

‘Warning: allergic to penicillin’: association between penicillin allergy status in 2.3 million NHS general practice electronic health records, antibiotic prescribing and health outcomes

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Background: The prevalence of reported penicillin allergy (PenA) and the impact these records have on health outcomes in the UK general population are unknown. Without such data, justifying and planning enhanced allergy services is challenging.

Objectives: To determine: (i) prevalence of PenA records; (ii) patient characteristics associated with PenA records; and (iii) impact of PenA records on antibiotic prescribing/health outcomes in primary care.

Methods: We carried out cross-sectional/retrospective cohort studies using patient-level data from electronic health records. Cohort study: exact matching across confounders identified as affecting PenA records. Setting: English NHS general practices between 1 April 2013 and 31 March 2014. Participants: 2.3 million adult patients. Outcome measures: prevalence of PenA, antibiotic prescribing, mortality, MRSA infection/colonization and *Clostridioides difficile* infection.

Results: PenA prevalence was 5.9% (IQR=3.8%–8.2%). PenA records were more common in older people, females and those with a comorbidity, and were affected by GP practice. Antibiotic prescribing varied significantly: penicillins were prescribed less frequently in those with a PenA record [relative risk (RR) =0.15], and macrolides (RR=4.03), tetracyclines (RR=1.91) nitrofurantoin (RR=1.09), trimethoprim (RR=1.04), cephalosporins (RR=2.05), quinolones (RR=2.10), clindamycin (RR=5.47) and total number of prescriptions were increased in patients with a PenA record. Risk of re-prescription of a new antibiotic class within 28 days (RR=1.32), MRSA infection/colonization (RR=1.90) and death during the year subsequent to 1 April 2013 (RR=1.08) increased in those with PenA records.

Conclusions: PenA records are common in the general population and associated with increased/altered antibiotic prescribing and worse health outcomes. We estimate that incorrect PenA records affect 2.7 million people in England. Establishing true PenA status (e.g. oral challenge testing) would allow more people to be prescribed first-line antibiotics, potentially improving health outcomes.

Introduction

Many patients have a record of penicillin allergy (PenA),^{1–4} but, when formally tested, only a small proportion are found to have a true PenA.^{1,5,6} ‘False’ PenA labels can arise for a number of reasons, including skin reactions to the penicillin that do not constitute a serious allergy risk, adverse effects that have been misclassified as an allergy and misidentification of infection symptoms. When antibiotic treatment is considered necessary, clinicians generally prescribe second-line antibiotic classes for these patients,⁷ which may

not be as effective, may impact more negatively on antimicrobial resistance and might not be as safe. For example, an increased risk of cardiovascular mortality has been reported following therapy with antibiotics often used as alternatives to penicillins, including clarithromycin,⁸ azithromycin^{9,10} and levofloxacin.⁹ The risk of MRSA infection is increased following cephalosporin,^{11,12} clindamycin¹³ and fluoroquinolone¹² prescribing. A recent analysis of general practice data has found a significant increased risk of MRSA and *Clostridioides* (*Clostridium*) *difficile* infection (CDI) in

patients with a PenA record, partly attributed to changes in antibiotic prescribing.¹⁴

PenA testing is available and reliable, so many patients who are falsely labelled as penicillin allergic could have their status safely reversed. However, PenA testing is available, but not commonly carried out, in general practice, partly due to GP uncertainty about referral criteria and knowledge about the test.¹⁵ Existing hospital allergy services are unable to meet the current demand for allergy testing.

Precise estimates of the prevalence of PenA records and their impact on the general population in the UK are not available. It is unclear the extent to which the worse patient outcomes attributed to PenA might be explained by comorbidity, age or other factors. If a record of PenA was associated with such increased risks, then confirmation of allergic status in advance of the need for antibiotics (a 'pre-emptive' strategy) in primary care may have important benefits for these individuals and for antibiotic stewardship.

To support a 'pre-emptive' testing strategy, we set out to: (i) determine the prevalence of PenA in UK general practice records; (ii) establish patient characteristics associated with a recorded PenA; and (iii) investigate the impact on antibiotic prescribing decisions and health outcomes.

Methods

Ethics approval

The study was approved by the School of Medicine Research Ethics Committee, University of Leeds (REF: SoMREC/13/101). The protocol/data request was also approved by the Project Committee at ResearchOne. ResearchOne is a research database that consists of de-identified clinical and administrative data drawn from the electronic patient records of ~6 million patients on SystmOne.¹⁶ ResearchOne has received a favourable opinion from NHS Research Ethics Committee North East–Newcastle and North Tyneside 1 (REF: 11/NE/0184) and an opinion from the National Information Governance Board and Secretary of State for Health that no recommendation of support for Section 251 approval is required as there is no disclosure of identifiable data (National Research Ethics Service Research Ethics Committee North East REC reference number 11/NE/0184).

Study design

This study comprised three parts.

Part 1

A cross-sectional study of adult patients in ResearchOne based on their electronic health records on 1 April 2013. The aim was to identify factors associated with the record of a PenA, allowing for clustering within practice.

Part 2

A retrospective cohort study with patients matched by the factors identified in Part 1. Patients were followed for 1 year until 31 March 2014 to establish the associated impact of a PenA record on several health outcomes.

Part 3

A retrospective cohort study that included only patients prescribed at least one antibiotic during the study year 1 April 2013 to 31 March 2014. Patient cohorts with and without a PenA record were matched by the factors identified in Part 1.

Setting and source data

Data comprised an extract from NHS general practices in England whose routine clinical data were included in ResearchOne at 29 June 2016. ResearchOne has been mainly used in quality improvement research and to develop a frailty index.¹⁷ Patient records included historical contributions from 400 general practices. The 1 year study period began on 1 April 2013. Matched case-control studies used a subset of the extract.

Participants

All adults (18–100 years old) with records on ResearchOne at the date of extraction were included. Eligible patients included those that had died since 1 April 2013. Patients >100 years of age were excluded to reduce the risk of inadvertent identification.

Variables

Variables included were PenA records and antibiotic prescriptions from the classes penicillins, cephalosporins, clindamycin, macrolides, tetracyclines, nitrofurantoin, trimethoprim, quinolones, carbapenems and aztreonam; date of prescription; and all prescriptions of drugs within the period 1 April 2013 to 31 March 2014. Additional variables included: age, gender, date of death, index of multiple deprivation (IMD),¹⁸ smoking status and practice identifier (anonymized). The IMD is the official measure of relative deprivation for neighbourhoods in England. England can be divided into 32844 neighbourhoods each with ~1500 residents (650 households) and these are ranked from 1 (most deprived area) to 32844 (least deprived) based on an aggregated measure of seven dimensions of deprivation.¹⁸ It is common practice to use the fifths of deprivation to give a summary of the deprivation where patients live, moving from the most deprived 20% through to the most affluent 20%. Comorbidities were included where data are routinely collected and where an impact on antibiotic prescribing or outcome from antibiotic prescribing might be anticipated. Clinical codes for these comorbidities were determined using the business rules defined in the NHS Quality Outcomes Framework (QOF).¹⁹ These included: cancer, coronary heart disease (CHD), chronic kidney disease (CKD), COPD, peripheral arterial disease (PAD), asthma, diabetes, stroke and transient ischaemic attack (TIA). Any new record of the following pathogens during the year of study was extracted: *C. difficile*, VRE and MRSA; no attempt was made to distinguish colonization from infection. Codes used were READ Codes (Version 3) – CTV3²⁰ and those used for the data extract are shown in the [Supplementary data](#) available at JAC Online; if any of these codes were present, the variable was considered to be present, otherwise they were considered to be not present.

PenA records were defined using READ codes specified by the research team. Patients were considered to have a PenA record if they had a record of either 'sensitivity' or 'allergy' to any penicillin class antibiotic agent (amoxicillin, ampicillin, penicillin V and G, flucloxacillin and piperacillin) recorded in their electronic health records on 1 April 2013. We combined allergy and sensitivity records because these terms are often used interchangeably.¹

Health outcomes

We ascertained if there was a record of a prescription of a subsequent antibiotic of a different class in the 28 days following the prescription of an index antibiotic agent; this has been used previously as a proxy marker of 'lack of treatment response'.²¹ Mortality and healthcare-associated infection (MRSA infection, CDI and VRE infection) at any time during the 1 year study period were included as additional health outcomes.

Selection bias

Data for all patients available on ResearchOne who fulfilled the inclusion criteria were used for the analyses.

Sample size

The sample comprised data for all patients on ResearchOne who fulfilled the inclusion criteria. We estimated that a population of 2 million with a prevalence of 10% would yield an estimate of prevalence with a standard error of 0.02%.

Statistical methods (including quantitative variables)

Part 1: cross-sectional study

Adjusted and unadjusted ORs were calculated from cross-tabulation of PenA records with potential factors affecting these records, and 95% CIs were reported. For convenience, continuous variables [age, GP practice list size and area deprivation (IMD)] were categorized. This reduced the risk of inadvertent identification further during analysis, enabled handling of non-linear effects and made interpretation of results easier. Adjusted ORs were calculated from a logistic regression model that included a random intercept term to account for clustering of patients within general practice. The intraclass correlation coefficient (ICC) is reported to enable the assessment of clustering.

Part 2: retrospective cohort study for associated health impacts

Two patient cohorts were formed according to the PenA records on 1 April 2013, and patients in the cohort with a PenA record were then exact matched to patients in the cohort without a PenA record. Exact matching was undertaken according to the factors identified in Part 1: age, sex, ethnicity, IMD, comorbidities (asthma, cancer, CHD, CKD, COPD, diabetes, PAD, smoking, stroke and TIA) and the proportion of patients with a PenA record within the general practice. Any continuous variables were finely categorized to allow the exact matching process. All patients in the PenA cohort were then matched, according to all the factors above; multiple subclasses were formed that differed only in their PenA status. This meant that each PenA patient could be matched to multiple patients without a PenA record, who shared the same characteristics. Practices were also categorized according to the percentage of patients within them with a PenA record, and these categories were used in the exact matching as an additional factor. Following matching, each binary outcome (MRSA, *C. difficile* and 1 year mortality) was modelled within a binomial model using a log link and including all of the matching factors as covariates as well as PenA record. This is the currently recommended approach, which demands the controlling of factors even after matching.²² Relative risk (RR) was reported from exponentiated coefficients along with 95% CI. The number of antibiotic prescriptions was modelled as a negative binomial regression with the same set of covariates. The incidence RR was calculated by exponentiating the coefficients. Patients were only counted once in this analysis. A propensity score-matched model was used for a sensitivity analysis.

Part 3: retrospective cohort study for antibiotic prescribing

A subset comprising all patients prescribed at least one antibiotic in the year 1 April 2013 to 31 March 2014 was used because only those having an infection requiring antibiotic treatment were considered with respect to type of antibiotic prescribed. Exact matching using the method of Part 2 was applied to the subset. Outcomes of interest were the prescription of specific antibiotic classes and were modelled by a binomial model with a log link function. Then exponentiated coefficients gave the RR of each antibiotic class. A value of the RR risk >1.000 meant that, according to the fitted model, the antibiotic class was more likely to be prescribed to those with a

PenA record than those without, after controlling for age, sex, ethnicity, IMD, smoking status, comorbidities (asthma, cancer, CHD, CKD, COPD, diabetes, PAD, stroke and TIA) and the proportion of patients with a PenA record within the general practice.

Results

Participants

A total of 2350803 adult patients met the inclusion criteria and comprised the initial population for cross-sectional analysis (Tables 1 and 2).

Prevalence of PenA records

Of the total patients, 139437 patients had a PenA record, giving a prevalence for the population of 5.9% (95% CI 5.9%–6.0%).

Characteristics of patients with a PenA record

Women were more likely to have a recorded PenA, even after adjustment for possible confounders (Table 1). The prevalence increased significantly with increasing age (Table 1). Rates of PenA varied considerably by general practice (IQR=3.8%–8.2%); from the random intercept term, the calculated ICC revealed that 7.2% of the variation in PenA records could be attributed to general practice. After adjustment, IMD status had a small, but significant, impact, with more affluent patients more likely to have a record of allergy. The exception was patients with 'unknown' IMD status, which was associated with lower odds of a record of PenA; IMD status was not available for 11.1% of patients. The selected comorbidities were all associated with small, but significantly, increased odds of having a PenA record, with asthma having the highest (Table 2).

Exact matching

In Part 2, 130571 of 139437 patients with a record of PenA were matched with 1892835 of 2211366 patients. Exact matching results are shown in Table 3. In Part 3, for those patients treated with an antibiotic, 45831 with a record of PenA were matched with 409687 patients with no record.

PenA records and antibiotic prescribing

In the exact matched analysis, patients with a PenA record received ~5% more antimicrobial prescriptions than those without a PenA record during the 12 month follow-up (Table 3). Macrolides, tetracyclines, cephalosporins, quinolones, clindamycin, nitrofurantoin and trimethoprim were all prescribed significantly more frequently in patients with a PenA record (Table 4). As expected, carbapenems and aztreonam were prescribed infrequently. Antibiotic prescribing patterns in the total population are shown in Table S1 and Table S2.

PenA record and health outcomes

Compared with patients without a PenA record, those with a record had significantly increased risk of death in the following year, re-prescription of a new antibiotic class within 28 days and MRSA infection/colonization (Tables 3 and 5, and Table S3). A PenA record

Table 1. Characteristics of patients with and without a PenA record in a sample of antibiotic-treated general practice patients in England

Characteristic	PenA record	No PenA record	Unadjusted OR (95% CI)	Adjusted OR ^a (95% CI)
Overall count	139437 (5.9%)	2211366		
Gender				
male	51754 (4.4%)	1115192	1.00 (ref.)	1.00
female	87683 (7.4%)	1096157	1.72 (1.70–1.74)	1.72 (1.70–1.74)
Age (years)				
18–24	10160 (4.0%)	245248	1.00	1.00
25–34	17611 (4.3%)	390920	1.09 (1.06–1.11)	1.10 (1.07–1.13)
35–44	22321 (5.7%)	373061	1.44 (1.41–1.48)	1.42 (1.38–1.45)
45–54	25760 (6.2%)	392976	1.58 (1.55–1.62)	1.49 (1.45–1.54)
55–64	22205 (6.5%)	318181	1.68 (1.64–1.73)	1.50 (1.46–1.53)
65–74	20338 (7.2%)	263051	1.87 (1.82–1.91)	1.50 (1.46–1.54)
75–100	21042 (8.5%)	227929	2.23 (2.17–2.28)	1.59 (1.55–1.64)
IMD (fifths)				
most deprived	22075 (5.3%)	396076	1.00	1.00
deprived	24618 (5.9%)	393822	1.12 (1.10–1.14)	1.04 (1.02–1.06)
average	27993 (6.7%)	389731	1.29 (1.27–1.31)	1.07 (1.05–1.09)
affluent	27380 (6.6%)	390678	1.26 (1.23–1.28)	1.07 (1.04–1.09)
most affluent	27178 (6.5%)	390902	1.25 (1.22–1.27)	1.07 (1.04–1.10)
unknown	10193 (3.9%)	250157	0.73 (0.71–0.75)	dropped
Practice list size				
0–4999	15656 (5.4%)	275288	1.00	1.00
5000–9999	52556 (5.9%)	834541	1.11 (1.09–1.13)	1.05 (0.98–1.12)
10000–14999	49688 (6.3%)	739903	1.18 (1.16–1.20)	1.17 (1.08–1.26)
15000–19999	15037 (6.2%)	229617	1.15 (1.13–1.18)	1.19 (1.05–1.34)
20000–75000	6285 (4.6%)	129614	0.85 (0.83–0.88)	0.99 (0.84–1.17)
unknown	215 (8.2%)	2403	1.57 (1.37–1.81)	dropped

^aThe adjusted analysis was undertaken with complete cases only, i.e. those with complete data for all covariates.

Table 2. Counts, percentages and ORs of PenA records compared with patient disease registration

Condition	PenA record	No PenA record	Unadjusted OR (95% CI)	Adjusted OR ^a (95% CI)
No conditions	43199 (4.6%)	886940	1.00	1.00
One condition	58041 (5.9%)	929994	1.28 (1.27–1.30)	–
Two conditions	24226 (8.1%)	275509	1.81 (1.78–1.84)	–
Three or more conditions	13971 (10.5%)	118923	2.41 (2.36–2.46)	–
Asthma	25052 (8.9%)	255637	1.68 (1.65–1.70)	1.58 (1.56–1.61)
Cancer	9827 (8.9%)	100723	1.59 (1.56–1.62)	1.18 (1.15–1.21)
CHD	8845 (9.1%)	88748	1.62 (1.58–1.66)	1.23 (1.20–1.26)
CKD	11228 (9.5%)	106585	1.73 (1.69–1.76)	1.18 (1.15–1.21)
COPD	8130 (10.7%)	67587	1.96 (1.92–2.01)	1.41 (1.37–1.45)
Diabetes mellitus	11280 (8.1%)	127784	1.44 (1.41–1.46)	1.18 (1.16–1.21)
PAD	1647 (9.5%)	15712	1.67 (1.59–1.76)	1.16 (1.10–1.22)
Smoker	74720 (6.5%)	1078500	1.21 (1.20–1.23)	1.11 (1.10–1.13)
Stroke	2782 (9.2%)	27591	1.61 (1.55–1.68)	1.15 (1.11–1.20)
TIA	2437 (9.8%)	22328	1.74 (1.67–1.82)	1.19 (1.13–1.24)

^aThe adjusted analysis was undertaken with complete cases only, i.e. those with complete data for all covariates. The analysis adjusted for all variables listed in Tables 1 and 2.

Table 3. Health outcomes in the exact matched cohort of general practice patients, with ($n=130\,571$) and without ($n=1\,892\,835$) a record of PenA

	RR	95% CI	P
Antibiotic prescribing			
any antibiotic	1.05	1.04–1.06	<0.001
Health outcome			
mortality	1.08	1.03–1.14	0.002
CDI	1.22	0.80–1.87	0.359
MRSA	1.90	1.50–2.41	<0.001

Table 4. Antibiotic prescribing patterns in an exact matched cohort of general practice patients, prescribed antibiotics, with and without a record of PenA

	RR	95% CI	P
Antibiotic			
clindamycin	5.47	4.83–6.20	<0.001
macrolide	4.03	3.99–4.08	<0.001
quinolone	2.10	2.02–2.19	<0.001
cephalosporin	2.05	1.99–2.12	<0.001
tetracycline	1.91	1.88–1.94	<0.001
nitrofurantoin	1.09	1.07–1.11	<0.001
trimethoprim	1.04	1.03–1.06	<0.001
penicillin	0.15	0.14–0.15	<0.001
carbapenem	–	–	–
monobactam	–	–	–
Health outcome			
re-prescription of a new antibiotic class within 28 days	1.33	1.31–1.35	<0.001

was associated with 6 in 1000 more deaths and 1 in 1000 more patients with MRSA. There was a non-statistically significant increase in risk of CDI. There were only two patients with VRE records and these were not analysed further. The propensity score-matched sensitivity analysis found equivalent results (data not shown).

Discussion

Key results

A record of PenA affected 1 in 17 general practice patients, with considerable variation between practices. PenA records were associated with increasing age, comorbidity and being female. After matching for demographic factors and comorbidities, a PenA record was associated with more antibiotic prescriptions, a different profile of antibiotic prescribing, a higher rate of re-prescription of a new antibiotic class within 28 days, greater MRSA burden and increased risk of death. There was little evidence of an impact on CDI, when confounding factors were taken into consideration.

Strengths and weaknesses

Use of routinely collected clinical data carries risk of bias, but exact matching was used to reduce this. Such studies are affected by data quality, so we purposefully chose conditions that are included in QOF because they are linked to health services payments and likely to be consistently and well recorded across general practices. There may be conditions that affect PenA recording that we have not included. The main concern with the use of exact matching is bias due to lack of matches; in this study, the matching rate was very high (94%), minimizing risk of bias due to lack of matches.

Drug reactions can be recorded in different ways on SystmOne and hence appear in ResearchOne as either ‘sensitivities’ or ‘allergies’, so they were considered interchangeable in the analysis. This might be an oversimplification, but from GP stakeholder consultations and the literature these terms seemed to be used interchangeably.²³ In addition, when patients move to a new GP there is a potential problem with the correctness and completeness of the data migration process between GP systems with respect to recorded allergies and sensitivities. For example, migration might omit sensitivities or might import at a coarser granularity. The more patient records move between practices, the more they are subject to any issues associated with these migration processes. IMD was not recorded in 11% of patients and this was associated with a lower rate of PenA records; we think that this may relate to patients whose postcodes were missing, invalid or newly assigned, or patients without a permanent residence, but it is possible that it reflects generally poor record keeping. While this might result in an underestimate of the overall prevalence of PenA records, it did not affect the exact matching analysis.

We did not standardize the counting of antibiotic prescriptions to average daily quantities (ADQs), but we were primarily concerned with choice of agent in this analysis, rather than dose-related effects. Methods of testing for, diagnosing and communicating MRSA infection and CDI vary between laboratories, but we could not see any reason why this would have a selective effect on either of our patient groups. We know that there is inconsistency and a lack of consensus on what information is transferred from hospital records to general practice electronic health records. For this reason, we also collected all MRSA-positive results and did not attempt to distinguish between MRSA colonization and infection.

ResearchOne data are likely to be representative of the general population because they came from a large number (400) of general practices in England. The similarity of our findings when compared with recent data from The Health Improvement Network (THIN)¹⁴ provides important validation of the use of these clinical databases in applied research, as these databases are derived from different electronic health record systems.

Prevalence of PenA records

An allergy to penicillin has previously been reported in 4.5%–15.6% of patients, depending on location and population, but none of these studies was based on a general adult population.^{1–4,24,25} Our estimate of prevalence is lower than the NICE estimate of 10%¹ probably because hospital patients are enriched for those with comorbidities. The observed variation in recording of PenA between general practices raises the possibility of under-recording and therefore an underestimate of its prevalence. There are differences in the reported prevalence of PenA between the USA,

Table 5. Health outcomes in the total cohort of general practice patients, with and without a record of PenA

Health outcome	PenA, n=139437	No PenA, n=2211366	P
Re-prescription of a new antibiotic class within 28 days, absolute number (%)	10111 (7.3)	89191 (4.0)	<0.001
Mortality, absolute number (%)	2056 (1.5)	20521 (0.9)	<0.001
CDI, absolute number (%)	26 (0.0)	256 (0.0)	0.027
MRSA, absolute number (%)	95 (0.1)	674 (0.0)	<0.001

which generally reports prevalence of >10%,^{2,3,24} and the UK and Europe where a lower prevalence has been reported,^{4,25} but these studies were often small (single institution) or undertaken in select patient groups. The importance of this figure lies in the number of patients who are likely to have a true allergy to penicillin; probably fewer than 10% of those with a record of PenA.¹ With a 5.9% prevalence of PenA records, an estimated 3 million UK adults are affected.

Patient characteristics associated with a PenA record

Older women with comorbidities were more likely to have a PenA record, while area deprivation (IMD) was associated with a reduced risk. General practice list size also had an effect, with increased records in medium sized practices. Studies that explore the health impacts of penicillin records clearly need to account for these confounding factors. All the factors identified increase the possibility of being prescribed an antibiotic and, presumably, the chance of having a reaction that is recorded as an allergy or sensitivity. All the selected comorbidities that we felt were likely to impact on infection risk were associated with a small, but significant, increased risk of a PenA record. Our assumption of increased infection risk was borne out by higher rates of all antibiotic prescriptions in patients with all the selected conditions (data not shown).

Effects on antibiotic prescribing

Even after matching for age, sex, IMD, smoking and comorbidities (asthma, cancer, CHD, CKD, COPD, diabetes, PAD, stroke and TIA) and prevalence of PenA records at the general practice, a PenA record was associated with altered and increased antibiotic prescribing. In keeping with previous mainly hospital-based studies, macrolides and tetracyclines were the most commonly prescribed antibiotics for patients with a PenA record,²⁶ while the biggest impact (increase in RR) of the record was on clindamycin, tetracyclines and quinolones, similar to a recent primary care-based analysis from the Netherlands, which also found that patients with a PenA record had a higher likelihood of receiving more than one antibiotic prescription (OR=2.56, 95% CI=2.05–3.20).⁷ This raises questions about the relative clinical effectiveness of non-penicillins and the possibility that patients with a PenA record receive less effective agents with more treatment failures. An alternative explanation is that patients with a PenA record are more prone to infection and also treatment failure. We attempted to account for this by controlling for comorbidities that are associated with an increased risk of infection, but the increased rate of antibiotic prescribing remained. Trimethoprim and nitrofurantoin prescribing

were included as a reference point because we initially thought these would not be affected by PenA status. The small, but significant, increase in trimethoprim RR might be accounted for by use in infections other than urinary tract infection (e.g. respiratory tract infections²¹) in patients with a PenA record. Higher rates of nitrofurantoin prescribing in patients with a PenA record may indicate health-seeking behaviour.

Effects on health outcomes

The observed increase in all-cause mortality in patients with a PenA record, even after matching for age, gender and comorbidity, was surprising given the low mortality from infections managed in general practice. Increased mortality has been described previously in a US hospital-based study, which found a 1.6-fold higher risk of dying during hospitalization associated with a PenA record (crude OR=1.56, 95% CI=1.20–2.04),²⁷ and it has been suggested that a PenA record might result in suboptimal therapy, particularly for hospitalized patients, where, for example, penicillins are considered treatment of choice for *Staphylococcus aureus* bloodstream infection.

Healthcare-associated infection pathogens

MRSA and CDI rates were low, as would be expected in a general practice population, but the risk of MRSA colonization/infection was higher among those with a PenA record. There were no records of VRE, confirming this as a pathogen whose relevance is currently restricted to secondary care. A recent study using THIN, a UK electronic health record database of general practice patients, also found an increased risk of MRSA in patients with a PenA of similar magnitude (multivariable adjusted HR=1.69).¹⁴ In the USA, penicillin-allergic hospital patients were found to have 23.4% (95% CI=15.6%–31.7%) more *C. difficile*, 14.1% (95% CI=7.1%–21.6%) more MRSA and 30.1% (95% CI=12.5%–50.4%) more VRE infections than expected compared with control subjects.³ Many factors affect the risk of MRSA infection, including antibiotic prescribing practices.²⁸ Observational studies show an association between MRSA colonization/infection and various classes of antibiotics: cephalosporins,^{11,12} carbapenems,¹³ clindamycin¹³ and fluoroquinolones,¹² so there is a plausible, potential mechanism for the increased risk. The THIN analysis found that half the increased risk of MRSA was mediated through fluoroquinolone, clindamycin and macrolide prescribing. While we saw a non-statistically significant increased risk of CDI in patients with a PenA (RR=1.22), the THIN analysis found a significantly increased risk of

CDI (adjusted HR=1.26), perhaps because of the longitudinal nature of that study allowing longer follow-up for each patient.¹⁴

Penicillin prescribing

Patients who report a PenA are not usually prescribed penicillins⁵ so finding that nearly 1 in 25 patients with a PenA record had been prescribed a penicillin, subsequent to the date of their allergy record, was unexpected. Possible explanations include: data entry errors or GPs consciously 'overruling' PenA alerts, perhaps because a patient may have an allergy to a specific agent, but can tolerate other penicillins. Re-prescription of a new antibiotic class within 28 days was associated with a PenA record; this has been used a marker of treatment response failure in some studies, but there are other explanations for why this may have occurred; for example, it is possible that patients returned when they noticed a penicillin had been prescribed, or experienced an adverse reaction or were non-compliant.

Conclusions

The prevalence of PenA records in adults in general practice suggests that there are 3 million affected patients in the UK. Identifying patients without a current PenA (e.g. by a pre-emptive PenA testing strategy) has the potential to improve antibiotic prescribing, enabling more patients to receive first-line therapy for infections. This antimicrobial stewardship strategy has potential to improve clinical outcomes and help contain antibiotic resistance. Current services are unlikely to cope with the increased demand that additional testing would require so service provision needs to be reviewed; a safe streamlined testing pathway is under evaluation to avoid overburdening the existing allergy service.

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Transparency declarations

C. C. B. is an NIHR Senior Investigator. C. B. is employed by TPP, the company that owns the SystmOne electronic health record system. All other authors: none to declare.

Supplementary data

Codes used for data extraction and Tables S1 to S3 are available as [Supplementary data](#) at JAC Online.

References

- NICE. *Drug Allergy: Diagnosis and Management of Drug Allergy in Adults, Children and Young People*. NICE Clinical Guideline 183. 2014.
- Macy E, Poon K-YT. Self-reported antibiotic allergy incidence and prevalence: age and sex effects. *Am J Med* 2009; **122**: 778.e1–7.
- Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin 'allergy' in hospitalized patients: a cohort study. *J Allergy Clin Immunol* 2014; **133**: 790–6.
- Borch JE, Andersen KE, Bindslev-Jensen C. The prevalence of suspected and challenge-verified penicillin allergy in a university hospital population. *Basic Clin Pharmacol Toxicol* 2006; **98**: 357–62.
- Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. *JAMA* 2001; **285**: 2498–505.
- Trubiano JA, Adkinson NF, Phillips EJ. Penicillin allergy is not necessarily forever. *JAMA* 2017; **318**: 82–3.
- Su T, Broekhuizen BDL, Verheij TJM et al. The impact of penicillin allergy labels on antibiotic and health care use in primary care: a retrospective cohort study. *Clin Transl Allergy* 2017; **7**: 18.
- Schembri S, Williamson PA, Short PM et al. Cardiovascular events after clarithromycin use in lower respiratory tract infections: analysis of two prospective cohort studies. *BMJ* 2013; **346**: f1235.
- Ray WA, Murray KT, Hall K et al. Azithromycin and the risk of cardiovascular death. *N Engl J Med* 2012; **366**: 1881–90.
- Svanstrom H, Pasternak B, Hviid A. Use of azithromycin and death from cardiovascular causes. *N Engl J Med* 2013; **368**: 1704–12.
- Fukatsu K, Saito H, Matsuda T et al. Influences of type and duration of antimicrobial prophylaxis on an outbreak of methicillin-resistant *Staphylococcus aureus* and on the incidence of wound infection. *Arch Surg* 1997; **132**: 1320–5.
- Crowcroft NS, Ronveaux O, Monnet DL et al. Methicillin-resistant *Staphylococcus aureus* and antimicrobial use in Belgian hospitals. *Infect Control Hosp Epidemiol* 1999; **20**: 31–6.
- Landman D, Chockalingam M, Quale JM. Reduction in the incidence of methicillin-resistant *Staphylococcus aureus* and ceftazidime-resistant *Klebsiella pneumoniae* following changes in a hospital antibiotic formulary. *Clin Infect Dis* 1999; **28**: 1062–6.
- Blumenthal KG, Lu N, Zhang Y et al. Risk of methicillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study. *BMJ* 2018; **361**: k2400.
- Wanat M, Anthierens S, Butler CC et al. Patient and prescriber views of penicillin allergy testing and subsequent antibiotic use: a rapid review. *Antibiotics (Basel)* 2018; **7**: 71.
- TPP. *ResearchOne: Transforming Data into Knowledge*. <http://www.researchone.org/systmone-user-faqs/>.
- Clegg A, Bates C, Young J et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing* 2016; **45**: 353–60.
- Department for Communities and Local Government. The English Index of Multiple Deprivation (IMD) 2015 – Guidance. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/464430/English_Index_of_Multiple_Deprivation_2015_-_Guidance.pdf.
- HSCIC. *Quality and Outcomes Framework*. <https://qof.digital.nhs.uk>.
- NHS Digital. *UK Read Code*. <https://data.gov.uk/dataset/f262aa32-9c4e-44f1-99eb-4900deada7a4/uk-read-code>.
- Currie CJ, Berni E, Jenkins-Jones S et al. Antibiotic treatment failure in four common infections in UK primary care 1991–2012: longitudinal analysis. *BMJ* 2014; **349**: g5493.
- Pearce N. Analysis of matched case-control studies. *BMJ* 2016; **352**: i969.
- Inglis JM, Caughey GE, Smith W et al. Documentation of penicillin adverse drug reactions in electronic health records: inconsistent use of allergy and intolerance labels. *Intern Med J* 2017; **47**: 1292–7.

- 24** Zhou L, Dhopeswarkar N, Blumenthal KG *et al.* Drug allergies documented in electronic health records of a large healthcare system. *Allergy* 2016; **71**: 1305–13.
- 25** Kerr JR. Penicillin allergy: a study of incidence as reported by patients. *Br J Clin Pract* 1994; **48**: 5–7.
- 26** Harris AD, Sauberman L, Kabbash L *et al.* Penicillin skin testing: a way to optimize antibiotic utilization. *Am J Med* 1999; **107**: 166–8.
- 27** Charneski L, Deshpande G, Smith SW. Impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients. *Pharmacotherapy* 2011; **31**: 742–7.
- 28** Monnet DL. Methicillin-resistant *Staphylococcus aureus* and its relationship to antimicrobial use: possible implications for control. *Infect Control Hosp Epidemiol* 1998; **19**: 552–9.

Supplementary data

Count	of Patients	with Patients without penicillin allergy
prescriptions/patient	penicillin record (%)	record (%)
0	86777 (62.2)	1624580 (73.5)
1	22197 (15.9)	288889 (13.1)
2	12263 (8.8)	136442 (6.2)
3	6086 (4.4)	60732 (2.8)
4	3633 (2.6)	34766 (1.6)
5	2268 (1.6)	19235 (0.9)
6	1520 (1.1)	12742 (0.6)
7	1059 (0.8)	8081 (0.4)
8	714 (0.5)	5480 (0.3)
9	535 (0.4)	3712 (0.2)
10	376 (0.3)	2789 (0.1)
11	296 (0.2)	2257 (0.1)
12	277 (0.2)	1990 (0.1)
13 or more	1436 (1.0)	9671 (0.4)
Mean No. antibiotic prescriptions (SD)	1.1 (2.9)	0.9 (2.5)

Table S1. Counts of antibiotic prescriptions in patients with and without a penicillin allergy record for the total, unmatched cohort of adult general practice patients.

Antibiotic class	Penicillin allergy record (%)	No penicillin allergy	p
Macrolide	30092 (21.6)	82770 (3.7)	<0.001
Tetracycline	15132 (10.9)	84890 (3.8)	<0.001
Nitrofurantoin	14450 (10.4)	132297 (5.9)	<0.001
Trimethoprim	10769 (7.7)	102778 (4.7)	<0.001
Penicillin	5866 (4.2)	420868 (19.0)	<0.001
Cephalosporin	4575 (3.3)	22997 (1.0)	<0.001
Quinolone	3703 (2.7)	19569 (0.9)	<0.001
Clindamycin	478 (0.3)	995 (0.0)	<0.001
Carbapenem	2 (0.0)	17 (0.0)	0.717
Monobactam	0 (0.0)	1(0.0)	1.000

Table S2. Number of patients with and without a record of penicillin allergy who were prescribed specified antibiotic classes/agents at least once during 2012-13.

	Penicillin allergy record	No penicillin allergy record
Health outcomes, absolute number (%)		
Mortality	1578 (1.2%)	11,300 (0.6%)
CDI	23 (0.0)	142 (0.0)
MRSA	78 (0.1)	422 (0.0)

Table S3. Health outcomes in the exact-matched cohort of general practice patients, with (n= 130571) and without (n= 1,892,835) a record of penicillin allergy. CDI, *Clostridioides difficile* infection. MRSA, Methicillin resistant *Staphylococcus aureus*.

Codes used for data extract

Comorbidity

Defined using clinical codes within Clinical Terms Version 3 (CTV3).

Asthma

c64u., c13K., c61e., c66U., c65Z., c14g., c195., c619., c11y., c64G., cA15., c648., c1D4., c41h., c531., c51B., x00z6, c251., c66F., c668., c612., c33z., c14x., c61W., c434., c71g., ck15., c66f., c43u., c66A., c41a., ck12., c13B., c64N., c1Cz., c1B., c31z., c13T., g221., x00Av, x00Aw, c43g., c66a., c61H., c221., c64., c41e., x00Af, c65C., c1b., c11e., c1E5., c732., c51w., c11o., c68., c41A., c1c1., c123., c663., c67y., c645., c74., c622., c312., c119., c112., c61A., c43h., c43q., H33z., H33z1, H33z0, c61w., c715., Xa0lZ, c151., x00l3, c61a., x00l0, c66J., c71b., c11i., c13O., c199., c13a., c1Dv., c64b., c134., cA21., c25z., c65U., c146., c13f., c61h., c14j., c652., c691., c31D., c11d., c64p., g24., c13F., c1EE., c71k., ck11., c41b., c747., c125., c65A., c66E., c14c., c13x., c61Z., c65g., c13g., c331., c224., c62., c43c., c66e., XE0ZP, c667., XE0ZR, c43r., XE0ZT, c13X., c61z., c65G., c61T., XaLPE, c1Cy., c1C., c12x., c1B3., c61S., c617., c11c., x02lG, g22., c13A., c64l., c719., x01EJ, c671., x01EG, x01EF, c1b3., c13S., c61s., c1C4., c647., c1D6., x01Ek, x01Ej, c11D., c67z., c11j., c1E1., c416., c14v., c61M., c43d., c43z., c13d., c41B., c116., c15y., c66N., c1EC., c316., H330z, c61m., c65R., c13e., c1cz., c19A., c621., c642., c154., c25v., c43m., c66W., c61F., c681., c65l., c142., c13j., c61t., c1Dy., c12w., x029g, H3301, H3300, c736., c61f., c11x., cA13., c41f., H330., c13J., c64F., c1D., c194., c51A., c11q., cA14., c319., c64m., c133., cA22., c252., c66l., c1C7., c41i., c33y., c64M., c193., c14y., x00bV, x00bU, c11g., c1B4., c61P., ck14., c71f., c43v., c1Dz., c658., c721., c31u., c13E., c13w., c65d., c149., c71a., c1E4., c13W., c66T., c65c., c65D., c51v., c11n., c65J., c432., c662., c143., c14b., c14r., c614., H33., c644., H3311, c672., c11z., c118., c1C3.,

c1C8., c43i., c111., c1D2., c25., c14f., x05Fg, c13y., c65M., c1b4., c13n., c61p., c61B., x05Fh, c418., XE0YQ, XE0YS, XE0YR, XE0YU, XE0YT, XE0YW, XE0YV, cA1z., XE0YX, c653., c66M., c64h., c13N., c61b., Ua1AX, c124., c65V., c147., c13i., c64a., c64E., c61i., c692., c643., c14k., c1D1., c684., cA2., c13l., c64A., c197., c65X., x01Cq, x01Cs, x01Cr, x01Cm, c744., c1cy., x01Ck, c14e., x05kq, c41j., c11., c198., c126., c43., c227., c731., c66d., c226., c71e., c666., H3120, c12z., c15., c13r., c31x., X101t, c71j., c148., c1Dw., c12y., c11b., c1E9., c64H., c13Y., c13., c222., c65L., c718., c13R., c144., c656., c31., c669., c438., c67., c19., c14w., X101y, c69., cA., c43e., c115., c61N., x0019, c41C., c437., c661., c1EB., c657., c411., c311., c73., c61n., c25x., c66Q., c33., c61G., H33zz, c153., c431., c43n., c66V., c1E., c64e., c61R., c61u., c25w., c713., c415., c13m., H3310, c735., c61g., c14z., x00zz, cA12., c31C., c51G., c14a., c64k., H331., c13M., c132., c318., c51n., c65S., c412., c64l., c66H., x00zA, c315., c253., c62x., c11p., c8b., c14h., g25., c41m., c33x., c192., H331z, c11f., c64L., c66h., c71i., c61Q., c66Y., c137., c741., x00Hy, x00Hx, x00Hz, c254., c333., c659., c66C., c31t., c13D., c722., c69z., c43w., c65e., c13v., c61X., c61J., ck1., Xa9zf, c43a., c66c., c72z., c1E7., c1E3., c65E., c13V., c61x., c313., c13q., c64y., c66S., c121., c665., c11m., c64K., c1c3., c14s., 173A., c66X., c65N., c419., c13Q., c673., c1C2., c62z., c414., c64w., c11w., Xa1hD, x01NO, x01Cl, c14t., c1D3., c61q., x00QV, c43j., c66Z., x00QU, c61C., c1cx., c66L., cA1y., c654., c41c., c65P., c64o., c13c., c61c., c13h., c61j., c71., c13o., X102D, c61D., c43A., c314., c341., c136., c683., c13H., x00CE, c196., H332., c65Y., c13z., c61d., c64v., c745., X1024, c66D., c31F., X1020, X1021, X1022, c41k., c131., cA16., c649., c51C., c43s., c66G., c51D., c742., c71d., c1Du., c19z., c66g., c61V., c43t., c65b., c1B1., c65W., ck13., c65H., c611., c51H., c1E8., c13C., c65B., c1b1., c13U., c61O., c439., c1E6., c11h., c1c., c13Z., x00gE, c51x., x00gG, x025g, c43f., c114., c67x., c117., x025h, x025i, x025j, c51E., c623., c31A., c25y., x00gF, c66P., c1EA., c1C1., XM0s2, c43o., c113., c152., c1C6., c64i., c65K., c64d.,

c31G., c13l., c61v., c1..., c734., c15z., c51F., x00l4, x00l2, cA11., c31B., x00l1, c64j., c13L., c64c., c135., c145., x02LJ, c65T., c651., c66K., c122., c14i., c342., x05Fi, c31E., g22z., c13G., c723., c191., c71h., ck16., c43y., c746., c255., c66B., c332., c41d., c12..., c65f., c733., c31w., c61Y., x006b, c43p., c43b., c66b., c433., c61K., c71c., X101u, c65F., c11a., c1E2., c613., c141., c61y., X101x, X101z, c64x., x0100, c14.., c1Dx., c13p., c11v., c436., Xaa7B, c413., c1B2., c61E., c1c2., c664., c64J., c66R., c616., c62y., c41g., c13P., c61r., c716., c1b2., c69y., c1C5., c1D5., c435., c14u., c11k., c61L., c717., c31v., c43k., c317., c1ED., c655., c65Q., c61l., c64n., c51i., c19B., c43x., c43B., c711., c417., c65O., c72y., c65a., c139., cA1.., c641., c61k., c41.., c682., c64g.

Cancer

B23.., B6162, B6163, XE2vT, B6161, XE2vR, B6168, XE2vP, XE2vQ, XE2vN, XE2vO, B616., B485., B545z, X78fN, X78fO, XE2vj, X78fK, X78fH, XE2vi, B6160, B44z., B6016, B6017, B6014, B6015, B6012, B6013, B6010, B6011, B601z, B6018, B6167, B21y., B6164, B601., B6165, B5452, B5451, B5450, XM00E, B545., B135., B68z., X78TD, X78TE, X78TF, X78TG, Xa0l6, X78TC, B241., B51z., X77nT, X77nQ, B053., B506., B45z., B4z.., B541., X78T4, B59z., X78T3, X78T8, X78T9, X78kT, X77nk, X77nj, B110., B1101, B1100, B47z., B161z, B511., B040., B937W, B074., X78fl, B110z, B1611, B1610, B1613, B1612, B161., B616z, B453., B172., B584., Byu4., Byu41, Byu43, Byu42, B56y., XaYdL, B471., B440., B143., Xa3HG, B66.., B46.., B350z, B200z, B11y., B42.., B44.., B344., B11y0, B11y1, XaYeq, B350., B6..., B3501, B3500, B671., B2001, B2000, B2003, B2002, B11yz, B200., B4A4., Xa0KG, B6023, B6022, X78e9, B6020, B6027, B6026, B6025, B6024, X78e2, B565z, X78e6, XaA0C, B602., Xa9EA, B615., B662., B6157, B6156, B544., B6154, B6153, B6152, B6151, B6150, B6158, B6531, X78es, B602z, B005., X78ek, X78ej, X78ei, X78eh, X78el, X78eg, X78ef, X78eY, X78eV, X78eH, X78eL, B4..., B615z, X78eE, B505., B48.., XE1wv, B052., B111z, B512z, B68y., XE1wn, Xa0ay,

X78SS, X78SU, X78ST, B111., B1110, B1111, B60y., XaB1i, XaB1h, XaB1b, B5121, B5120, XaB1g, XaB1e, B934., B041., X78Se, X78Sd, X78Sg, X78Sf, X78Si, X78Sh, X78Sk, X78Sj, B14., Byu5B, Byu5A, X78OK, B67y., B67y0, X78OW, Xa0TY, X78OP, B305z, X78OX, B064z, B305D, B305A, B305C, B305B, B160., X78Oz, B305., B332z, B3059, B3058, B3055, B3054, B3057, B3056, B3051, B3050, B3053, B3052, B173., XaDc9, XaDc8, XaDc7, XaDc6, XaDc5, Byu5., B0640, Byu52, Byu53, Byu50, Byu51, Byu56, Byu57, Byu54, Byu55, B452., Byu59, XM0pb, B561z, B4700, B4701, XM0ps, B470., B5810, XM0pv, B142., Xa0TF, B441., B327z, Xa0TD, XM0pZ, Xa0TE, B18., B5610, B5613, B5612, B5615, B5614, B470z, B5616, B05z0, B347., B17z., B05z., B561., B3275, B3274, B3277, B3276, B3271, B3270, B3273, B3272, B006., B3279, B3278, B681., B11z., B327., Xa9AP, B572., Xa0Dr, Xa9AA, Xa9AM, Xa9AN, Xa9AO, B670., B2012, B2013, XaELM, XaELL, XaELK, XaELJ, XaELI, Xa9Aa, Xa0Ti, B201., B614z, B1z1., XaMeL, XE2t9, Xa9A0, Xaa1P, B614., B6140, B6141, B6142, B6143, B6144, B6145, B6146, B543., B6148, Xa36e, X78RR, X78RS, X78RP, X78RV, X78RT, X78RU, B6108, B6260, B065., B22., B554., B504., B6268, X78dW, B16z., B22z., XaJM3, B610., B3371, B14z., B66z., XaE6L, B112., X20FX, B513., XaBBP, B072z, B60z., X78hl, X78hn, Xa3AG, B072., B073z, B0720, B0721, B20y., B163., B304z, B304., X78IW, B224z, B3044, B3042, B3043, B3040, B3041, Byu6., Xa84V, X78N6, X78N1, B170., X78NG, X78NB, X78NL, Byu8., B2241, B2240, B224., Byu81, Byu80, B6021, Byu82, XaDbr, B613z, B141., X78ap, B5602, B5603, B5600, B5601, B5606, B5607, B5604, B5605, B5608, XaB1p, B346., Xalt4, B560., B3264, B3265, B3262, B3263, B3260, B3261, B503., B1z., B682., B326., B50., B573., XSA0M, B202., B35., B326z, B44y., B673., B495., X78cQ, X78cP, X78cS, X78cR, B25., X78cT, Xa3eR, Xa3eS, Xa3eP, Xa3eQ, Xa3eT, Xa3eU, X78ci, B5420, B5421, B660., Xa3eF, Xa3eG, Xa3eJ, Xa3eK, Xa3eH, Xa3el, Xa3eN, Xa3eO, Xa3eL, Xa3eM, B5609, B138., B31z0, B542z, XM1QO, B555., ByuA2,

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B6225, B6224, B6227, B6226, B493., XE1y7, B16..., B622., B553z, Xa0GA, B34..., B512., Xa0Ei, B6134, B6137, B622z, B6131, B480., Xa0TG, B6132, B6138, B553., B5530, B5531, B5532, Xa0Eq, B613., B083., Xa97v, Xa97w, Xa97t, Xa97u, Xa97r, Xa97s, Xa97p, Xa97q, B4A..., Xa97z, Xa97x, Xa97y, Xa0EY, ByuD9, B03y., B5500, Xa97o, B64y2, B123., B64y0, B64y1, B64y., B241z, B522., Xa0ik, Xa1qs, Xa9FE, Xa9FD, B4y..., X78kl, Xa9FC, X78kn, X78ka, X78kc, X78kb, X78ke, X78kd, X78kg, X78kf, X78ky, X78kx, X78kz, X78kq, X78kp, X78ks, X78kr, X78kw, X78kv, XM00F, B0730, B43y., B2412, B2413, B2410, B2411, X78kY, X78kX, X78kZ, X78kS, X78kU, B130., X78kV, B104., B49z., B3z..., X78Y6, B1503, X78Y1, B054., Xa99n, X78YK, X78YR, X78YP, X78gr, X78Yb, B2z0., B432., X78Yz, X78Yy, X78Yx, B5812, B5811, XaBAx, XaBAp, XaBAw, XaBAu, B015., XaBAk, XaBAo, XaBAn, XaBAm, XaBAI, Xa36T, B581., B316., Xa36m, Xa36k, Xa36h, B487., Xa36d, Xa36c, Xa36b, Xa36a, Xa3A8, Xa3A9, Xa3A6, Xa3A7, Xa3A4, Xa3A5, Xa36r, B59..., Xa3AJ, Xa3AK, Xa3AH, Xa3AI, Xa3AF, B581z, Xa3AD, Xa3AE, Xa3AB, Xa3AC, XaBA5, Xa3AA, XaZdD, XaZdF, B52z., B24z., B62y0, B67..., XaZdn, Xa0Dj, B3114, Xa0Di, B62y4, B47..., B302z, Xa0Dd, XaYj0, XE1x9, B2..., XaYj4, XE1x3, X78HT, XE1x1, XE1x7, XE1x5, B3111, B3112, X00ZB, B43..., B5821, Xa0DF, Xa0DG, Xa0DX, B330., Xa0DP, B1z1z, B63y., B45..., XE1xj, XE1xh, XaYje, XE1xn, XE1xl, XE1xb, XE1xf, XE1xd, XE1xz, XE1xx, B492., XE1xr, XE1xp, XE1xv, XE1xt, B630., XE1xJ, XE1xH, XE1xN, B21..., XE1xL, XaYjl, XE1xB, B020., Xa0Rp, XE1xF, XE1xD, B1z11, XE1xZ, Xa0Rn, XE1xX, Xa0Ri, Xa0Rk, XE1xR, XE1xP, XE1xV, B6300, XE1xT, B6126, B6127, B6124, X78ji, B182., B6123, B6120, B6121, B6128, X78je, B080., X78jy, B612., B481., X78jJ, B67yz, XaEJe, XaEJg, XaEJf, XaEJi, XaEJh, B57..., B612z, B122., B340., B55..., X78j2, X78j3, X78j1, X78j7, X78j4, B10z., B00z0, XM1FM, B620z, B23y., X78g0, X78XA, B49..., X78XD, B514., X78XH, B0641, Xa8Jb, X78XN, X78XO, C333z, B62z1, B62z0, B62z3, B62z2, B62z5, B62z4, X78Xf, X78Xg, X78Xh, B64z., X78Xq, B131., B064.,

B242., X78Xw, X78Xx, X78Xy, B62z., C333., B103., XE1vY, XaYv2, C3331, C3330, C3332, Byu58, XaBBZ, Xa1ne, Xa1na, Xa1nb, X78X8, X78X9, B057., XE11b, Xa3BI, Xa3BH, Xa3BN, Xa3BM, Xa3BL, Xa3BG, Xa3BF, B08y., Xa3BZ, Xa3BX, B517z, B34y0, X78b8, B34y., Xa3Bc, Xa3Bb, Xa3Ba, Xa3Bd, B431., B114., Xa0SY, B014., B580., B34yz, B431z, XM0pq, B5y., XE1yp, XE1yr, XE1yx, XE1yz, XE1yd, XE1yf, XE1yb, B222z, XE1yl, XE1yn, Xa39z, B444., XE1yj, B231., XE1yT, XE1yV, XE1yP, XE1yR, B6206, XE1yX, XE1yZ, XE1yD, XE1yF, B61z8, B61z6, B61z7, B61z4, B61z5, B61z2, B61z3, B61z0, B61z1, XE1y5, B222., XE1y1, XE1y3, XE1y9, XaYk0, B13y., B2221, B2220, B48yz, Xa0U5, B50y., B642., B3y., B611z, Xa0G9, B00zz, B3400, B3401, B2131, B2130, B2133, B2132, B1z0., B58y8, XM1FE, B213., B58y3, B58y2, B58y1, B58y0, B58y7, B58y6, B58y5, B58y4, B6113, B6112, B6111, B6110, B6117, B6116, B6115, B6114, B2zy., B6118, Xa0Ge, B081., B611., B486., B213z, B620., B340z, B6207, B58yz, B6205, B6204, B6203, B6202, B6201, B6200, B0zy., Xa0GN, B204., B6208, B60., X78i2, X78i1, Xa1oQ, B5101, K5510, Xa99z, X30L8, B5103, X30L7, B5617, B5242, B5243, B5240, B5241, B5246, B64., B5244, B5245, B5619, Xa0ko, G753., B5618, B10y., X78iu, X78it, X78ip, B243., X78if, X78id, XaEY9, X78io, Xa99w, X78Uq, X78iC, B136., C332., B45y0, B102., B12z., B45y., B430z, X78IR, B65., Xa34D, B5011, B5010, B18z., B056., X78b1, B501., B524., X78WM, X78WO, X78WN, X78WF, C332z, X78WT, X78WQ, X78WP, X78WS, X78WR, X78Wm, X78WI, X78Wo, X78Wn, X78Wi, X78Wh, X78Wk, X78Wj, B4300, B4301, B4302, B4303, B115., X78Wy, B430., X78Wz, Xa0S9, B017., B3370, Byu12, Byu13, Byu10, Byu11, Byu1., B314., B0z0., B3372, B587., B1zz., B00., B48y., B02., B6z0., B314z, B590., B230., B309., B223., B1..., B332., X78bU, X00eS, B3321, B3320, B2230, B2231, Xa0T8, Xa0T9, B35z., Xa0T2, Xa0T3, Xa0T0, Xa0T1, Xa0T7, Xa0T4, Xa0T5, B692., B35z0, Xa0TZ, Xa0TX, B565., Xa0TS, Xa0TP, Xa0TH, Xa0TI, B223z, Xa0TM, B5654, Xa0TA, B5651, B5650, B5653, B5652, Xa0Tr, B022.,

Xa0Tt, Xa0Tu, Xa0Tj, Xa0Tk, Xa0Th, B35zz, B212., Xa0To, B343., B1800, B1801, B1802, Xa9EH, B6104, B6105, B6106, B6107, B6100, B6101, B6102, B6103, X78ha, XE2xB, X78hk, B33y., X78hm, B180., X78hS, B674., B621., B6210, B6211, B6212, B6213, B6214, B6215, B6216, B6217, B6218, B0zz., X78h0, X78h1, B610z, X78h7, B6512, B180z, B51y0, B07z., B621z, B2010, XaFsw, B0z1., X78VL, B2011, X78VK, Xa3rj, X78VT, X78VS, B500z, X78VQ, X78Vm, X78Vj, XE1yL, X78Vi, X78JV, B62x., B137., B18yz, B101., Xa0jn, B5000, B5001, B5002, B5003, C331., B18y., B0511, B0510, XaKWz, B0512, X00eT, B5151, B051., B18y6, B18y5, B18y4, B18y3, B18y2, B18y1, B18y0, B6135, B315z, Xa0bJ, B6136, B3..., B6130, B010., B6133, B116., X78IL, B042., B016., B3150, B3151, B3152, B3153, Byu25, Byu24, B586., Byu2., B073., B22y., XaYii, XaYij, XaYil, XaYim, XaYin, B220z, B52y., B442., B591., B333z, XaYis, Xa0WG, XaYil, B3088, B3089, XaYiL, XaYiN, B3082, B3083, B3080, B3081, B3086, B174., B3084, B3085, B308., B4510, B201z, B220., B333., B3330, B3331, B3332, B3333, B3334, B3335, B308B, B308C, B2201, B308A, B0732, XaYi5, B308D, B308z, XaEGU, XaPQD, B691., B451z, B564., XaFrK, XaFrH, XaFrl, XaFrN, XaFrL, XaFrM, B211., XaFrF, XaFrG, XaFrD, XaFrE, XaFrR, XaFrS, XaFrQ, B5642, XaFrT, B5641, XaFrj, XaFrk, XaFrh, XaFri, XaFrn, XaFro, XaFrl, XaFrm, XaFrc, XaYgm, XaFrf, XaFrg, XaFrd, XaFre, XaFrz, B342., XaFry, XaFrr, XaFrs, XaFrp, XaFrq, XaFrv, XaFrw, XaFrt, XaFru, Xaa1N, B6147, B33z., B564z, XaFr8, XaFr6, XaFr7, XaFr4, XaFr5, B6005, B6004, B6007, B6006, B6001, B6000, B6003, B6002, X78g1, B6008, B23z., X78g2, B515z, B600., B21z., B6166, B06..., XaC1Q, B51yz, B501z, B134., X78gq, X78gp, X78gs, B600z, X78gd, B53..., X78ga, B48z., X78gc, X78gb, B62y8, X78gY, B51y., B62y1, B62y2, B62y3, X78gQ, B62y5, X78gS, B62y7, X78gM, X78gL, X78gO, X78gN, X78gK, B51y1, X78gA, B100., B507., XE209, XE1yN, XE201, XE203, XE205, XE207, B02y., B510z, B16y., B050., X78U7, B117., XE1yH, B210., B34z., XE20H, XE20J, XE20N, B5105, XE20B, XE20D, B5100, XE20F,

B5102, XE20X, B510., B41..., XE20T, XE20V, X78Ut, B62y., X78Ig, B450z, B3356, B04z., Xa3EW, B443., B3141, B6z..., B592., B651z, B450., B175., B585., Byu3., Xa3Ec, Xa3Ea, Byu30, Byu31, Byu32, Byu33, Xa3En, B4500, B4501, Xa059, B64yz, B2210, B2211, X78kh, B690., X78kk, B221., B00y., B31..., B221z, B33..., XaBmX, B55z., B345., Xa05A

Coronary Heart Disease

G33z., X2009, X2008, XaEgZ, X2007, X2006, G33z2, G35..., G31..., G30z., Ua1eH, XalwM, XE0WC, XE0WA, XE0WG, XE0WE, G307., XalwY, G351., XaINf, XaJX0, X200a, X200Z, X200Y, X200X, Xalf1, X200S, X200R, X200Q, X200P, X200W, X200V, X200U, X200T, X200K, X200J, X200I, X200H, X200O, X200N, X200M, X200L, X200C, Xa1dR, X200A, Xa1dP, X200G, G304., X200E, X200D, G30yz, G311., G350., G3..., G33..., Gyu35, Gyu34, Gyu36, Gyu30, Gyu33, Gyu32, G3110, XM0rN, G343., G305., G33z0, G33z1, G30y2, G34yz, XaD2h, XaD2i, G30y0, G30y1, XaD2b, XaD2d, XaD2e, XaD2f, XE2uV, G30y., G311z, G353., XaD2g, Xa1dQ, G34y., XSDT6, G34y1, G302., G340., G3401, G3400, G31yz, G303., XaYYq, G300., G308., Xa7nH, G312., XaAzi, G31y1, G31y0, G31y2, G3y..., G3z..., G301., G3010, G3011, G30..., XaG1Q, XE0Ui, XE0Uh, XE2aA, Xa0YL, G330z, XaAC3, XaFsH, XaFsG, G34z., XaEXt, G301z, G34..., G3300, G330., G306.

Chronic Kidney Disease

XaO3s, XaLHG, XaLHJ, XaO3t, XaLHH, XaLHI, XaO41, XaO40, XaNbo, XaO3x, XaO3y, XaO3z, XaLHK, XaO3p, XaO3q, XaO3r, XaO42, XaNbn, XaO3u, XaO3v, XaO3w

Chronic Obstructive Pulmonary Disease

H313., H31yz, X102z, H582., H311., X101n, X101r, H32z., H32..., H30z., H31..., H4641, H321., H31z., XE0ZN, H312z, H310z, X101l, XaZd1, H3y0., XE0YM, H322., XaEIW, H3z..., XaIND, H320z, H32yz, H3..., XaEIV, XE0YP, H3201, H32y., XaEIY, X101m, H3202, X101o, H310., X101i, X101k, H31y1, H31y., H3122, H3121, X101q, H32y0, H32y2, X101j,

H311z, XE0YL, XE0YO, XE0YN, H320., XaN4a, Hyu30, Hyu31, H3200, Xaa7C, Xa35l, H4640, H3y., X101p

Diabetes

XaFmK, X40JS, X40JA, XaFmM, XaFmL, XaEnq, Xa4g7, XaFmA, XalzM, X40JZ, X40JY, XalzN, XalzQ, XalzR, XaOPu, XaOPt, XaEno, XaEnn, X40JO, C10., XaJIL, X40JJ, X40JI, C1011, C1096, C1097, XaFWG, C1095, XaF04, C1093, XaKyX, C1091, C1031, XaKyW, XaJIR, XaFWI, XaJQp, C1090, XaJIM, XaFn8, XaELP, XaFn7, XaMzl, XaELQ, XSETp, X008t, XM1Xk, XaFn9, X40J5, Xalrf, XaEnp, X40JG, C1086, C1030, C1092, C1094, XaJUI, XaF05, C1085, X40J6, C1087, X40J4, C1081, C1080, C1083, C1082, C1089, C1088, C1010, XaFm8, XSETH, XSETK, XaJSr, X40JC, X40JB

Peripheral Arterial Disease

G73z., XE0VP, XE0VR, Xa0IV, Gyu74, XaZJa

Smoker

Ub1tW, Ub1tV, Ub1tU, Ub1tT, Ub1tS, Ub1tR, 137J., XaQ8V, 1373., 137N., 137Q., 137H., XE0ol, 137P., 137T., Ub1tK, Ub1tJ, Ub1tl, 1379., 137F., 137D., 1378., Xallu, XaWNE, 1375., XaluQ, 137B., 137K., Xaltg, Xa1bv, XE0or, XE0oq, XE0op, 1372., XE0ok, 1374., XE0oi, XE0oo, XE0on, XE0om, 137C., XE0oj, XaBSp, XalkW, 137A., XalkX, XalkY, XaJX2, 137G., 137R., 1377., Ub1na, XaLQh, 1376., 137M., 137O., 137Z., Ub0p2, Ub0p3, Ub0p1, XaZIE

Stroke

XaB4Z, Xa0Bj, G64z., G61z., G610., G66., G618., G611., G668., X00D1, X00D3, X00D5, X00D4, X00D7, X00D6, X00D9, X00D8, XaQbK, XaQbM, Xa00R, Xa00P, Xa00Q, Xa6YV, G661., Xa00N, Xa00O, Xa00L, Xa00M, Xa00J, Xa00K, Xa00I, XaEGq, G612., G63y0, G63y1, X00DA, X00DC, X00DB, X00DE, X00DD, X00DG, X00DF, X00DI, X00DK, X00DJ, G660., X00DL, X00DO, X00DN, X00DQ, X00DP, X00DS, X00DR, X00DT, XE0VJ,

XE0VF, G613., G663., XaBM5, XaBM4, G6410, XaJgQ, G641., G614., XE0X2, Xa1hE, G662., G6400, Xa0kZ, X00DM, G664., G61.., G615., XE2aB, G640., Gyu6F, Gyu6G, XaBED, XaBEC, G616., G667., Gyu62, Gyu63, Gyu66, Gyu64, Gyu65, G6760

Stroke (TIA)

G65z., XE0X0, Fyu55, G651., G65.., G650., G652., G65z0, G654., G65y., X00DU, G65z1, X00DW, XE0VK, XaEGK, G6510, XaX16, G653., X00DV

Drugs

Defined using chapters within the British National Formulary (BNF).

Penicillin

05.01.01

Cephalosporin

05.01.02.01

Monobactam

05.01.02.03

Tetracycline

05.01.03

Macrolide

05.01.05

Quinolone

05.01.12

Carbapenem

05.01.02.02

Clindamycin

05.01.06

Sulfonamides/Trimethoprim

05.01.08

Nitrofurantoin

05.01.13

Allergies

Defined using clinical codes within Clinical Terms Version 3 (CTV3).

Penicillin

14L1., Xa5sN, Xa5sO, Xa5sL, Xa5sM, Xa5sJ, Xa5sK, Xa5sH, Xa5sI, Xa5sZ, Xa5sX, Xa5sY, Xa5sV, Xa5sW, Xa5sT, Xa5sU, Xa5sR, Xa5sS, Xa5sP, Xa5sQ, Xa5sn, Xa5so, Xa5sl, Xa5sm, Xa5sj, Xa5sk, Xa5sh, Xa5si, Xa5sf, Xa5sg, Xa5sd, Xa5se, Xa5sb, Xa5sc, Xa5sa, ZV140, Xa5sp, Xa5sq

Cephalosporin

Xa5tl, Xa5tH, Xa5tG, Xa5tF, Xa5tE, Xa5tD, Xa5tC, Xa5tB, Xa5tA, Xa5t9, Xa5t8, Xa5t7, Xa5t6, Xa5t5, Xa5t4, Xa5t3, Xa5t2, Xa5t1, Xa5t0, Xa5sz, Xa5sx, Xa5sy, Xa5sv, Xa5sw

Monobactam

Xa5tR, Xa5tQ

Tetracycline

Xa5tt, Xa5ts, Xa5tr, Xa5tq, Xa5tp, Xa5to, Xa5tn, Xa5tm, Xa5tl, Xa5tk

Macrolide

Xa5ru, Xa5rw, Xa5rv, Xa5rx

Quinolone

Xa5sF, Xa5sG, Xa5sD, Xa5sE, Xa5sB, Xa5sC, Xa5sA, Xa5s8, Xa5s9

Carbapenem

Xa5su

Clindamycin

Xa5tN

Sensitivities

See Drugs

Infections

Defined using clinical codes within Clinical Terms Version 3 (CTV3).

Methicillin resistant *Staphylococcus aureus*

XaEJ0, XE0R6, Xa1xy

Clostridium difficile

X303u, A3Ay2

Vancomycin-resistant enterococci

XaCM2, XaZKS

Ethnicities

Defined using clinical codes within Clinical Terms Version 3 (CTV3).

9S3.., XM1SC, XaJRj, XaBz8, 9SA6., XaJSG, XaFwF, 9SA2., XaJRM, XE2Nw, 9T1.., XaJQx, 9T17., XaFwz, XM1S9, XaJRh, XaR4p, XaJRF, XE2Ny, XM1S4, XaFx0, XaJRE, XaJSU, 9SA4., 9T19., XaJRX, XaJR0, XE0oc, XaJRB, XaJSd, XaJRN, 9T..., XaW95, 9SA5., 9S43., XM1S8, XaJSY, XaJSa, XM1S5, XaJQu, XaJRP, XaJRC, XaJSO, 9T1Z., XaJRK, XaJR1, XaJRM, XM1S7, XaVw5, XM1SB, XaJRd, 9SAC., 134D., 9T16., 9T1A., XM1SI, 9SB1., XaJR5, XaJSH, XaJRA, XaJSW, 134L., XM1SF, XaJR4, 134G., 9S1.., XaJSS, 134K., XaJQw, XaJRe, XaJSf, XE2Nx, XaQEb, XE2Nz, XaFwG, XaFx1, 9S..., XaJSQ, XaJSD, 9S41., 134P., 9T12., XaJR8, XaJQv, 9SA9., 134H., XM1SD, 134F., Xa8Es, XE2Nt, XaJSC, XaJSB, XaJSZ, XaJRY, XaJRW, XaJRH, XaJQy, 9SAB., XaJQz, 134E., X76Gp, XaJR9, 9T1C., XaJRS, XaJR2, XaJSX, XS7AU, 9T15., XaJRb, 9T1Y., XaN9x, XaJRV, 134O., XaJRI, XaJRU, XaJSI, XaJSe, XaJRC, XaJRD, XaJRa, 9T14.,

XaJRG, 134M., 9S8., 9SAD., XM1SE, 134B., 9T1E., 9T13., XaJRf, 9S7., XaJSF, XaJRg, 9S51., XM1S6, XaJSE, 9T1B., XaJSb, XaJSM, XaJSP, XaJRO, 9T11., XaJRZ, 9S42., XaFwH, XaJSL, XM1SH, XaJSJ, XaJR7, XaJST, 9SA., XaJRR, XaFwy, XE2Nv, 9S45., 9SZ., XaJSV, XM1S3, XM1SG, XaR61, 134J., 9SB., XaQEa, 9SA8., XE2O0, XaJSg, 9T18., XaIB6, XaFwE, 9SAA., XM1SA, XaE4A, 9SB2., XaR4o, 9S4., XaJR3, XaJRI, 9SB3., XaJRI, 9S5., 9SA3., 9SB4., 9S44., XE2Nu, 9SA7., XaJSK, XaIB5, 134C., Xaluh, XaJSN, XaJRk, XaJSR, 134I., XaBEN, 9S47., 9S2., Xalui, 9S6., XaJSc, XaJRQ, XaW8w, XaJRL, XaFwD, XaBz7, 9S48., 9S52., XaJR6, XaE4B, 9SA1., XaFx2, XaJRT, 9S46., XaJRJ