Unilateral earache	162358006	Upper
Bilateral earache	162359003	Upper
Has a sore throat	162388002	Upper
Throat pain	162397003	Upper
Pain in throat	162397003	Upper
[D]Throat pain	162397003	Upper
Throat discomfort	162397003	Upper
Throat soreness	162397003	Upper
Sore throat	162397003	Upper
Pain in the pharynx	162397003	Upper
Pharyngeal pain	162397003	Upper
O/E - follicular tonsillitis	164256007	Upper
O/E - granular pharyngitis	164260005	Upper
Acute tonsillitis	17741008	Upper
Acute tonsillitis NOS	17741008	Upper
[X]Acute tonsillitis due to other specified organisms	17741008	Upper
Throat infection - tonsillitis	17741008	Upper
Mild Tonsillitis	17741008	Upper
Streptococcal sore throat with scarlatina NOS	186357007	Upper
Streptococcal sore throat with scarlatina	186357007	Upper
Vincent's angina	186963008	Upper
Vincent's pharyngitis	186963008	Upper
Vincent's angina - pharyngitis	186963008	Upper
Non-suppurative otitis media with eustachian tube disorders	194237006	Upper
Acute non-suppurative otitis media - serous	194240006	Upper
Acute serous otitis media	194240006	Upper
Acute suppurative otitis media	194281003	Upper
Acute suppurative otitis media NOS	194281003	Upper
ASOM - Acute suppurative otitis media	194281003	Upper
Acute suppurative otitis media due to disease EC	194282005	Upper
Bilateral suppurative otitis media	194286008	Upper
Recurrent acute otitis media	194287004	Upper
Acute left otitis media	194288009	Upper
Acute right otitis media	194289001	Upper
Acute bilateral otitis media	194290005	Upper
Acute myringitis without otitis media	194311006	Upper
Unspecified acute tympanitis	194311006	Upper
Acute gangrenous pharyngitis	195655000	Upper
Acute phlegmonous pharyngitis	195656004	Upper
Acute ulcerative pharyngitis	195657008	Upper
Acute bacterial pharyngitis	195658003	Upper
Acute bacterial pharyngitis NOS	195658003	Upper
Acute pneumococcal pharyngitis	195659006	Upper
Acute staphylococcal pharyngitis	195660001	Upper
Acute viral pharyngitis	195662009	Upper
Viral sore throat NOS	195662009	Upper
Acute erythematous tonsillitis	195666007	Upper
Acute follicular tonsillitis	195667003	Upper
Acute ulcerative tonsillitis	195668008	Upper
Acute catarrhal tonsillitis	195669000	Upper
Acute exudative tonsillitis	195669000	Upper
Acute gangrenous tonsillitis	195670004	Upper
Acute bacterial tonsillitis	195671000	Upper
Acute bacterial tonsillitis NOS	195671000	Upper
Acute pneumococcal tonsillitis	195672007	Upper

Acute staphylococcal tonsillitis	195673002	Upper
Acute viral tonsillitis	195676005	Upper
Recurrent acute tonsillitis	195677001	Upper
RAT - Recurrent acute tonsillitis	195677001	Upper
Acute oedematous laryngitis	195680000	Upper
Acute ulcerative laryngitis	195681001	Upper
Acute catarrhal laryngitis	195682008	Upper
Acute phlegmonous laryngitis	195683003	Upper
Acute haemophilus influenzae laryngitis	195684009	Upper
Acute suppurative laryngitis	195686006	Upper
Tracheopharyngitis	195707008	Upper
Pharyngotracheitis	195707008	Upper
Tracheopharyngitis	195707008	Upper
Recurrent upper respiratory tract infection	195708003	Upper
Pharyngolaryngitis	195709006	Upper
Pharyngitis keratosa	195779005	Upper
Recurrent sinusitis	195788001	Upper
Pansinusitis	195790000	Upper
Lingular tonsillitis	195804009	Upper
Influenza with laryngitis	195923003	Upper
Influenza with pharyngitis	195924009	Upper
Acute epiglottitis with obstruction	222008	Upper
Vincent's tonsillitis	232417005	Upper
Vincent's laryngitis	232427004	Upper
Simple chronic pharyngitis	2365002	Upper
Granular pharyngitis	2365002	Upper
Chronic granular pharyngitis	2365002	Upper
Fusobacterial necrotising tonsillitis	240444009	Upper
Lemierre's syndrome	240444009	Upper
Gangosa - tertiary yaws	24078009	Upper
Rhinopharyngitis mutilans	24078009	Upper
Acute epiglottitis (non-streptococcal)	266337001	Upper
Acute tracheitis	26650005	Upper
Acute tracheitis NOS	26650005	Upper
Sore throat symptom NOS	267102003	Upper
Sore throat symptom	267102003	Upper
Acute otitis media with effusion	270490007	Upper
Non-suppurative otitis media	275481002	Upper
Nonsuppurative otitis media NOS	275481002	Upper
Sore throat - chronic	275488008	Upper
Persistent sore throat	275488008	Upper
Acute laryngitis and/or tracheitis	276443001	Upper
Acute laryngitis and tracheitis	276443001	Upper
Acute laryngitis/tracheitis	276443001	Upper
Viral upper respiratory tract infection	281794004	Upper
URTI - Viral upper respiratory tract infection	281794004	Upper
Catarrhal otitis media	29350000	Upper
Acute epiglottitis	29608009	Upper
Acute myringitis	297009	Upper
Viral ear infection	312137007	Upper
Acute secretory otitis media	359609001	Upper
[X]Other acute nonsuppurative otitis media	359609001	Upper
Acute non-suppurative otitis media	359609001	Upper
Acute nonsuppurative otitis media NOS	359609001	Upper
Acute nonsupp. otitis media	359609001	Upper
Acute nonsuppurative otitis media	359609001	Upper
[X]Acute pharyngitis due to other specified organisms	363746003	Upper
Acute pharyngitis	363746003	Upper
Acute pharyngitis NOS	363746003	Upper
Pharyngitis	363746003	Upper
Sinusitis	36971009	Upper
Acute laryngotracheitis without obstruction	37948003	Upper
Chronic purulent otitis media	38394007	Upper
Chronic suppurative otitis media	38394007	Upper
[X]Other chronic suppurative otitis media	38394007	Upper
Chronic otitis media with effusion, purulent	38394007	Upper
Chronic secretory otitis media, purulent	38394007	Upper
CSOM - Chronic suppurative otitis media	38394007	Upper
Otitis media with effusion - purulent	38394007	Upper
Chronic otitis media with perforation	38394007	Upper
Purulent otitis media NOS	39288006	Upper
Purulent otitis media	39288006	Upper
Suppurative otitis media	39288006	Upper
Throat infection - pharyngitis	405737000	Upper
Pharyngitis	405737000	Upper
Irritation of the throat	405737000	Upper
Acute laryngitis with obstruction	408669002	Upper
Streptococcal tonsillitis	41582007	Upper
Acute rhinosinusitis	431231008	Upper
Streptococcal sore throat	43878008	Upper

Streptococcal pharyngitis	43878008	Upper
Streptococcal sore throat NOS	43878008	Upper
Septic sore throat	43878008	Upper
Strep throat	43878008	Upper
Viral laryngitis	441551009	Upper
Inflammation of larynx due to virus	441551009	Upper
Aero-otitis media	49252004	Upper
Barotrauma, otitic	49252004	Upper
Aero-otitis media	49252004	Upper
Acute epiglottitis without obstruction	49908003	Upper
Acute pansinusitis	5028002	Upper
Acute non-suppurative otitis media - mucoid	52353000	Upper
Acute mucoid otitis media	52353000	Upper
Other upper respiratory infections of multiple sites	54150009	Upper
Upper respiratory infection NOS	54150009	Upper
Upper respiratory infection	54150009	Upper
URTI - Infection of the upper respiratory tract	54150009	Upper
Upper respiratory tract infection	54150009	Upper
URI - Upper respiratory infection	54150009	Upper
Other acute upper respiratory infections	54398005	Upper
[X]Acute upper respiratory infections	54398005	Upper
Acute upper respiratory infection	54398005	Upper
AURTI - Acute upper respiratory tract infection	54398005	Upper
Acute upper respiratory tract infection	54398005	Upper
Laryngotracheitis	55130001	Upper
Acute laryngopharyngitis	55355000	Upper
Acute laryngotracheitis with obstruction	59967003	Upper
Atrophic pharyngitis	63866002	Upper
Acute tracheitis without obstruction	64369009	Upper
Acute laryngotracheitis	64375000	Upper
Acute laryngotracheitis NOS	64375000	Upper
Acute laryngitis/tracheitis	64375000	Upper
Rhinorrhoea	64531003	Upper
Nasal catarrh - acute	64531003	Upper
Nasal discharge	64531003	Upper
Rhinorrhea	64531003	Upper
Discharge from nose	64531003	Upper
[X]Otitis media in other diseases classified elsewhere	65363002	Upper
Otitis media	65363002	Upper
OM - Otitis media	65363002	Upper
Acute laryngitis	6655004	Upper
Acute laryngitis NOS	6655004	Upper
Acute ethmoidal sinusitis	67832005	Upper
Acute maxillary sinusitis	68272006	Upper
Acute antritis	68272006	Upper
Viral epiglottitis	70976000	Upper
Croup	71186008	Upper
Acute sanguinous otitis media	77478005	Upper
Acute sanguinous otitis media	77478005	Upper
Acute non-suppurative otitis media with haemotympanum	77478005	Upper
Acute non-suppurative otitis media - sanguinous	77478005	Upper
Acute non-suppurative otitis media - bloody	77478005	Upper
Acute sphenoidal sinusitis	77919000	Upper
Acute upper respiratory infection of multiple sites	78337007	Upper
Frontal sinusitis	78737005	Upper
Chronic mucoid otitis media	78868004	Upper
Glue ear	78868004	Upper
Chronic mucoid otitis media	78868004	Upper
Chronic mucoid otitis media NOS	78868004	Upper
Chronic otitis media with effusion, other	78868004	Upper
Mucoid otitis media	78868004	Upper
Chronic otitis media with effusion	78868004	Upper
Chronic secretory otitis media, mucoid	78868004	Upper
Chronic otitis media with effusion, mucoid	78868004	Upper
Chronic middle ear effusion	78868004	Upper
Otitis media with effusion	78868004	Upper
Secretory otitis media	78868004	Upper
Chronic secretory otitis media	78868004	Upper
Serous otitis media	80327007	Upper
Acute nasopharyngitis	82272006	Upper
Acute rhinitis	82272006	Upper
Acute infective rhinitis	82272006	Upper
Acute bacterial laryngitis	849571000000102	Upper
Streptococcal laryngitis	85083002	Upper
Acute tracheitis with obstruction	8519009	Upper
Croup	85915003	Upper
Acute suppurative otitis media - tympanic membrane ruptured	86279000	Upper
Acute suppurative otitis media with spontaneous rupture of ear drum	86279000	Upper
Acute suppurative otitis media with discharge	86279000	Upper
Hypertrophic pharyngitis	87326000	Upper

Maxillary sinusitis	88348008	Upper
Aerosinusitis	88548007	Upper
Barotrauma - sinuses	88548007	Upper
Barotrauma - sinuses	88548007	Upper
Sinus barotrauma	88548007	Upper
Tonsillitis	90176007	Upper
Acute frontal sinusitis	91038008	Upper
[X]Otitis media in bacterial diseases classified elsewhere	95882006	Upper
Bacterial ear infection	95882006	Upper

Appendix 2A. Codes for included antibiotics

ProdCodeId	TermfromEMIS
1070441000033113	Phenoxymethylpenicillin Capsules 250 mg
1076641000033113	Phenoxymethylpenicillin Paediatric syrup 125 mg/5 ml
1068741000033112	Phenoxymethylpenicillin Potassium Capsules 250 mg
1071541000033115	Phenoxymethylpenicillin Potassium Elixir 125 mg/5 ml
1071641000033119	Phenoxymethylpenicillin Potassium Elixir 250 mg/5 ml
1071441000033116	Phenoxymethylpenicillin Potassium Elixir 62.5 mg/5 ml
1080241000033118	Phenoxymethylpenicillin Potassium Tablets 125 mg
1082641000033116	Phenoxymethylpenicillin Potassium Tablets 250 mg
1078241000033114	Phenoxymethylpenicillin Suspension 125 mg/5 ml
1078541000033111	Phenoxymethylpenicillin Syrup 125 mg/5 ml
1078641000033112	Phenoxymethylpenicillin Syrup 250 mg/5 ml
1081841000033112	Phenoxymethylpenicillin Tablets 125 mg
1182841000033110	Rommix 125 Susp Paediatric suspension 125 mg/5 ml
1183841000033117	Rommix Tablets 500 mg
37241000033112	Almodan 125 mg/5 ml syrup (Teva UK Ltd)
55641000033117	Amix 125 oral suspension (Ashbourne Pharmaceuticals Ltd)
46141000033118	Amix 250 capsules (Ashbourne Pharmaceuticals Ltd)
55741000033114	Amix 250 oral suspension (Ashbourne Pharmaceuticals Ltd)
45641000033115	Amix 500 capsules (Ashbourne Pharmaceuticals Ltd)
56841000033114	Amoram 125 mg/5 ml oral suspension (LPC Medical (UK) Ltd)
45441000033117	Amoram 250 mg capsules (LPC Medical (UK) Ltd)
56941000033118	Amoram 250 mg/5 ml oral suspension (LPC Medical (UK) Ltd)
45541000033116	Amoram 500 mg capsules (LPC Medical (UK) Ltd)
3079841000033112	Amoxicillin 125 mg/1.25 ml oral suspension paediatric
3079641000033111	Amoxicillin 125 mg/5 ml oral suspension
3080041000033117	Amoxicillin 125 mg/5 ml oral suspension sugar free
13707941000033117	Amoxicillin 1 g dispersible tablets sugar free
3079141000033118	Amoxicillin 250 mg capsules
3079741000033119	Amoxicillin 250 mg/5 ml oral suspension
3080141000033118	Amoxicillin 250 mg/5 ml oral suspension sugar free
3079941000033116	Amoxicillin 3 g oral powder sachets sugar free
3079241000033113	Amoxicillin 500 mg capsules
13827741000033111	Amoxicillin 500 mg/5 ml oral suspension sugar free
52841000033110	Amoxil 125 mg/1.25 ml paediatric oral suspension (GlaxoSmithKline UK Ltd)
55941000033112	Amoxil 125 mg/5 ml syrup sucrose free (GlaxoSmithKline UK Ltd)
44041000033113	Amoxil 250 mg capsules (GlaxoSmithKline UK Ltd)
56041000033119	Amoxil 250 mg/5 ml syrup sucrose free (GlaxoSmithKline UK Ltd)
53941000033113	Amoxil 3 g oral powder sachets sucrose free (GlaxoSmithKline UK Ltd)
44141000033112	Amoxil 500 mg capsules (GlaxoSmithKline UK Ltd)
625941000033118	Galenamox 125 mg/5 ml oral suspension (Galen Ltd)
620241000033118	Galenamox 250 mg capsules (Galen Ltd)
625841000033114	Galenamox 250 mg/5 ml oral suspension (Galen Ltd)
620341000033111	Galenamox 500 mg capsules (Galen Ltd)
1671741000033118	Respillin 250 mg capsules (Kent Pharma (UK) Ltd)
1671841000033111	Respillin 500 mg capsules (Kent Pharma (UK) Ltd)
2186941000033119	Amiclav 250 mg/125 mg tablets (Ashbourne Pharmaceuticals Ltd)
94641000033110	Augmentin 125/31 SF oral suspension (GlaxoSmithKline UK Ltd)
94741000033118	Augmentin 250/62 SF oral suspension (GlaxoSmithKline UK Ltd)
93141000033115	Augmentin 375 mg dispersible tablets (GlaxoSmithKline UK Ltd)
94941000033115	Augmentin 375 mg tablets (GlaxoSmithKline UK Ltd)
95041000033115	Augmentin 625 mg tablets (GlaxoSmithKline UK Ltd)
94841000033111	Augmentin-Duo 400/57 oral suspension (GlaxoSmithKline UK Ltd)
5697041000033116	Co-amoxiclav 125 mg/31 mg/5 ml oral suspension
366941000033113	Co-amoxiclav 125 mg/31 mg/5 ml oral suspension sugar free
317741000033113	Co-amoxiclav 250 mg/125 mg dispersible tablets sugar free
370041000033115	Co-amoxiclav 250 mg/125 mg tablets
5697141000033117	Co-amoxiclav 250 mg/62 mg/5 ml oral suspension
367041000033114	Co-amoxiclav 250 mg/62 mg/5 ml oral suspension sugar free
367541000033116	Co-amoxiclav 400 mg/57 mg/5 ml oral suspension sugar free
370141000033116	Co-amoxiclav 500 mg/125 mg tablets
1594141000033117	Co-amoxiclav 875 mg/125 mg tablets
2290941000033119	Ranclav 125 mg/31 mg/5 ml SF oral suspension (Ranbaxy (UK) Ltd)
2290741000033117	Ranclav 375 mg tablets (Ranbaxy (UK) Ltd)
98441000033116	Azithromycin 200 mg/5 ml oral suspension
3955441000033115	Azithromycin 250 mg tablets

1572841000033112	Azithromycin 500 mg tablets
4823141000033118	Clamelle 500 mg tablets (Actavis UK Ltd)
1557141000033118	Zithromax 200 mg/5 ml oral suspension (Pfizer Ltd)
1713741000033116	Zithromax 500 mg tablets (Pfizer Ltd)
96941000033113	Azithromycin 250 mg capsules
1553141000033111	Zithromax 250 mg capsules (Pfizer Ltd)
6030241000033111	Clarie XL 500 mg tablets (Teva UK Ltd)
3838541000033117	Clarithromycin 125 mg granules straws
278241000033118	Clarithromycin 125 mg/5 ml oral suspension
3838641000033116	Clarithromycin 187.5 mg granules straws
282141000033118	Clarithromycin 250 mg granules sachets
3838741000033113	Clarithromycin 250 mg granules straws
287441000033111	Clarithromycin 250 mg tablets
1830541000033112	Clarithromycin 250 mg/5 ml oral suspension
277841000033115	Clarithromycin 500 mg modified-release tablets
285341000033110	Clarithromycin 500 mg tablets
3838841000033115	Clarosip 125 mg granules for oral suspension straws (Grunenthal Ltd)
3838941000033111	Clarosip 187.5 mg granules for oral suspension straws (Grunenthal Ltd)
3839041000033119	Clarosip 250 mg granules for oral suspension straws (Grunenthal Ltd)
805741000033118	Klaricid 250 mg tablets (Abbott Laboratories Ltd)
805441000033113	Klaricid 500 tablets (Abbott Laboratories Ltd)
805341000033119	Klaricid Adult 250 mg granules sachets (Viatris UK Healthcare Ltd)
805141000033117	Klaricid Paediatric 125 mg/5 ml oral suspension (Viatris UK Healthcare Ltd)
1830641000033113	Klaricid Paediatric 250 mg/5 ml oral suspension (Viatris UK Healthcare Ltd)
804941000033116	Klaricid XL 500 mg tablets (Viatris UK Healthcare Ltd)
415841000033119	Demix 100 capsules (Ashbourne Pharmaceuticals Ltd)
415941000033110	Demix 50 capsules (Ashbourne Pharmaceuticals Ltd)
3089341000033112	Doxycycline 100 mg capsules
3089541000033117	Doxycycline 20 mg tablets
1603241000033119	Doxycycline 50 mg capsules
7871241000033116	Doxycycline 50 mg/5 ml oral suspension
2104341000033112	Doxylar 100 mg capsules (Sandoz Ltd)
2104241000033119	Doxylar 50 mg capsules (Sandoz Ltd)
2637141000033110	Periostat 20 mg tablets (Alliance Pharmaceuticals Ltd)
1514941000033119	Vibramycin 100 mg capsules (Pfizer Ltd)
1515041000033119	Vibramycin 50 capsules (Pfizer Ltd)
1705841000033113	Vibramycin Acne Pack 50 mg capsules (Pfizer Ltd)
2193041000033114	Vibrox 100 mg capsules (Kent Pharma (UK) Ltd)
3089441000033118	Doxycycline 100 mg dispersible tablets sugar free
5150141000033114	Doxycycline 40 mg modified-release capsules
5150241000033119	Efracea 40 mg modified-release capsules (Galderma (UK) Ltd)
1523841000033118	Vibramycin-D 100 mg dispersible tablets (Pfizer Ltd)
534141000033113	Erymax 250 mg gastro-resistant capsules (Teva UK Ltd)
534241000033118	Erythromycin 250 mg gastro-resistant capsules
1924941000033118	Erythromycin 250 mg gastro-resistant tablets
2890541000033117	Kerymax 250 mg gastro-resistant capsules (Kent Pharma (UK) Ltd)
1183741000033110	Rommix 250 EC tablets (Ashbourne Pharmaceuticals Ltd)
1436941000033111	Tiloryth 250 mg gastro-resistant capsules (Tillomed Laboratories Ltd)
537641000033110	Erythromycin ethyl succinate 125 mg/5 ml oral suspension
537441000033113	Erythromycin ethyl succinate 125 mg/5 ml oral suspension sugar free
537741000033118	Erythromycin ethyl succinate 250 mg/5 ml oral suspension
537541000033114	Erythromycin ethyl succinate 250 mg/5 ml oral suspension sugar free
538841000033112	Erythromycin ethyl succinate 500 mg tablets
537841000033111	Erythromycin ethyl succinate 500 mg/5 ml oral suspension
537941000033115	Erythromycin ethyl succinate 500 mg/5 ml oral suspension sugar free
540141000033115	Erythroped A 500 mg tablets (Advanz Pharma)
537241000033112	Erythroped Forte SF 500 mg/5 ml oral suspension (Advanz Pharma)
536141000033119	Erythroped PI SF 125 mg/5 ml oral suspension (Advanz Pharma)
537341000033119	Erythroped SF 250 mg/5 ml oral suspension (Advanz Pharma)
539541000033115	Erythrocin 250 tablets (Advanz Pharma)
539641000033119	Erythrocin 500 tablets (Advanz Pharma)
536941000033117	Erythromycin stearate 250 mg tablets
13300741000033118	Erythromycin stearate 500 mg tablets
854441000033117	Lymecycline 408 mg capsules
1414641000033119	Tetralysal 300 capsules (Galderma (UK) Ltd)
1076141000033115	Phenoxymethylpenicillin 125 mg/5 ml oral solution
3923541000033116	Phenoxymethylpenicillin 125 mg/5 ml oral solution sugar free
1081941000033116	Phenoxymethylpenicillin 250 mg tablets
1076241000033110	Phenoxymethylpenicillin 250 mg/5 ml oral solution
3923641000033115	Phenoxymethylpenicillin 250 mg/5 ml oral solution sugar free
2130541000033115	Tenkicin 250 mg tablets (Kent Pharma (UK) Ltd)
3541000033113	Achromycin 250 mg capsules (Wyeth Pharmaceuticals)
1414841000033118	Tetracycline 250 mg capsules
1428041000033114	Tetracycline 250 mg tablets

Appendix 2B. Codes for included specific antibiotics if accompanied with a history of COPD/bronchiectasis

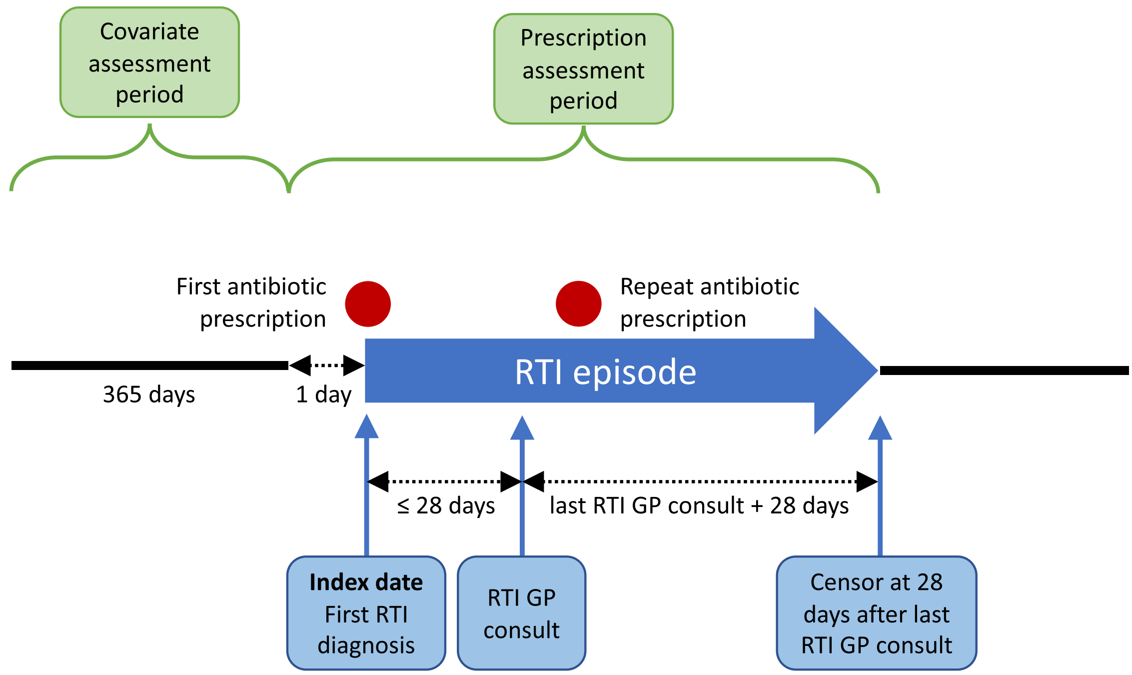
ProdCodeId	TermfromEMIS
227841000033116	Cefaclor M/R tablets 500 mg
439041000033115	Distaclor Capsules 250 mg
453841000033111	Distaclor Mr M/R tablets 500 mg
798041000033114	Keflex-C Chewable tablets 125 mg
798141000033113	Keflex-C Chewable tablets 250 mg
3914841000033111	Suprax Capsules 400 mg
289541000033118	Co-Trimoxazole Mixture 480 mg/5 ml
317941000033111	Co-Trimoxazole Dispersible tablets 480 mg
325641000033115	Co-Trimoxazole Drapsules 480 mg
327741000033117	Co-Trimoxazole Forte tablets dispersible 960 mg
327841000033110	Co-Trimoxazole Tablets 960 mg
353241000033118	Co-Trimoxazole Paediatric s/f dispersible tablets 120 mg
353741000033112	Co-Trimoxazole Paediatric mixture 240 mg/5 ml
353941000033110	Co-Trimoxazole Paediatric suspension 240 mg/5 ml
354041000033112	Co-Trimoxazole Paediatric tablets 120 mg
372541000033112	Co-Trimoxazole Tablets forte 960 mg
2617541000033112	Bacticlor MR 375 mg tablets (Ranbaxy (UK) Ltd)
230941000033110	Cefaclor 125 mg/5 ml oral suspension
230741000033112	Cefaclor 125 mg/5 ml oral suspension sugar free
220441000033115	Cefaclor 250 mg capsules
231741000033119	Cefaclor 250 mg/5 ml oral suspension
230841000033119	Cefaclor 250 mg/5 ml oral suspension sugar free
227741000033114	Cefaclor 375 mg modified-release tablets
219741000033111	Cefaclor 500 mg capsules
460341000033118	Distaclor 125 mg/5 ml oral suspension (Flynn Pharma Ltd)
460441000033112	Distaclor 250 mg/5 ml oral suspension (Flynn Pharma Ltd)
433941000033116	Distaclor 500 mg capsules (Flynn Pharma Ltd)
452341000033110	Distaclor MR 375 mg tablets (Flynn Pharma Ltd)
803141000033116	Keftid 125 mg/5 ml oral suspension (Strides Pharma UK Ltd)
797641000033116	Keftid 250 mg capsules (Strides Pharma UK Ltd)
803241000033111	Keftid 250 mg/5 ml oral suspension (Strides Pharma UK Ltd)
797741000033113	Keftid 500 mg capsules (Strides Pharma UK Ltd)
220541000033119	Cefadroxil 500 mg capsules
3084141000033110	Cefalexin 500 mg capsules
232341000033112	Ceporex 125 mg/5 ml syrup (Strides Pharma UK Ltd)
220941000033113	Ceporex 250 mg capsules (Strides Pharma UK Ltd)
235141000033115	Ceporex 250 mg tablets (Strides Pharma UK Ltd)
232441000033118	Ceporex 250 mg/5 ml syrup (Strides Pharma UK Ltd)
221041000033115	Ceporex 500 mg capsules (Strides Pharma UK Ltd)
235241000033110	Ceporex 500 mg tablets (Strides Pharma UK Ltd)
232541000033117	Ceporex 500 mg/5 ml syrup (Strides Pharma UK Ltd)
802741000033110	Keflex 125 mg/5 ml oral suspension (Flynn Pharma Ltd)
796841000033118	Keflex 250 mg capsules (Flynn Pharma Ltd)
803341000033118	Keflex 250 mg tablets (Flynn Pharma Ltd)
802841000033117	Keflex 250 mg/5 ml oral suspension (Flynn Pharma Ltd)
796941000033114	Keflex 500 mg capsules (Flynn Pharma Ltd)
803441000033112	Keflex 500 mg tablets (Flynn Pharma Ltd)
3084041000033111	Cefalexin 250 mg capsules
3084241000033115	Cefalexin 250 mg tablets
3084341000033113	Cefalexin 500 mg tablets
3084441000033119	Cefalexin 125 mg/5 ml oral suspension
3084541000033118	Cefalexin 250 mg/5 ml oral suspension
3084641000033117	Cefalexin 500 mg/5 ml oral suspension
4373141000033119	Cefalexin 250 mg/5 ml oral suspension sugar free
5747941000033119	Cefalexin 125 mg/5 ml oral suspension sugar free
230041000033114	Cefixime 100 mg/5 ml oral suspension
232741000033113	Cefixime 200 mg tablets
12395841000033112	Cefixime 400 mg tablets
1398741000033113	Suprax 200 mg tablets (Sanofi)
1393841000033111	Suprax Paediatric 100 mg/5 ml oral suspension (Sanofi)
967441000033110	Nicef 250 mg capsules (Strides Pharma UK Ltd)
967541000033111	Nicef 500 mg capsules (Strides Pharma UK Ltd)
1506041000033114	Velosef 250 mg capsules (Bristol-Myers Squibb Pharmaceuticals Ltd)
1506141000033113	Velosef 500 mg capsules (Bristol-Myers Squibb Pharmaceuticals Ltd)
1511941000033116	Velosef 250 mg/5 ml syrup (Bristol-Myers Squibb Pharmaceuticals Ltd)
3084741000033114	Cefradine 250 mg capsules
3084841000033116	Cefradine 500 mg capsules
3085141000033111	Cefradine 250 mg/5 ml oral solution
235441000033111	Cefuroxime 125 mg tablets
230141000033113	Cefuroxime 125 mg/5 ml oral suspension
233041000033118	Cefuroxime 250 mg tablets
228941000033111	Cefuroxime 125 mg granules sachets
1556241000033110	Zinnat Suspension 125 mg granules sachets (GlaxoSmithKline UK Ltd)
1557041000033117	Zinnat 125 mg/5 ml oral suspension (GlaxoSmithKline UK Ltd)
1557341000033115	Zinnat 250 mg tablets (GlaxoSmithKline UK Ltd)
1558241000033114	Zinnat 125 mg tablets (GlaxoSmithKline UK Ltd)

1582841000033117	Ciproxin 250 mg/5 ml oral suspension (Bayer Plc)
1582941000033113	Ciprofloxacin 250 mg/5 ml oral suspension
259341000033118	Ciprofloxacin 100 mg tablets
260241000033112	Ciprofloxacin 250 mg tablets
258841000033116	Ciprofloxacin 500 mg tablets
259041000033115	Ciprofloxacin 750 mg tablets
259441000033112	Ciproxin 100 mg tablets (Bayer Plc)
259641000033114	Ciproxin 250 mg tablets (Bayer Plc)
258741000033114	Ciproxin 500 mg tablets (Bayer Plc)
258941000033112	Ciproxin 750 mg tablets (Bayer Plc)
1626241000033115	Levofloxacin 250 mg tablets
1626341000033113	Levofloxacin 500 mg tablets
1698741000033115	Tavanic 250 mg tablets (Sanofi)
1698841000033113	Tavanic 500 mg tablets (Sanofi)
10220241000033110	Evoxil 500 mg tablets (Kent Pharma (UK) Ltd)
2890241000033119	Moxifloxacin 400 mg tablets
2890341000033112	Avelox 400 mg tablets (Bayer Plc)
986441000033114	Norfloxacin 400 mg tablets
1496041000033116	Utinor 400 mg tablets (Organon Pharma (UK) Ltd)
1407541000033110	Tarivid 400 mg tablets (Sanofi)
1002541000033118	Ofloxacin 200 mg tablets
1002641000033117	Ofloxacin 400 mg tablets
1409341000033111	Tarivid 200 mg tablets (Sanofi)
373541000033118	Co-trimoxazole 160 mg/800 mg tablets
366841000033117	Co-trimoxazole 40 mg/200 mg/5 ml oral suspension sugar free
373441000033119	Co-trimoxazole 80 mg/400 mg tablets
289441000033119	Co-trimoxazole 80 mg/400 mg/5 ml oral suspension
1267541000033110	Septrin Adult 80 mg/400 mg/5 ml oral suspension (Aspen Pharma Trading Ltd)
1275641000033110	Septrin tablets (Aspen Pharma Trading Ltd)
1272641000033118	Septrin Paediatric 40 mg/200 mg/5 ml oral suspension (Aspen Pharma Trading Ltd)
1275741000033118	Septrin Forte 160 mg/800 mg tablets (Aspen Pharma Trading Ltd)
3104641000033111	Sulfamethoxypyridazine 500 mg tablets
953941000033117	Nalidixic acid 300 mg/5 ml oral suspension
954741000033117	Nalidixic acid 500 mg tablets
964941000033112	Negram 300 mg/5 ml oral suspension (Sanofi-Synthelabo Ltd)
965141000033111	Negram 500 mg tablets (Sanofi)
1494941000033113	Uriben 300 mg/5 ml oral suspension (Rosemont Pharmaceuticals Ltd)

Appendix 3. Geographical distribution of all RTI patients who were prescribed an antibiotic during the study period in the full CPRD Aurum set versus the sample of 530 general practices

	RTI patients with an antibiotic	
	Full CPRD set	Sampled set
	1483 Practices	530 Practices
Region	1726,463 Unique RTI patients with an antibiotic	676,141 Unique RTI patients with an antibiotic
North East	3%	3%
North West	21%	18%
Yorkshire and The Humber	3%	4%
East Midlands	3%	3%
West Midlands	17%	18%
East of England	5%	6%
South West	18%	15%
South Central	19%	21%
London	11%	12%

Appendix 4. Schema depicting study RTI and prescription outcome definitions



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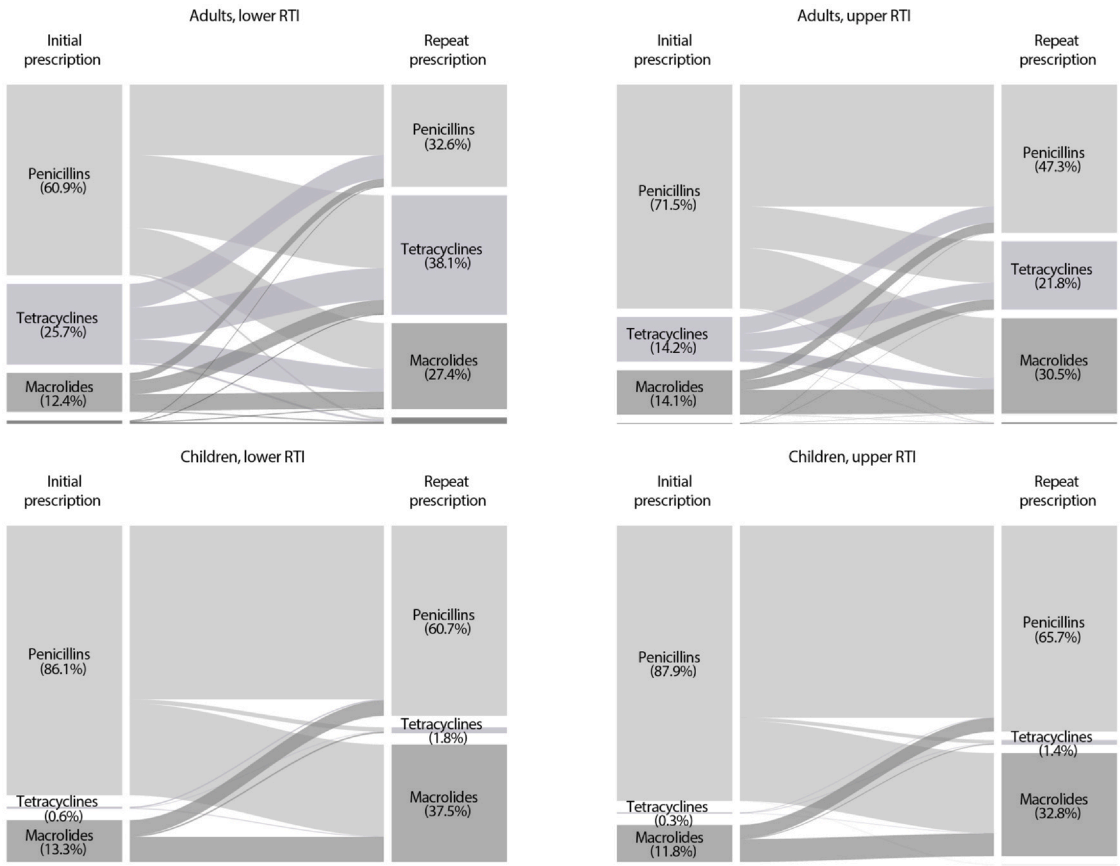
In sensitivity analyses, the maximum allowed time between consecutive GP RTI consults was set at 14 and 21 days. Antibiotic prescriptions on the day before RTI diagnosis was included as this is likely to be associated to the RTI itself, but merely reflects delayed RTI diagnosis recording. A total of 3480 episodes (0.4%) started with an antibiotic on the day before the start of the RTI episode.

Appendix 5. Switch patterns between initial and within-episode repeat antibiotics



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Appendix 6. Coverage of GP practices, person time and most frequently used RTI related codes

	Adults		Children	
	Lower RTI	Upper RTI	Lower RTI	Upper RTI
RTI episodes (N)	217,788	440,621	25,114	222,441
Unique RTI patients (N)	167,258	334,554	18,135	156,194
Any GP consult among study population (N)	9884,531	14,356,812	428,794	3157,980
Physicians (N)	5984	6607	3702	6007
Practices (N)	528	529	524	529
Annual consults per patient (N)	14.8	10.7	5.9	5.1
Annual consults per physician among RTI patients (N)	413	543	29	131
Annual consults per practice among RTI patients (N)	4680	6784	205	1492
Most frequently used RTI related codes	Lower respiratory tract infection N = 160,750 (74%)	Acute tonsilitis N = 100,688 (23%)	Lower respiratory tract infection N = 18,379 (73%)	Acute tonsilitis N = 64,688 (29%)
	Lower resp tract infection N = 42,945 (20%)	Acute sinusitis N = 61,992 (14%)	Lower resp tract infection N = 5080 (20%)	Otitis media N = 48,636 (22%)
	Acute bronchitis N = 10,975 (5%)	Sore throat symptom N = 58,261 (13%)	Acute bronchiolitis N = 776 (3%)	Upper respiratory infection N = 24,041 (11%)
	Acute wheezy bronchitis N = 720 (< 1%)	Upper respiratory infection N = 40,823 (9%)	Acute bronchitis N = 523 (2%)	Tonsilitis N = 20,143 (9%)
	Bronchitis N = 625 (< 1%)	Otitis media N = 33,405 (8%)	Acute wheezy bronchitis N = 95 (< 1%)	Sore throat symptom N = 17,701 (8%)
	Chest infection – unspecific bronchitis N = 567 (< 1%)	Sinusitis N = 33,122 (8%)	Bronchitis N = 67 (< 1%)	Viral upper respiratory tract infection N = 6692 (3%)
	LRTI – Lower respiratory tract infection N = 369 (< 1%)	Tonsilitis N = 30,694 (7%)	Chest infection – unspecific bronchitis N = 36 (< 1%)	Ear infection N = 4181 (2%)
	Bronchitis NOS N = 306 (< 1%)	Acute pharyngitis N = 8265 (2%)	LRTI – Lower respiratory tract infection N = 31 (< 1%)	Upper respiratory infection NOS N = 3810 (2%)
	Acute tracheobronchitis N = 140 (< 1%)	Ear infection N = 7664 (2%)	Bronchitis NOS N = 25 (< 1%)	Earache symptoms N = 3496 (2%)
	Acute viral bronchitis N = 131 (< 1%)	Viral upper respiratory tract infection N = 7184 (2%)	Acute bacterial bronchitis N = 23 (< 1%)	Acute suppurative otitis media N = 2695 (1%)

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