Title: The effectiveness of pneumococcal vaccination in adults with common immune mediated inflammatory diseases: a UK wide study using data from the Clinical Practice Research Datalink Gold.

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Abstract

Background

The effectiveness of pneumococcal vaccination in people with common immune mediated inflammatory diseases (IMIDs) has not been evaluated. We investigated the effectiveness of pneumococcal vaccination in preventing respiratory morbidity and mortality in this population.

Methods

We conducted three nested case-control studies using data from the Clinical Practice Research Datalink Gold, linked to hospitalization and mortality records. Adults with incident common IMIDs diagnosed between 1997 and 2019 were followed up from the first diagnosis date to the occurrence of an outcome or date of last follow-up. Cases were people with IMIDs hospitalised for pneumonia, death due to pneumonia, or primary-care consultation for lower respiratory tract infection (LRTI) respectively. Cases were age and sex matched to up to ten contemporaneous controls using incidence density sampling.

We defined pneumonia using hospital discharge diagnoses, death due to pneumonia using death certification data, and primary-care consultation for LRTI as present when primary-care consultation and antibiotic prescription occurred on the same date.

Findings

1,884 patients with and 10,476 patients without pneumonia hospitalization; 781 patients that died due to pneumonia and 4,540 patients who were alive on the index

date; and 10,549 patients with LRTI and 43,981 patients without were included in the nested case-control analyses.

On multivariable analysis, pneumococcal vaccination was negatively associated with hospitalisation for pneumonia (aOR (95%CI) 0.70 (0.60, 0.81), death certified due to pneumonia (aOR (95%CI) 0.60 (0.48, 0.76) and LRTI (aOR (95%CI) 0.76 (0.72, 0.80). There was no association between wellness checks (negative control exposure) and pneumonia or death due to pneumonia. Wellness check was associated positively with LRTI.

Interpretation

Pneumococcal vaccination is protective against pneumonia and death due to pneumonia without apparent residual confounding. However, residual unmeasured confounding cannot be fully excluded in observational research which includes nested case-control study.

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Research in context:

Evidence before this study: Patients with inflammatory diseases are at an increased risk of pneumococcal pneumonia. Vaccination against pneumococcus using the 23-valent pneumococcal polysaccharide vaccine (PPV 23) is widely recommended for this vulnerable group. However, vaccine uptake remains low. Immunosuppression reduces vaccine induced immunity, including that elicited by the PPV 23. Whether vaccination against pneumococcus with the PPV 23 – the most widely used vaccine against pneumococcus globally and recommended for use in adults in the UK - prevents pneumonia and its complications in this population is not well understood. This lack of evidence is a major barrier to vaccination in people with IMIDs. We searched PubMed for randomised controlled trials (RCTs) and observational studies published between database inception and December 21, 2023, using the terms (pneumoco* AND vaccin*) AND (effica* OR effective*) AND (trial OR cohort OR case-control) AND (rheumat* OR psoria* OR lupus OR colitis OR Crohn*) with no language restrictions to identify pre-existing evidence. We identified one underpowered clinical trial conducted in Japan that did not detect efficacy for pneumococcal vaccination on clinical outcomes.

Added value of this study: Using a UK wide cohort of patients with rheumatoid arthritis, psoriatic arthritis, axial spondylarthrosis, reactive arthritis, inflammatory bowel

disease, and systemic lupus erythematosus, we conducted three separate nested case control studies that included 1,884 patients hospitalised due to pneumonia and 10,476 patients without such hospital admission; 781 patients that died due to pneumonia and 4,540 patients who were alive on index date; and 10,549 patients with antibiotic treated LRTI and 43,981 patients without. On multivariable analysis, pneumococcal vaccination was associated negatively with hospitalisation for pneumonia (adjusted Odds Ratio (aOR), 0.70 [95% Confidence Interval (CI) 0.60,0.81]), death due to pneumonia (aOR, 0.60 [95% CI 0.48,0.76]) and LRTI (aOR, 0.76 [95% CI 0.72,0.80]). There was no evidence for waning immunity over time. There was no association between attending for a routine wellness check, a negative control exposure, and either hospitalisation or death due to pneumonia. Attending a routine wellness check was associated with LRTI suggesting residual confounding.

Implications of all the available evidence: This study reported that pneumococcal vaccination prevents hospitalisation and death due to pneumonia in people with common immune mediated inflammatory diseases with protective effect present across a range of prognostic factors. The extent of protection was comparable to what has been reported in other at-risk conditions. This evidence should be used to promote vaccination in this vulnerable population. Due to a lack of evidence on aetiology of pneumonia, we were unable to ascertain vaccine efficacy on pneumococcal pneumonia.

Introduction Common immune mediated inflammatory diseases (IMIDs) such as rheumatoid arthritis (RA), psoriasis +/- arthritis (PsA), inflammatory bowel disease (IBD), and systemic lupus erythematosus (SLE) affect 1 in 30 adults in the UK and are treated with corticosteroid sparing immune suppressing drugs (1-3). These conditions are associated with an increased risk of infection with *Streptococcus pneumoniae*, the commonest cause of community acquired pneumonia, with rate ratios ranging from 4.0-4.4 for pneumococcal pneumonia and 2.2-6.5 for invasive pneumococcal disease (4-6). Consequently, vaccination with the pneumococcal vaccine is recommended for adults with IMIDs, and pneumococcal polysaccharide vaccine (PPV23) is the main vaccine used globally (7-9).

The effectiveness of pneumococcal vaccines for clinically relevant outcomes, such as pneumococcal pneumonia and its complications such as death, is not well understood in people with IMIDs. To our knowledge, only one randomised placebo controlled trial has evaluated the efficacy of PPV23 in preventing pneumonia in people with RA and it did not demonstrate vaccine efficacy, potentially due to a lack of power (10). However, a retrospective study on the clinical effectiveness of PPV23 in people with RA reported a relative risk of 9.7 for pneumonia in the non-vaccinated individuals (11). Trials of vaccinations in immunosuppressed people are short-term, typically only report on serological outcomes, and demonstrate that the pneumococcal vaccine is immunogenic in people with IMIDs, albeit the serological response might be diminished when compared to the healthy population (12-14).

Lack of knowledge about vaccine efficacy and concerns about disease flare underlie vaccine hesitancy in people with IMIDs (15-17). According to our patient and public

engagement, it is imperative to provide evidence on the benefit from pneumococcal vaccine in people with IMIDs in order to improve the vaccine uptake. Thus, the objectives of this study were to investigate the association between pneumococcal vaccination and hospitalisation due to pneumonia, death due to pneumonia, and primary-care managed lower-respiratory tract infection (LRTI) in people with common IMIDs.

Methods Data from the Clinical Practice Research Datalink (CPRD) Gold linked to hospitalization and mortality records were used. Incepted in the year 1987, CPRD Gold is an anonymised longitudinal database of electronic health records of >14 million people in the UK. CPRD participants are representative of the UK population in terms of age, sex, and ethnicity (18). CPRD includes information on demographics, lifestyle factors, and diagnoses. The latter are stored as Read codes – a hierarchical coded thesaurus of clinical terms. Information about primary-care prescriptions and immunisations, including date of vaccination, is also recorded. The data are enhanced by linkage with hospitalisation (Hospital Episode Statistics (HES)) and mortality records (Office of National Statistics (ONS)).

Approval CPRD Research Data Governance (Reference 21_000614).

Study design Nested case-control study.

Study period 1 April 1997 to 31 December 2019. The start time was selected to coincide with the time CPRD commenced linkage to hospitalisation and mortality data.

Population Adults aged ≥18 years diagnosed with either RA, IBD, axial spondyloarthritis (AxSpA, i.e., PsA, reactive arthritis, or ankylosing spondylitis) or SLE, with at least one prescription of either methotrexate, azathioprine, 5-mercaptopurine, sulfasalazine, 5-aminosalicylate, mycophenolate, leflunomide, ciclosporin, tacrolimus or sirolimus, and alive and contributing data to CPRD in the study period. Patients were required to have ≥one year disease free registration period in their current GP surgery before the first record of the diagnosis.

Exposure Pneumococcal vaccination was the exposure of interest. It was defined using product and Read codes (Supplementary material page 3). In patients with ≥two

vaccinations, the latest record of vaccination prior to the index date was used to define the vaccination date (9).

Outcomes [1] hospitalisation due to pneumonia, [2] death due to pneumonia recorded as either a primary or contributing cause of death, and [3] primary-care managed LRTI. A sensitivity analysis considered death due to pneumonia where this was the primary cause of death. Hospitalisation and death due to pneumonia were defined using ICD codes in the linked HES and ONS datasets respectively (Supplementary material page 3). ICD codes for hospital acquired pneumonia were not considered to define the case status. Primary-care managed LRTI was defined as primary-care consultation for LRTI and antibiotic prescription on the same date.

Nested case-control studies Separate nested-case control studies were undertaken for the three outcomes. Patients with incident IMIDs diagnosed after the age of 18 years were followed up from the date of IMID diagnosis to the earliest date of outcome, transfer out of practice, last data collection from the practice, death, or study end.

Controls were individuals without the outcome of interest during the follow-up period that were alive and were contributing data to the CPRD on the date on which their matched case had an outcome of interest. As many as 10 controls were matched to each case for age (±5 years) and sex using incidence density sampling without replacement, whereby the index case was matched to controls drawn from the full risk set (19). Controls were allocated an index date corresponding to the outcome date of their matched case. Receipt of pneumococcal vaccine and covariates were ascertained using data prior to the index date.

Covariates We selected covariates to minimise confounding. These were age, sex, practice level Index of Multiple Deprivation (IMD, quintiles), body mass index (BMI, kg/m^2), alcohol consumption (current, ex-, never), smoking status (current, ex-, never), Charlson's comorbidity index (CCI), immunosuppression (i.e., immune suppressing drugs and corticosteroid prescription within 30-days prior to index date), IMID type, factors that reflect health seeking behaviour (i.e., influenza vaccination, shingles vaccination, number of primary care consultation, number of hospital admissions and number of prescriptions in 12-months prior to index date), and additional risk-factors indicating pneumococcal vaccination (9).

Statistical analyses Multivariable unconditional logistic regression was used to assess the association between pneumococcal vaccination as an exposure and each of the three outcomes. Multiple imputation using chained equations was used to impute missing data for smoking, alcohol, and body mass index using Stata command *mi impute*. The imputation model included all listed confounders, exposure, and case-control indicator (20). Ten imputations were carried out as the extent of missing data was modest.

Adjusted odds ratios (aOR) and 95% confidence interval (CI) were calculated and combined using Rubin's rule across the imputed datasets, with vaccination as the exposure of interest. Three models were constructed: model 1 included age and sex, model 2 included age, sex, BMI, alcohol, smoking, IMD, number of primary care consultations in 12 months prior to index date, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date, IMID type, immune suppressing

drug and CCI, and model 3 included all variables in model 2 alongside at-risk conditions (chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia outcome) and treatment (corticosteroid prescription within 30 days of index date) that may indicate the need for pneumococcal vaccination. The number of vaccinations received was not included in the model because in the UK, booster pneumococcal vaccinations are only indicated in people at risk of rapid decline in antibody levels i.e., those with splenic dysfunction, asplenia, and chronic kidney disease, and consequently those receiving multiple doses may not be more protected against pneumococcal disease.

Exploratory subgroup analyses were undertaken according to IMID type, age (<65 years or ≥65 years), CCI (<median vs ≥median) and additional indication for pneumococcal vaccination (present vs absent). A post-hoc subgroup analysis was undertaken for sex and index year (≤2011 vs ≥2012). A sensitivity analysis was undertaken in patients in whom pneumonia was the primary cause of death. A post-hoc sensitivity analysis was undertaken for patients treated with immune-suppressive corticosteroid sparing drugs and methotrexate within 30-days prior to the index date.
We assessed the extent of unmeasured confounding using E-value, defined as the minimum strength of association that an unmeasured confounder would need to have with both vaccination status and the outcome, conditional on the measured covariates, to cancel the observed association between vaccination and outcome of interest. The higher the E-value, the less likely for unmeasured confounding to explain away the observed exposure-outcome association (21). Additionally, we used NHS wellness check (Supplementary material page 3) as a negative exposure variable to explore the

role of unmeasured confounding in this study analyses (22). Data management and analysis were performed in Stata v17, Stata Corp LLC, Texas, USA.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. GN and AA had full access to the data in the study.

Results

Data from 12,360 patients (7,326, 59.3% female) of whom 1,884 were hospitalised due to pneumonia were included in the analysis that evaluated the association between vaccination and hospitalization due to pneumonia (Supplementary material page 2). Patients hospitalised with pneumonia, compared to those without a hospital admission due to pneumonia, were more likely to be current smokers (380 (20.2%) vs 1,560 (14.9%)), ex-smokers (779 (41.4%) vs 3690 (35.2%)), prescribed corticosteroids (339 (18%) vs 699 (6.7%)), have diabetes (321 (17%) vs 1,409 (13.5%)), chronic respiratory disease (415 (22%) vs 1,034 (9.9%)), chronic heart disease (373 (19.8%) vs 1361 (12.6%)), and received influenza vaccination in the last 12-months (1,174 (62.3%) vs 4,484 (42.8%)). They had more primary-care prescriptions and consultations in the last 12-months (median 66 vs 23; and 54 vs 27 respectively) (Table 1).

Data from 5,321 patients (3,112, 58.5% female) of whom 781 died due to pneumonia were included in the analysis that evaluated the association between vaccination and death due to pneumonia (Supplementary material page 2). Among them, pneumonia was the primary cause of death in 649 cases. Patients who died of pneumonia, compared to their controls, were more likely to be current smokers (122 (15.6%) vs 499 (11%)), received influenza vaccination in the previous 12-months (508 (65%) vs 2,463 (54.3%)), have RA (504 (64.5%) vs 2,497 (55%)), chronic heart disease (230 (29.5%) vs 798 (17.6%)), chronic respiratory disease (230 (29.5%) vs 587 (12.9%)), chronic kidney disease (226 (28.9%) vs 1,105 (24.3%)), diabetes (153 (19.6%) vs 655 (14.4%)), prescribed corticosteroid in the preceding 30-days (177 (22.7%) vs 415

(9.1%)) and had more primary-care prescriptions and consultations in the last 12-months (median 93 vs 39; and 64 vs 33 respectively).

Data from 54,530 patients (33,605, 61.6% female) of whom 10,549 were diagnosed with LRTI were included in the analysis that evaluated the association between vaccination and LRTI (Figure S1). The proportion of patients with a diagnosis of chronic respiratory disease, corticosteroid prescription within previous 30-days and vaccination against influenza was higher among patients with LRTI compared to those without LRTI (1,282 (12.2%) vs 3,956 (9%), 1,939 (18.4%) vs 3,135 (7.1%), 5,714 (54.2% vs 17,108 (38.9%) respectively). Additionally, the number of prescriptions and primary-care consultations in the previous 12-months was higher in patients with LRTI than in those without LRTI (median 45 vs 22; and 43 vs 27 respectively). There was no appreciable difference in either moderate or heavy alcohol intake between cases and controls in the three nested case-control studies.

Vaccinations occurred both before and after the diagnosis of an IMID was recorded in the CPRD (Supplementary material page 38). On multivariate analysis, pneumococcal vaccination was associated with significantly lower odds of hospitalisation for pneumonia (aOR, 0.70 [95% CI 0.60,0.81]), death due to pneumonia (aOR, 0.60 [95% CI 0.48,0.76]) and LRTI (aOR, 0.76 [95% CI 0.72,0.80]) (Table 2). In a sensitivity analysis, pneumococcal vaccination was associated with significantly lower odds of death due to pneumonia where pneumonia was recorded as the primary cause of death (aOR, 0.65 [95% CI 0.51,0.83]). 567 (4.6%), 52 (1%) and 2099 (3.9%) people whose data were included in the nested case control studies examining the association between pneumococcal vaccination and hospitalization due to pneumonia, death due to pneumonia and LRTI received >1 pneumococcal

vaccinations respectively. The results were unchanged upon excluding them (Supplementary material page 39). There were only 97 cases with the details of causative organism recorded in the HES dataset, therefore pneumococcal pneumonia could not be analysed separately as an. outcome.

In subgroup analyses, pneumococcal vaccination protected from LRTI regardless of age, IMID type, CCI, and additional indication for vaccination (Table 3). Similarly, vaccination protected against pneumonia hospitalisation and death across age, comorbidity and IMID type except for people with AxSpA, IBD, and high CCI in whom the protective effect lacked statistical significance (Table 4, 5). Compared to not being vaccinated, both vaccination within and prior to 5-years of index date were negatively associated with hospitalization for pneumonia (aOR, 0.82 [95% CI 0.69,0.97]) and 0.62, [95% CI 0.53,0.73]) respectively) and death due to pneumonia (aOR, 0.70 [95% CI 0.53,0.92]) and 0.55, [95% CI 0.43,0.71]) respectively), while the evidence for LRTI was inconsistent (aOR, 0.96, [95% CI 0.90-1.02]) and 0.61, [95% CI 0.57,0.65]) respectively) (Model-3). Comparable vaccine effectiveness was observed when the data were analysed restricted to those prescribed any immune-suppressing corticosteroid sparing drug and those prescribed methotrexate within the 30-days preceding the index date (Supplementary material page 40). Vaccine effectiveness was comparable when the data analyses were stratified for sex and calendar year in which the case experienced an outcome (Table S4).

No patient was vaccinated on the index date. 10 (0.5%), 11 (1.4%), 50 (0.5%) patients in the hospitalization due to pneumonia, death due to pneumonia, and LRTI requiring antibiotics case-control study were vaccinated within 14 days of the index date. The

results did not change when data were analysed excluding them. Similarly, the results were unchanged in a complete case analysis (Supplementary material page 41).

The E-values for the association of pneumococcal vaccination with hospitalisation for pneumonia, death due to pneumonia, and LRTI were 2.21, 1.96, and 1.81 respectively. There was no association between NHS wellness check (negative exposure) and hospitalisation for pneumonia (aOR 0.92, [95% CI 0.74, 1.15]) and death due to pneumonia (aOR 0.90, [95% CI 0.63, 1.29]). A positive association was observed between the NHS wellness check and LRTI (aOR 1.13, [95% CI 1.03, 1.23]).

Discussion This large study found that pneumococcal vaccine protected against hospitalisation for pneumonia, death certified due to pneumonia and LRTI in people with common IMIDs. The protective effect was observed in those recently prescribed an immune-suppressing steroid sparing drug, methotrexate, corticosteroids, and was present regardless of comorbidity burden, age, sex, and type of IMID but was weaker in people with IBD and AxSpA. There was no evidence of waning of immunity over time. These findings are supported by immunogenicity studies which have shown that the humoral response to PPV23 is present in people with inflammatory conditions treated with immune-suppressing drugs although serologic titres are lower for strains such as the 6B and 23F serotypes and in the context of B-cell depleting therapy (12, 13).

To our knowledge, this is the first study to demonstrate the clinical effectiveness of PPV23 across a broad range of common IMIDs. A few studies considered vaccine effectiveness in individual IMIDs or in groups of similar IMIDs and reported variable magnitude of protection (11, 23, 24). These studies mainly assessed the effectiveness of pneumococcal conjugated vaccines (PCV) and not that of a single dose PPV 23 vaccine that is commonly used in routine adult vaccinations in the UK and in many countries across the globe (9). In a recent Swedish study, PCV 7 reduced the risk of pneumonia and serious infections in people with inflammatory arthritis by 53% (24). Vaccination with PPV 23 in combination with PCV 13 but not alone was protective against severe pneumococcal disease among US veterans withIBD (HR [95% CI] 0.17 [0.14,0.22]) and 1.10 [0.99,0.21] respectively). Similarly, receipt of an additional dose of PPV23 showed a protective effect against severe pneumococcal disease in IBD (HR [95% CI] 0.80 [0.67,0.95]) (23). In RA patients treated with methotrexate, PPV23

had an adequate doubling of median antibody levels with vaccinated patients being 10 times less likely to develop pneumonia over a 10-year period than the unvaccinated (11). On the other hand, a randomised double-blind trial on the clinical efficacy of PPV23 in preventing pneumonia in RA patients did not demonstrate vaccine efficacy, potentially due to low power (25).

Our estimate of vaccine effectiveness against pneumonia are comparable to the findings from general population studies (26, 27). In the Cochrane meta-analysis, PPV23 protected against all-cause pneumonia by 29% (95% CI 3%-48%) in the general population (26). Similarly, in observational studies, pneumococcal vaccine associated with a reduced risk of pneumococcal community acquired pneumonia (HR 0.49 (95% CI 0.29, 0.84), all-cause community acquired pneumonia (HR 0.75 (95% CI 0.58, 0.98) in those 60 years in age or older (27), and hospitalisation for pneumonia (HR 0.74 (95% CI 0.59, 0.92) in the elderly (28).

Our study found that pneumococcal vaccination protected against respiratory morbidity and mortality in common IMIDs irrespective of age and comorbidity burden. Previous studies in people aged ≥ 65 years have reported similar findings of protection against invasive pneumococcal disease ranging from 23% to 56% (29-31). However, in certain conditions, such diabetes and HIV infection, PPV 23 has been shown to be less effective(32, 33). In our study, protection against death due to pneumonia conferred by vaccination in patients with high comorbidity burden score lacked statistical significance, although this could be due to few events. The protective effect against pneumonia hospitalisation in people with greater comorbidity with high event numbers was statistically significant.

Although not evaluated in a multivariate analysis in our study, corticosteroid prescription within the previous 30-days was two to three-fold more common in cases diagnosed with LRTI, hospitalized due to pneumonia, and among those who died due to pneumonia than in their age and sex matched controls. This finding is consistent with previous reports of an association between corticosteroid prescription and hospitalization for pneumonia (34) suggesting that such patients ought to be flagged in primary-care for prioritisation for pneumococcal vaccination.

The main strength of our study is the use of data from a nationally representative dataset that originated during routine care of patients in the NHS. Healthcare in the NHS is free at the point of delivery for all UK residents. We included patients with a range of common inflammatory conditions that are usually treated with corticosteroids sparing immunosuppressive drugs thereby indicating pneumococcal vaccination in the UK. The abovementioned factors increase the generalisability of our findings. We used both primary-care record of IMID diagnosis and prescription of immune-suppressing drug to define our population, thereby improving the internal validity of the findings. We also assessed outcomes of clinical importance namely, hospitalisation due to pneumonia, death due to pneumonia and primary-care consultation for LRTI that required treatment with antibiotics. In the UK, hospital discharge summaries include information on reasons for hospitalisation and are completed by doctors. Similarly, death certification is done by doctors. Both hospital discharge diagnoses and cause of death are regarded as having high validity. Primary care consultation for LRTI that were treated with antibiotics was selected as an outcome because these infections may include community acquired pneumonia. However, this is a non-specific outcome

and should be interpreted with caution. It is possible that LRTI may be misdiagnosed viral illness for which patients were prescribed antibiotics due to risk averse prescribing in those with immunosuppression. This was reflected in an association of the negative control exposure with LRTI and a low E value.

Our study has several weaknesses. Despite the outcomes studied being of clinical relevance, they were hospitalization and death due to all-cause pneumonia. These are therefore not specific to *Streptococcus Pneumoniae* against which the vaccine is designed to protect against (9). Additionally, PPV23 is the only vaccine recommended to be used in adults in the UK, making it difficult to assess other vaccine types using this dataset. People vaccinated elsewhere rather than in primary-care were not included in this study because the actual date of their vaccination could not be established. However, these comprise a very small proportion of vaccinated individuals in the UK given majority of vaccinations happen in primary-care where in this setting PPV23 is reimbursed by the state. We were unable to assess the impact of biologics on vaccine effectiveness because data on prescriptions of biological agents are not recorded in the CPRD. This is likely to be a particular issue for those with AxSpA and PsA who are often treated with biologic monotherapy. However, some patients in our study would have been treated with biologics. We could not separately investigate vaccine effectiveness in people with less common IMIDs such as SLE because of the small sample size. We did not include patients with vasculitis, polymyalgia rheumatica, and rare connective tissue diseases such as systemic sclerosis and polymyositis and the findings should not be extrapolated to them. Despite controlling for confounding, unmeasured confounding and healthy user bias might have inflated vaccine effectiveness particularly against LRTI but it is ethically

challenging to support an RCT of vaccination in this at-risk population. Additionally, we assumed the data to be missing at random and did not undertake sensitivity analysis to assess the validity of these assumptions. It is possible that variables not in our imputation model could have explained patterns of missing data, in which case data would be missing not at random. The results we presented were similar to those from a complete case analysis which provides a degree of reassurance. Finally, many cases could not be matched to controls.

In conclusion, pneumococcal vaccine prevents respiratory morbidity and mortality in people with common IMIDs. These findings should be used to promote pneumococcal vaccination in this at-risk group.

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Author contribution

Conceptualisation: Abhishek. Methodology: Abhishek, Grainge, Card, Van-Tam, Mallen, Nakafero. Project administration: Abhishek, Nakafero. Resources: Abhishek, Nakafero. Software: Abhishek, Nakafero, Grainge. Supervision: Abhishek, Grainge, Van-Tam, Card, Mallen. Validation: Abhishek. Visualisation: Nakafero. Writing – original draft: Abhishek, Nakafero. Writing– review & editing: Abhishek, Grainge, Card, Van-Tam, Mallen, Nakafero. All authors had full access to the data in the study and Dr Nakafero and Prof Abhishek directly accessed and verified the underlying data reported in the manuscript. All authors had final responsibility for the decision to submit for publication.

Data sharing statement Data used in the study are from the Clinical Practice Research Datalink (CPRD). Due to CPRD licencing rules, we are unable to share data used in this study with third parties. The data used in this study may be obtained directly from the CPRD. Study protocol is available from www.cprd.com.

Table 1: Demographic and clinical characteristics of patients included in the Nested Case-Control Study

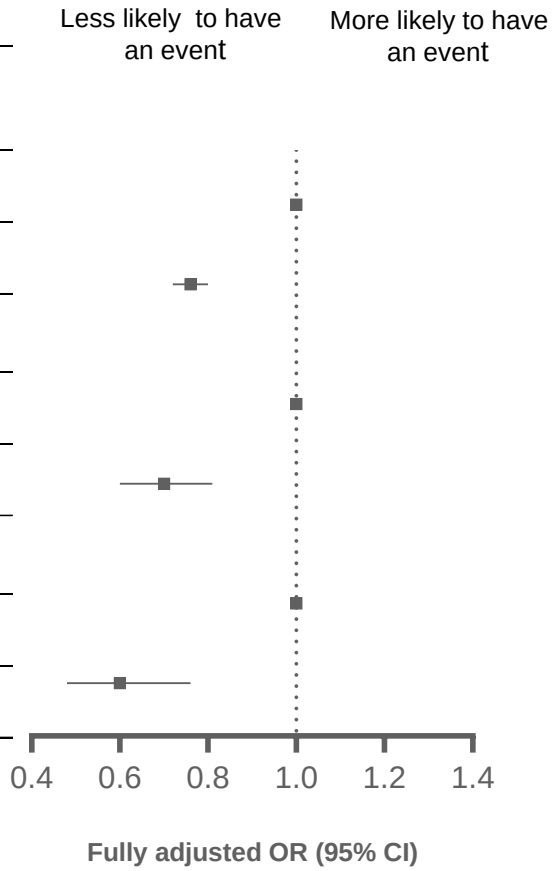
	Primary care consultation for LRTI requiring antibiotics		**Hospitalisation for pneumonia**		**Death due to pneumonia**	
Variables	**Cases (n=10,549)**	**Controls (n=43,981)**	**Cases (n=1,884)**	**Controls (n= 10,476)**	**Cases (n=781)**	**Controls (n=4,540)**
Continuous variables; median (IQR)						
Age; mean (SD)	55 (16)	54 (16)	63 (15)	60 (15)	71 (11)	69 (11)
Body mass index (BMI)	27 (23.6,31.4)	26.3 (23.2,30.1)	26 (22.7,30.1)	26.2 (23.2,29.8)	24.4 (21.1,28.2)	26 (23.1,29.4)
Missing BMI values	697 (6.6)	3,130 (7.1)	147 (7.8)	746 (7.1)	79 (10.1)	305 (6.7)
Charlson's comorbidity index	1 (0,2)	1 (0,2)	2 (0,3)	1 (0,2)	2 (1,4)	1 (0,3)
Index of Multiple deprivation	3 (2,5)	3 (2,4)	3(2,5)	3 (2,4)	3 (2,5)	3 (2,4)
Number of prescriptions±	45 (20,84)	22 (1,57)	66 (32,116)	23 (0,61)	93 (57,153)	39 (1,78)
Number of consultations±	43 (27,61)	27 (3,48)	54 (35,74)	27 (1,47)	64 (45,86)	33 (9,53)
Number of hospitalisations±	0 (0,0)	0 (0,0)	2 (1,3)	0 (0,1)	2 (1,4)	0 (0,1)
Categorical variables; n (%)						
Sex						
Male	3,952 (37.5)	16,973 (38.6)	788 (41.8)	4,246 (40.5)	338 (43.3)	1,871 (41.2)
Female	6,597 (62.5)	27,008 (61.4)	1,096 (58.2)	6,230 (59.5)	443 (56.7)	2,669 (58.8)
Smoking status						
Non-smoker	4,490 (42.6)	21,253 (48.3)	692 (36.7)	5,073 (48.4)	306 (39.2)	2,153 (47.4)
Current smoker	2,425 (22.9)	8,574 (19.5)	380 (20.2)	1,560 (14.9)	122 (15.6)	499 (11.0)
Ex-smoker	3,499 (33.2)	13,730 (31.2)	779 (41.4)	3,690 (35.2)	333 (42.6)	1,833 (40.4)
Missing	135 (1.3)	424 (1.0)	33 (1.8)	153 (1.5)	20 (2.6)	55 (1.2)
Alcohol consumption (units/week):						
Non-drinker	2,293 (21.7)	9,427 (21.4)	495 (26.3)	2,274 (21.7)	220 (28.2)	1,004 (22.1)
Low drinker (1-14)	5,639 (53.5)	24,036 (54.7)	879 (46.7)	5,627 (53.7)	338 (43.3)	2,466 (54.3)
Moderate (15-21)	410 (3.9)	1,866 (4.2)	68 (3.6)	430 (4.1)	17 (2.2)	178 (3.9)
Hazardous (> 21)	600 (5.7)	2,480 (5.6)	111 (5.9)	610 (5.8)	40 (5.1)	229 (5.0)
Former drinker	392 (3.7)	1,275 (2.9)	73 (3.9)	355 (3.4)	46 (5.9)	171 (3.8)
Missing	1,215 (11.5)	4,897 (11.1)	258(13.7)	1,180 (11.3)	120 (15.4)	492 (10.8)
Previous influenza vaccination±	5,714 (54.2)	17,108 (38.9)	1,174 (62.3)	4,484 (42.8)	508 (65.0)	2,463 (54.3)
Previous shingles vaccination	101 (1.0)	490 (1.1)	28 (1.5)	137 (1.3)	8 (1.0)	46 (1.0)
At-risk conditions						
Diabetes	1,266 (12.0)	5,084 (11.6)	321 (17.0)	1,409 (13.5)	153 (19.6)	655 (14.4)
Chronic kidney disease	1,129 (10.7)	6,029 (13.7)	421 (22.4)	1,935 (18.5)	226 (28.9)	1,105 (24.3)
Chronic liver disease	63 (0.6)	337 (0.8)	23 (1.2)	80 (0.8)	12 (1.5)	30 (0.7)
Chronic respiratory disease	1,282 (12.2)	3,956 (9.0)	415 (22.0)	1,034 (9.9)	230 (29.5)	587 (12.9)
Chronic heart disease	983 (9.3)	4,135 (9.4)	373 (19.8)	1,316 (12.6)	230 (29.5)	798 (17.6)
Asplenia	6 (0.1)	18 (0.04)	-/- (0.2)	-/- (0.04)	-	-

	Primary care consultation for LRTI requiring antibiotics		Hospitalisation for pneumonia		Death due to pneumonia	
Immunosuppression	176 (1.7)	849 (1.9)	68 (3.6)	199 (1.9)	24 (3.1)	87 (1.9)
Corticosteroid prescription	1,939 (18.4)	3,135 (7.1)	339 (18.0)	699 (6.7)	177 (22.7)	415 (9.1)
IMID type						
Rheumatoid arthritis	5,053 (47.9)	19,862 (45.2)	1,066 (56.6)	5,174 (49.4)	504 (64.5)	2,497 (55.0)
Inflammatory bowel syndrome	3,692 (35.0)	17,443 (39.7)	635 (33.7)	4,013 (38.3)	226 (28.9)	1,619 (35.7)
Systemic lupus erythematosus	370 (3.5)	1,069 (2.4)	63 (3.3)	197 (1.9)	17 (2.2)	76 (1.7)
Spondlyloarthritis	1,434 (13.6)	5,607 (12.8)	120 (6.4)	1,092 (10.4)	34 (4.4)	348 (7.7)
Steroid sparing drug						
5-ASA/sulfasalazine	5,260 (49.9)	23,299 (53.0)	946(50.2)	5,588 (53.3)	377 (48.3)	2,402 (52.9)
Immune suppressing drugs	5,289 (50.1)	20,682 (47.0)	938 (49.8)	4,888 (46.7)	404 (51.7)	2,138 (47.1)

± 12 months prior to indexdate;-/- number of participants < 5 were suppressed to comply with the CPRD guidelines; IQR: Interquartile range; SD: Standard deviation; Spondyloarthritis: psoriatic arthritis, ankylosing spondyloarthritis and reactive arthritis; corticosteroid prescription within 30 days prior to indexdate; 5-ASA: aminosalicylates; Immune suppressing drugs: methotrexate, leflunomide, azathioprine, ciclosporin, mycophenolate, mercaptopurine, tacrolimus/sirolimus.

Table 2: Pneumococcal vaccine effectiveness in immune mediated inflammatory condition. The figure displays results of model 3.

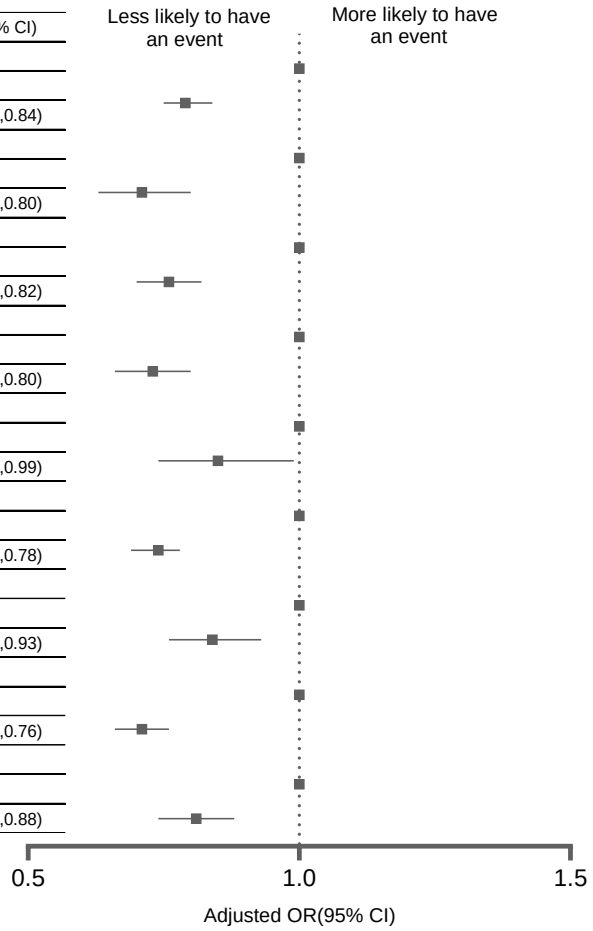
Outcomes	Cases n (%)	Controls n (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Primary care consultation for LRTI requiring antibiotics					
Unvaccinated	5,299 (50.2)	22,035 (50.1)	1	1	1
Vaccinated	5,250 (49.8)	21,946 (49.9)	0.94 (0.90,0.99)	0.73 (0.70,0.77)	0.76 (0.72,0.80)
Hospitalisation for pneumonia					
Unvaccinated	639 (33.9)	4,182 (39.9)	1	1	1
Vaccinated	1,245 (66.1)	6,294 (60.1)	1.09 (0.98,1.23)	0.71 (0.62,0.82)	0.70 (0.60,0.81)
Death due to pneumonia					
Unvaccinated	200 (25.6)	1,168 (25.7)	1	1	1
Vaccinated	581 (74.4)	3,372 (74.3)	0.86 (0.72,1.03)	0.64 (0.51,0.81)	0.60 (0.48,0.76)



OR: odds ratio; CI, confidence interval; Model 1 adjusted for matching variables (age and sex); Model 2 adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to indexdate, number of hospital admission in 12 months prior to indexdate, influenza vaccination in 12 months prior to indexdate, shingles vaccination in 12 months prior to indexdate deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory) drug ; Model 3 (Fully adjusted model): Model 2 covariates plus at-risk conditions for pneumococcal vaccination (chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia outcome), corticosteroid prescription within 30 days of indexdate

Table 3: The association of pneumococcal vaccine and LRTI requiring antibiotics: Subgroup analyses (model 3).

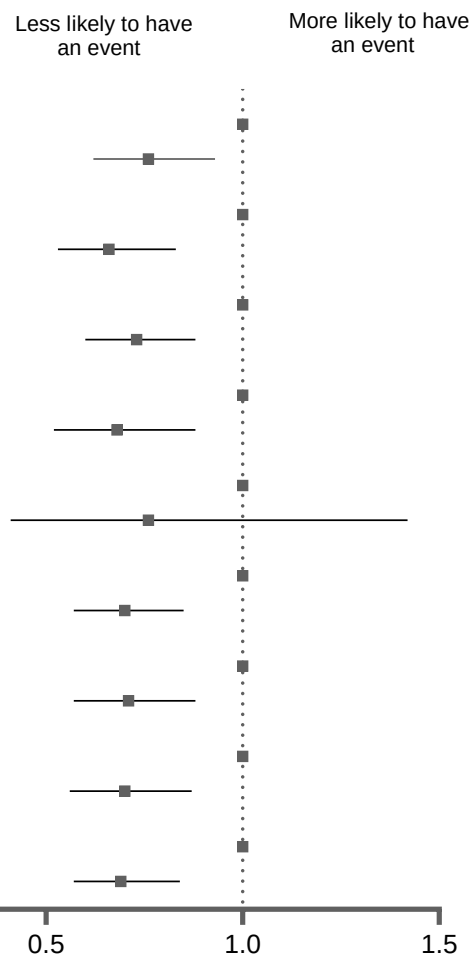
Subgroup	Cases, n (%)	Controls, n (%)	aOR*(95% CI)
< 65 years			
Vaccinated, No	4,695 (61.9)	19,598 (61.3)	1
Vaccinated, Yes	2,886 (38.1)	12,384 (38.7)	0.79 (0.75,0.84)
≥65 years			
Vaccinated, No	604 (20.4)	2,437 (20.3)	1
Vaccinated, Yes	2,364 (79.7)	9,562 (79.7)	0.71 (0.63,0.80)
RA			
Vaccinated, No	2,035 (40.3)	7,677 (38.7)	1
Vaccinated, Yes	3,018 (59.7)	12,185 (61.4)	0.76 (0.70,0.82)
IBD			
Vaccinated, No	2,261 (61.2)	10,627 (60.9)	1
Vaccinated, Yes	1,431(38.8)	6,816 (39.1)	0.73 (0.66,0.80)
SpA			
Vaccinated, No	806 (56.2)	3,160 (56.4)	1
Vaccinated, Yes	628 (43.8)	2,447 (43.6)	0.85 (0.74,0.99)
CCI low (≤ median)			
Vaccinated, No	4,505 (60.3)	18,193 (60.4)	1
Vaccinated, Yes	2,965 (39.7)	11,916 (39.6)	0.74 (0.69,0.78)
CCI high (>median)			
Vaccinated, No	794 (25.8)	3,842 (27.7)	1
Vaccinated, Yes	2,285 (74.2)	10,030 (72.3)	0.84 (0.76,0.93)
At-risk condition present			
Vaccinated, No	1,488 (32.2)	4,598 (28.7)	1
Vaccinated, Yes	3,137 (67.8)	11,436 (71.3)	0.71 (0.66,0.76)
At-risk condition absent			
Vaccinated, No	3,811 (64.3)	17,437 (62.4)	1
Vaccinated, Yes	2,113 (35.7)	10,510 (37.6)	0.81 (0.74,0.88)



*adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to indexdate, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date, deprivation score, inflammatory condition, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory), chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia), corticosteroid prescription within 30 days of index date, -/-:few observations leading to failure of model convergence.

Table 4: The association of pneumococcal vaccine and hospitalisation due to pneumonia: Subgroup analyses (model 3).

Subgroup	Cases, n (%)	Controls, n (%)	aOR*(95% CI)
< 65 years			
Vaccinated, No	458 (50.5)	3,365 (56.1)	1
Vaccinated, Yes	449 (49.5)	2,631 (43.9)	0.76 (0.62,0.93)
≥65 years			
Vaccinated, No	181 (18.5)	817 (18.2)	1
Vaccinated, Yes	796 (81.5)	3,663 (81.8)	0.66 (0.53,0.83)
RA			
Vaccinated, No	297 (27.9)	1,688 (32.6)	1
Vaccinated, Yes	769 (72.1)	3,486 (67.4)	0.73 (0.60,0.88)
IBD			
Vaccinated, No	264 (41.6)	1,887 (47.0)	1
Vaccinated, Yes	371 (58.4)	2,126 (53.0)	0.68 (0.52,0.88)
SpA			
Vaccinated, No	45 (37.5)	525 (48.1)	1
Vaccinated, Yes	75 (62.5)	567 (51.9)	0.76 (0.41,1.42)
CCI low (≤ median)			
Vaccinated, No	434 (46.9)	3,303 (51.5)	1
Vaccinated, Yes	492 (53.1)	3,116 (48.5)	0.70 (0.57,0.85)
CCI high (>median)			
Vaccinated, No	205 (21.4)	879 (21.7)	1
Vaccinated, Yes	753 (78.6)	3,178 (78.3)	0.71 (0.57,0.88)
At-risk condition +nt			
Vaccinated, No	279 (23.8)	993 (21.7)	1
Vaccinated, Yes	895 (76.2)	3,570 (78.2)	0.70 (0.56,0.87)
At-risk condition -nt			
Vaccinated, No	360 (50.7)	3,189 (53.9)	1
Vaccinated, Yes	350 (49.3)	2,724 (46.1)	0.69 (0.57,0.84)

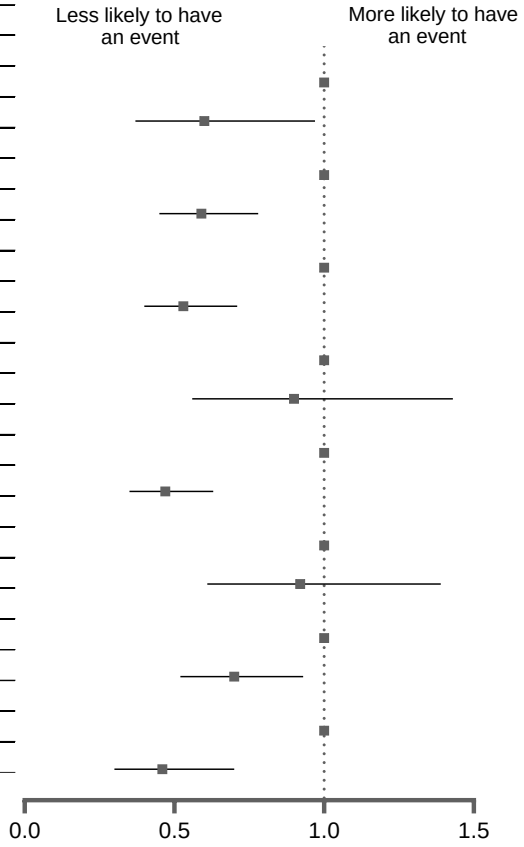


*adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to indexdate, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date, deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory) drug, chronic heart disease, diabetes immunosuppression, chronic liver

disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia), corticosteroid prescription within 30 days of index date, -/-:few observations leading to failure of model convergence.

Table 5: The association of pneumococcal vaccine and death due to pneumonia: subgroup analyses (model-3).

Subgroup	Cases, n (%)	Controls, n (%)	aOR*(95% CI)
< 65 years			
Vaccinated, No	73 (38.0)	633 (41.4)	1
Vaccinated, Yes	119 (62.0)	898 (58.7)	0.60 (0.37,0.97)
≥65 years			
Vaccinated, No	127 (21.6)	535 (17.8)	1
Vaccinated, Yes	462 (78.4)	2,474 (82.2)	0.59 (0.45,0.78)
RA			
Vaccinated, No	138 (27.4)	585 (23.4)	1
Vaccinated, Yes	366 (72.6)	1,912 (76.6)	0.53 (0.40,0.71)
IBD			
Vaccinated, No	45 (19.9)	458 (28.3)	1
Vaccinated, Yes	181 (80.1)	1,161 (71.7)	0.90 (0.56,1.43)
CCI low (≤ median)			
Vaccinated, No	144 (32.4)	962 (30.3)	1
Vaccinated, Yes	301 (67.6)	2,212 (69.7)	0.47 (0.35,0.63)
CCI high (>median)			
Vaccinated, No	56 (16.7)	206 (15.1)	1
Vaccinated, Yes	280 (83.3)	1,160 (84.9)	0.92 (0.61,1.39)
At-risk condition +nt			
Vaccinated, No	124 (21.2)	426 (17.4)	1
Vaccinated, Yes	462 (78.8)	2,024 (82.6)	0.70 (0.52,0.93)
At-risk condition -nt			
Vaccinated, No	76 (39.0)	742 (35.5)	1
Vaccinated, Yes	119 (61.0)	1,348 (64.5)	0.46 (0.30,0.70)



*adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to indexdate, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date, deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory), chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia), corticosteroid prescription within 30 days of index date, -/-:few observations leading to failure of model convergence.

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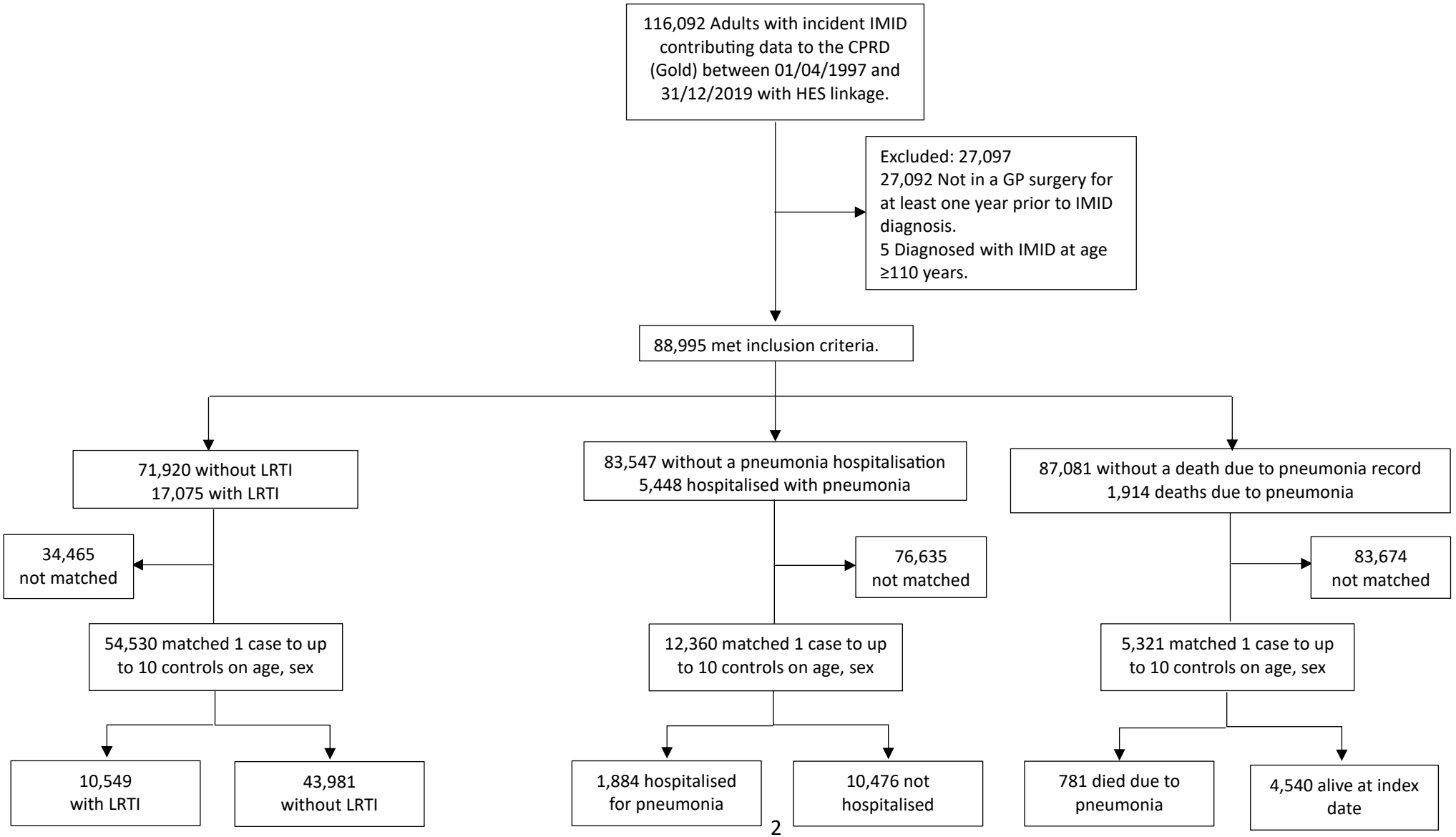
Supplementary material

Figure S1: Study population selection criteria: Nested case-control study cohorts



IMID: Immune mediated inflammatory diseases; CPRD: Clinical Practice Research Datalink; HES: Hospital Episode Statistics; LRTI: Lower respiratory tract infection

Table S1: code lists

A. Pneumococcal vaccination codes

Medcodes

medcode	readcode	readterm
5764	7L19700	Subcutaneous injection of Pneumovax II
11363	6572	Pneumococcal vaccination
30411	9Oo..00	Pneumococcal vaccination administration
36826	6572000	Pneumococcal vaccination given
53198	657K.00	Booster pneumococcal vaccination
97759	657P.00	Pneumococcal vaccination given by other healthcare provider

Product codes

prodcode	Description
821	Pneumococcal polysaccharide conjugated vaccine (adsorbed) suspension for injection 0.5ml vials
832	Pneumococcal polysaccharide vaccine solution for injection 0.5ml vials
930	Pneumovax II vaccine solution for injection 0.5ml vials (sanofi pasteur MSD Ltd)
1327	PNEUMOVAX VAC
3684	Pnu-Imune vaccine solution for injection 0.5ml vials (Wyeth Pharmaceuticals)
15482	PNEUMOVAC PLUS VACCINE VAC
42602	Prevenar 13 vaccine suspension for injection 0.5ml pre-filled syringes (Pfizer Ltd)
42612	Pneumococcal polysaccharide conjugated vaccine (adsorbed) suspension for injection 0.5ml pre-filled syringes
42991	Pneumococcal 10-valent saccharide conjugated absorbed vaccine
50264	Pneumovax II vaccine solution for injection 0.5ml pre-filled syringes (sanofi pasteur MSD Ltd)
50338	Prevenar vaccine suspension for injection 0.5ml pre-filled syringes (Pfizer Ltd)
53159	Synflorix vaccine suspension for injection 0.5ml pre-filled syringes (GlaxoSmithKline UK Ltd)
4530007	PNEUMOVAX VAC
6007001	PNEUMOCOCCAL 23-VALENT POLYSACCHARIDE vaccine

6008001	PNEUMOVAX II vaccine
7920001	PNEUMOCOCCAL 7-VALENT SACCHARIDE CONJUGATED adsorbed vaccine
9289001	PREVENAR vaccine
10904001	PNU-IMUNE vaccine

B: Pneumonia

ICD10	Description
J13	Pneumonia due to Streptococcus pneumoniae
J14	Pneumonia due to Haemophilus influenzae
J15	Bacterial pneumonia, not elsewhere classified
J15.0	Pneumonia due to Klebsiella pneumoniae
J15.1	Pneumonia due to Pseudomonas
J15.2	Pneumonia due to streptococcus
J15.3	Pneumonia due to streptococcus, group B
J15.4	Pneumonia due to other streptococci
J15.5	Pneumonia due to Escherichia coli
J15.6	Pneumonia due to other Gram-negative bacteria
J15.7	Pneumonia due to Mycoplasma pneumoniae
J15.8	Other bacterial pneumonia
J15.9	Bacterial pneumonia, unspecified
J16	Pneumonia due to other infectious organisms, not elsewhere classified
J16.0	Chlamydia pneumonia
J16.8	Pneumonia due to other specified infectious organisms
J18	pneumonia, organism unspecified
J18.0	Bronchopneumonia, unspecified
J18.1	Lobar pneumonia, unspecified
J18.2	Hypostatic pneumonia, unspecified
J18.8	Other pneumonia, organism unspecified

J18.9	Pneumonia, unspecified
J85.1	Absess of lung with pneumonia
J85.2	Absess of lung without pneumonia

C: Lower respiratory infection

Medcode	Readcode	Readterm
68	H06z011	Chest infection
152	H302.00	Wheezy bronchitis
293	H06z111	Respiratory tract infection
312	H060.00	Acute bronchitis
556	H27..00	Influenza
1019	H061.00	Acute bronchiolitis
1382	H060w00	Acute viral bronchitis unspecified
2476	H07..00	Chest cold
2581	H06z000	Chest infection NOS
3163	H300.00	Tracheobronchitis NOS
3358	H06z100	Lower resp tract infection
4519	14B3.11	H/O: bronchitis
4899	H06z200	Recurrent chest infection
5818	17...00	Respiratory symptoms
5909	H312011	Chronic wheezy bronchitis
5978	H060.11	Acute wheezy bronchitis
6124	H062.00	Acute lower respiratory tract infection
6475	R06..00	[D]Respiratory system and chest symptoms
7074	H5yy.11	Respiratory infection NOS
7092	H30..12	Recurrent wheezy bronchitis
8025	H0...00	Acute respiratory infections
9043	H060600	Acute pneumococcal bronchitis

11072	H060300	Acute purulent bronchitis
14791	H27y100	Influenza with gastrointestinal tract involvement
15626	H310000	Chronic catarrhal bronchitis
15774	H271000	Influenza with laryngitis
16388	H27z.00	Influenza NOS
16468	R06zz00	[D]Respiratory system and chest symptoms NOS
17185	H061200	Acute bronchiolitis with bronchospasm
17359	H30..11	Chest infection - unspecified bronchitis
17917	H061z00	Acute bronchiolitis NOS
18451	H061500	Acute bronchiolitis due to respiratory syncytial virus
20198	H060z00	Acute bronchitis NOS
21061	H3y0.00	Chronic obstruct pulmonary dis with acute lower resp infect
21113	H0z..00	Acute respiratory infection NOS
21145	H060400	Acute croupous bronchitis
21492	H060800	Acute haemophilus influenzae bronchitis
23488	H271z00	Influenza with respiratory manifestations NOS
23663	17ZZ.00	Respiratory symptom NOS
24316	H24..11	Chest infection with infectious disease EC
24800	H060x00	Acute bacterial bronchitis unspecified
25603	H310.00	Simple chronic bronchitis
27819	H312.00	Obstructive chronic bronchitis
29273	H060C00	Acute bronchitis due to parainfluenza virus
29617	H271100	Influenza with pharyngitis
29669	H06..00	Acute bronchitis and bronchiolitis
31363	H27yz00	Influenza with other manifestations NOS
31886	H060A00	Acute bronchitis due to mycoplasma pneumoniae
37447	H06z112	Acute lower respiratory tract infection
41137	H06z.00	Acute bronchitis or bronchiolitis NOS
43362	H060700	Acute streptococcal bronchitis

43625	H271.00	Influenza with other respiratory manifestation
44525	H312z00	Obstructive chronic bronchitis NOS
44611	D410300	Polycythaemia due to cyanotic respiratory disease
46052	H20y000	Severe acute respiratory syndrome
46157	H27y000	Influenza with encephalopathy
46397	P8z..00	Respiratory system anomaly NOS
47472	H27y.00	Influenza with other manifestations
47638	R06z.00	[D]Other respiratory system and chest symptoms
48593	H060D00	Acute bronchitis due to respiratory syncytial virus
49794	H060900	Acute neisseria catarrhalis bronchitis
54533	H061000	Acute capillary bronchiolitis
54739	Hyu8400	[X]Respiratory disorders in other diseases CE
61118	H310z00	Simple chronic bronchitis NOS
63697	43jQ.00	Avian influenza virus nucleic acid detection
64716	7N22y00	[SO]Specified respiratory tract NEC
64890	H060E00	Acute bronchitis due to rhinovirus
65916	H060F00	Acute bronchitis due to echovirus
66043	H31y.00	Other chronic bronchitis
66228	H061600	Acute bronchiolitis due to other specified organisms
66397	Hyu1.00	[X]Other acute lower respiratory infections
69192	H061300	Acute exudative bronchiolitis
70630	Hyu8.00	[X]Other diseases of the respiratory system
70815	H464z00	Chronic respiratory conditions due to chemical fumes NOS
71370	H060200	Acute pseudomembranous bronchitis
73100	Hyu1000	[X]Acute bronchitis due to other specified organisms
91123	43jz.00	Parainfluenza type 3 nucleic acid detection
93153	H060B00	Acute bronchitis due to coxsackievirus
94130	43jx.00	Parainfluenza type 1 nucleic acid detection
94858	43jy.00	Parainfluenza type 2 nucleic acid detection
94930	H29..00	Avian influenza

96017	4JU5.00	Influenza B virus detected
96018	4JU2.00	Influenza H3 virus detected
96019	4JU0.00	Influenza H1 virus detected
96286	4JUF.00	Human parainfluenza virus detected
97062	4JU4.00	Influenza A virus, other or untyped strain detected
97279	Hyu0700	[X]Influenza+other manifestations, virus not identified
97605	Hyu0600	[X]Influenza+oth respiratory manifestatns,virus not identifd
97936	Hyu0500	[X]Influenza+other manifestations,influenza virus identified
98102	H2A..11	Influenza A (H1N1) swine flu
98103	1W0..00	Possible influenza A virus H1N1 subtype
98115	1J72.11	Suspected swine influenza
98125	1J72.00	Suspected influenza A virus subtype H1N1 infection
98129	H2A..00	Influenza due to Influenza A virus subtype H1N1
98143	4J3L.00	Influenza A virus H1N1 subtype detected
98156	4JU3.00	Influenza H5 virus detected
98257	Hyu0400	[X]Flu+oth respiratory manifestations,'flu virus identified
99214	Hyu1100	[X]Acute bronchiolitis due to other specified organisms
99762	14B9.00	History of acute lower respiratory tract infection
101775	H060100	Acute membranous bronchitis
103785	H58y500	Respiratory bronchiolitis associated interstitial lung dis
572	H26..00	Pneumonia due to unspecified organism
886	H25..00	Bronchopneumonia due to unspecified organism
1576	H231.00	Pneumonia due to mycoplasma pneumoniae
1849	H21..00	Lobar (pneumococcal) pneumonia
3683	H261.00	Basal pneumonia due to unspecified organism
4910	H56y100	Interstitial pneumonia
5202	H20..00	Viral pneumonia
5324	H28..00	Atypical pneumonia

5612	H224.00	Pneumonia due to staphylococcus
6094	H2z..00	Pneumonia or influenza NOS
6181	H061400	Obliterating fibrous bronchiolitis
9389	H20..11	Chest infection - viral pneumonia
9639	H260.00	Lobar pneumonia due to unspecified organism
10086	H2...00	Pneumonia and influenza
11202	H530z00	Abscess of lung NOS
11849	H2y..00	Other specified pneumonia or influenza
12061	H22y200	Pneumonia - Legionella
12423	H223.00	Pneumonia due to streptococcus
13573	H270000	Influenza with bronchopneumonia
14976	H20z.00	Viral pneumonia NOS
15308	A3A4.00	Legionella
15912	H270.00	Influenza with pneumonia
16287	H25..11	Chest infection - unspecified bronchopneumonia
17025	H233.00	Chlamydial pneumonia
19400	H26..11	Chest infection - pnemonia due to unspecified organism
19992	AC21.00	Lung echinococcus granulosus
21185	H53..00	Abscess of lung and mediastinum
22795	H22..11	Chest infection - other bacterial pneumonia
23095	H22z.00	Bacterial pneumonia NOS
23546	H220.00	Pneumonia due to klebsiella pneumoniae
23726	H24y700	Pneumonia with varicella
25694	H23..00	Pneumonia due to other specified organisms
26125	H312300	Bronchiolitis obliterans
27519	H24y200	Pneumonia with pneumocystis carinii
27641	A789300	HIV disease resulting in Pneumocystis carinii pneumonia
28634	H22..00	Other bacterial pneumonia
29005	H530.00	Abscess of lung
29166	H21..11	Chest infection - pneumococcal pneumonia

29457	H270.11	Chest infection - influenza with pneumonia
30437	H243.00	Pneumonia with whooping cough
30591	H221.00	Pneumonia due to pseudomonas
30653	H23..11	Chest infection - pneumonia organism OS
31269	H201.00	Pneumonia due to respiratory syncytial virus
32172	A551.00	Postmeasles pneumonia
33478	H20y.00	Viral pneumonia NEC
33730	H530000	Single lung abscess
34251	H23z.00	Pneumonia due to specified organism NOS
34274	H246.00	Pneumonia with aspergillosis
34659	H53z.00	Abscess of lung and mediastinum NOS
34732	A054.00	Amoebic lung abscess
35082	H243.11	Pneumonia with pertussis
35189	H530300	Abscess of lung with pneumonia
35220	AD63.00	Pneumocystosis
35745	H270z00	Influenza with pneumonia NOS
36675	H202.00	Pneumonia due to parainfluenza virus
37711	H530100	Multiple lung abscess
37881	H222.00	Pneumonia due to haemophilus influenzae
40299	AB24.11	Pneumonia - candidal
40498	H24..00	Pneumonia with infectious diseases EC
41034	H240.00	Pneumonia with measles
41084	A221.11	Woolsorters' disease
41404	AB50100	Primary pulmonary blastomycosis
41589	H061100	Acute obliterating bronchiolitis
43286	H241.00	Pneumonia with cytomegalic inclusion disease
43884	H22yz00	Pneumonia due to bacteria NOS
45161	A221.00	Pulmonary anthrax
45425	H22y100	Pneumonia due to proteus
47295	A205.00	Pneumonic plague, unspecified

47973	A54x400	Herpes simplex pneumonia
48481	AB24.00	Candidiasis of lung
48804	H222.11	Pneumonia due to haemophilus influenzae
49398	H24y600	Pneumonia with typhoid fever
50408	A730.00	Ornithosis with pneumonia
50867	H22y.00	Pneumonia due to other specified bacteria
52071	H247000	Pneumonia with candidiasis
52384	H22yX00	Pneumonia due to other aerobic gram-negative bacteria
52520	Hyu0800	[X]Other viral pneumonia
53753	Hyu0H00	[X]Other pneumonia, organism unspecified
53947	Hyu0D00	[X]Pneumonia in viral diseases classified elsewhere
53969	H247z00	Pneumonia with systemic mycosis NOS
54540	AB30.00	Primary pulmonary coccidioidomycosis
54551	AB40700	Chronic pulmonary histoplasmosis capsulati
54906	AB65000	Pulmonary cryptococcosis
57667	H530200	Gangrenous pneumonia
58896	A022200	Salmonella pneumonia
59951	AB42.00	Pulmonary histoplasmosis
60119	H230.00	Pneumonia due to Eaton's agent
60299	H22y011	E.coli pneumonia
60482	H24y300	Pneumonia with Q-fever
61623	H24y000	Pneumonia with actinomycosis
62408	AC12.11	Lung fluke disease
62623	H242.00	Pneumonia with ornithosis
62632	H270100	Influenza with pneumonia, influenza virus identified
63763	Hyu0A00	[X]Other bacterial pneumonia
63858	H223000	Pneumonia due to streptococcus, group B
64306	A391.00	Pulmonary actinomycosis
65419	H22y000	Pneumonia due to escherichia coli
66362	H24z.00	Pneumonia with infectious diseases EC NOS

67836	H200.00	Pneumonia due to adenovirus
67901	H24y100	Pneumonia with nocardiasis
69782	H24y.00	Pneumonia with other infectious diseases EC
70559	H24yz00	Pneumonia with other infectious diseases EC NOS
70710	A203.00	Primary pneumonic plague
72182	H24y400	Pneumonia with salmonellosis
73340	A39y000	Pulmonary nocardiosis
73735	H232.00	Pneumonia due to pleuropneumonia like organisms
91481	AB40600	Acute pulmonary histoplasmosis capsulati
96332	AyuEU00	[X]Other pulmonary aspergillosis
98381	Hyu0B00	[X]Pneumonia due to other specified infectious organisms
98782	H24y500	Pneumonia with toxoplasmosis
100742	AB63300	Allergic bronchopulmonary aspergillosis
101292	AB41500	Histoplasma duboisii with pneumonia
101507	AB40500	Histoplasma capsulatum with pneumonia
102918	4JU1.00	Influenza H2 virus detected
103404	H247100	Pneumonia with coccidioidomycosis
104121	H2B..00	Community acquired pneumonia
104264	H2C..00	Hospital acquired pneumonia
106300	H203.00	Pneumonia due to human metapneumovirus
106908	H244.00	Pneumonia with tularaemia
111027	Hyu0C00	[X]Pneumonia in bacterial diseases classified elsewhere
111655	Hyu0G00	[X]Pneumonia in other diseases classified elsewhere

D: Antibiotics

Prodcode	Product_name
22029	amiclav 250mg/125mg tablets (ashbourne pharmaceuticals ltd)
11634	amix 125 oral suspension (ashbourne pharmaceuticals ltd)
11613	amix 250 capsules (ashbourne pharmaceuticals ltd)
21844	amix 250 oral suspension (ashbourne pharmaceuticals ltd)

18786 amix 500 capsules (ashbourne pharmaceuticals ltd)
29697 amopen 125mg/5ml liquid (yorkshire pharmaceuticals ltd)
30498 amopen 250mg capsule (yorkshire pharmaceuticals ltd)
31423 amopen 250mg/5ml liquid (yorkshire pharmaceuticals ltd)
17711 amopen 500mg capsule (yorkshire pharmaceuticals ltd)
12378 amoram 125mg/5ml oral suspension (lpc medical (uk) ltd)
9243 amoram 250mg capsules (lpc medical (uk) ltd)
22438 amoram 250mg/5ml oral suspension (lpc medical (uk) ltd)
22415 amoram 500mg capsules (lpc medical (uk) ltd)
8906 amoxicillin 125mg / clavulanic acid 31mg/5ml oral suspension
13285 amoxicillin 125mg / clavulanic acid 31mg/5ml oral suspension
53942 amoxicillin 125mg / clavulanic acid 62.5mg/5ml oral suspension
41835 amoxicillin 125mg powder (ivax pharmaceuticals uk ltd)
3742 amoxicillin 125mg sugar free chewable tablets
13848 amoxicillin 125mg sugar free powder
485 amoxicillin 125mg/1.25ml oral suspension paediatric
42822 amoxicillin 125mg/5ml mixture (celltech pharma europe ltd)
28872 amoxicillin 125mg/5ml mixture (crosspharma ltd)
41818 amoxicillin 125mg/5ml oral solution (berk pharmaceuticals ltd)
42240 amoxicillin 125mg/5ml oral solution (co-pharma ltd)
29337 amoxicillin 125mg/5ml oral solution (neo laboratories ltd)
62 amoxicillin 125mg/5ml oral suspension
33690 amoxicillin 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
34857 amoxicillin 125mg/5ml oral suspension (actavis uk ltd)
42545 amoxicillin 125mg/5ml oral suspension (almus pharmaceuticals ltd)
50002 amoxicillin 125mg/5ml oral suspension (bristol laboratories ltd)
32622 amoxicillin 125mg/5ml oral suspension (generics (uk) ltd)
23238 amoxicillin 125mg/5ml oral suspension (ivax pharmaceuticals uk ltd)
48038 amoxicillin 125mg/5ml oral suspension (kent pharmaceuticals ltd)
52685 amoxicillin 125mg/5ml oral suspension (phoenix healthcare distribution ltd)

28875 amoxicillin 125mg/5ml oral suspension (ranbaxy (uk) ltd)
43229 amoxicillin 125mg/5ml oral suspension (sandoz ltd)
55047 amoxicillin 125mg/5ml oral suspension (sandoz ltd)
28870 amoxicillin 125mg/5ml oral suspension (teva uk ltd)
56561 amoxicillin 125mg/5ml oral suspension (waymade healthcare plc)
503 amoxicillin 125mg/5ml oral suspension sugar free
33696 amoxicillin 125mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
34679 amoxicillin 125mg/5ml oral suspension sugar free (actavis uk ltd)
53078 amoxicillin 125mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
36054 amoxicillin 125mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
52122 amoxicillin 125mg/5ml oral suspension sugar free (bristol laboratories ltd)
31014 amoxicillin 125mg/5ml oral suspension sugar free (generics (uk) ltd)
24150 amoxicillin 125mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34384 amoxicillin 125mg/5ml oral suspension sugar free (kent pharmaceuticals ltd)
52857 amoxicillin 125mg/5ml oral suspension sugar free (phoenix healthcare distribution ltd)
29858 amoxicillin 125mg/5ml oral suspension sugar free (sandoz ltd)
34638 amoxicillin 125mg/5ml oral suspension sugar free (teva uk ltd)
55626 amoxicillin 125mg/5ml oral suspension sugar free (waymade healthcare plc)
1391 amoxicillin 250mg / clavulanic acid 125mg tablets
7636 amoxicillin 250mg / clavulanic acid 62mg/5ml oral suspension
13262 amoxicillin 250mg / clavulanic acid 62mg/5ml oral suspension
42809 amoxicillin 250mg capsule (c p pharmaceuticals ltd)
31661 amoxicillin 250mg capsule (co-pharma ltd)
28882 amoxicillin 250mg capsule (crosspharma ltd)
34435 amoxicillin 250mg capsule (ddsa pharmaceuticals ltd)
33222 amoxicillin 250mg capsule (lagap)
32872 amoxicillin 250mg capsule (mepra-pharm)
34714 amoxicillin 250mg capsule (neo laboratories ltd)
45267 amoxicillin 250mg capsule (regent laboratories ltd)
9 amoxicillin 250mg capsules

25484 amoxicillin 250mg capsules (a a h pharmaceuticals ltd)
33343 amoxicillin 250mg capsules (actavis uk ltd)
54796 amoxicillin 250mg capsules (boston healthcare ltd)
54491 amoxicillin 250mg capsules (bristol laboratories ltd)
30745 amoxicillin 250mg capsules (generics (uk) ltd)
34042 amoxicillin 250mg capsules (ivax pharmaceuticals uk ltd)
30528 amoxicillin 250mg capsules (kent pharmaceuticals ltd)
54271 amoxicillin 250mg capsules (mawdsley-brooks & company ltd)
51536 amoxicillin 250mg capsules (milpharm ltd)
30743 amoxicillin 250mg capsules (ranbaxy (uk) ltd)
48006 amoxicillin 250mg capsules (sandoz ltd)
23967 amoxicillin 250mg capsules (teva uk ltd)
54185 amoxicillin 250mg capsules (wockhardt uk ltd)
870 amoxicillin 250mg sugar free chewable tablets
42815 amoxicillin 250mg/5ml mixture (celltech pharma europe ltd)
33570 amoxicillin 250mg/5ml mixture (crosspharma ltd)
40238 amoxicillin 250mg/5ml mixture (mepra-pharm)
45317 amoxicillin 250mg/5ml oral solution (neo laboratories ltd)
427 amoxicillin 250mg/5ml oral suspension
33165 amoxicillin 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
34760 amoxicillin 250mg/5ml oral suspension (actavis uk ltd)
41090 amoxicillin 250mg/5ml oral suspension (almus pharmaceuticals ltd)
55018 amoxicillin 250mg/5ml oral suspension (bristol laboratories ltd)
33689 amoxicillin 250mg/5ml oral suspension (generics (uk) ltd)
32640 amoxicillin 250mg/5ml oral suspension (ivax pharmaceuticals uk ltd)
51382 amoxicillin 250mg/5ml oral suspension (phoenix healthcare distribution ltd)
55499 amoxicillin 250mg/5ml oral suspension (ranbaxy (uk) ltd)
56223 amoxicillin 250mg/5ml oral suspension (sandoz ltd)
37755 amoxicillin 250mg/5ml oral suspension (sandoz ltd)
53924 amoxicillin 250mg/5ml oral suspension (sigma pharmaceuticals plc)

27725	amoxicillin 250mg/5ml oral suspension (teva uk ltd)
585	amoxicillin 250mg/5ml oral suspension sugar free
34232	amoxicillin 250mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
40243	amoxicillin 250mg/5ml oral suspension sugar free (actavis uk ltd)
54222	amoxicillin 250mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
42732	amoxicillin 250mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
49065	amoxicillin 250mg/5ml oral suspension sugar free (bristol laboratories ltd)
31535	amoxicillin 250mg/5ml oral suspension sugar free (generics (uk) ltd)
33699	amoxicillin 250mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34855	amoxicillin 250mg/5ml oral suspension sugar free (kent pharmaceuticals ltd)
34775	amoxicillin 250mg/5ml oral suspension sugar free (teva uk ltd)
17746	amoxicillin 375mg soluble tablets
1140	amoxicillin 3g oral powder sachets sugar free
33383	amoxicillin 3g oral powder sachets sugar free (a a h pharmaceuticals ltd)
40168	amoxicillin 3g oral powder sachets sugar free (kent pharmaceuticals ltd)
28130	amoxicillin 3g oral powder sachets sugar free (teva uk ltd)
41734	amoxicillin 3g powder (actavis uk ltd)
15192	amoxicillin 400mg / clavulanic acid 57mg/5ml sugar free oral suspension
5662	amoxicillin 500mg / clarithromycin 500mg / lansoprazole 30mg triple pack
13216	amoxicillin 500mg / clavulanic acid 125mg tablets
38684	amoxicillin 500mg capsule (c p pharmaceuticals ltd)
35570	amoxicillin 500mg capsule (crosspharma ltd)
34885	amoxicillin 500mg capsule (ddsa pharmaceuticals ltd)
44854	amoxicillin 500mg capsule (lagap)
34912	amoxicillin 500mg capsule (neo laboratories ltd)
48	amoxicillin 500mg capsules
33692	amoxicillin 500mg capsules (a a h pharmaceuticals ltd)
53627	amoxicillin 500mg capsules (accord healthcare ltd)
26157	amoxicillin 500mg capsules (actavis uk ltd)
52820	amoxicillin 500mg capsules (alliance healthcare (distribution) ltd)

47640	amoxicillin 500mg capsules (almus pharmaceuticals ltd)
55527	amoxicillin 500mg capsules (boston healthcare ltd)
52771	amoxicillin 500mg capsules (bristol laboratories ltd)
23740	amoxicillin 500mg capsules (generics (uk) ltd)
29463	amoxicillin 500mg capsules (ivax pharmaceuticals uk ltd)
33706	amoxicillin 500mg capsules (kent pharmaceuticals ltd)
52058	amoxicillin 500mg capsules (medreich plc)
54725	amoxicillin 500mg capsules (milpharm ltd)
34852	amoxicillin 500mg capsules (ranbaxy (uk) ltd)
31801	amoxicillin 500mg capsules (sandoz ltd)
34001	amoxicillin 500mg capsules (teva uk ltd)
55394	amoxicillin 500mg capsules (wockhardt uk ltd)
1722	amoxicillin 500mg dispersible tablets
2281	amoxicillin 500mg sugar free chewable tablets
4582	amoxicillin 750mg soluble tablets
9343	amoxicillin 750mg sugar free powder
439	amoxicillin with clavulanic acid dispersible tablets
2171	amoxil 125mg/1.25ml paediatric oral suspension (glaxosmithkline uk ltd)
2153	amoxil 125mg/5ml syrup sucrose free (glaxosmithkline uk ltd)
133	amoxil 250mg capsules (glaxosmithkline uk ltd)
1812	amoxil 250mg/5ml syrup sucrose free (glaxosmithkline uk ltd)
2174	amoxil 3g oral powder sachets sucrose free (glaxosmithkline uk ltd)
847	amoxil 500mg capsules (glaxosmithkline uk ltd)
49590	amoxil 500mg capsules (lexon (uk) ltd)
51436	amoxil 500mg capsules (mawdsley-brooks & company ltd)
56700	amoxil 500mg capsules (necessity supplies ltd)
15148	amoxil 500mg dispersible tablet (smithkline beecham plc)
4010	amoxil 750mg sachets (glaxosmithkline uk ltd)
4154	amoxil fiztab 125mg tablet (bencard)
1637	amoxil fiztab 250mg tablet (bencard)

7737	amoxil fiztab 500mg tablet (bencard)
31571	amoxycillin
32505	amoxycillin
27897	amoxycillin
7592	amoxycillin 125 mg cap
22469	amoxycillin 125mg/31mg clavulanic acid
25034	amoxycillin 125mg/62mg clavulanic acid
7581	amoxycillin 125mg/62mg clavulanic acid syr
27886	amoxycillin 250/clavulanic acid 125 disp
19795	amoxycillin 250mg/clavulanic acid 125mg
1570	amoxycillin 500 mg tab
2902	amoxycillin fiztab 125 mg tab
1393	amoxycillin fiztab 250 mg tab
22293	amoxycillin trihydrate sachet
21982	amoxycillin trihydrate sachet
31286	amoxymed 125mg/5ml oral solution (medipharma ltd)
3669	amoxymed 250mg capsule (medipharma ltd)
33109	amrit 125mg/5ml liquid (bhr pharmaceuticals ltd)
27714	amrit 250mg capsule (bhr pharmaceuticals ltd)
33110	amrit 250mg/5ml liquid (bhr pharmaceuticals ltd)
33112	amrit 500mg capsule (bhr pharmaceuticals ltd)
27495	arpimycin 125mg/5ml liquid (rosemont pharmaceuticals ltd)
36544	arpimycin 125mg/5ml oral suspension (rosemont pharmaceuticals ltd)
24220	arpimycin 250mg/5ml liquid (rosemont pharmaceuticals ltd)
36514	arpimycin 250mg/5ml oral suspension (rosemont pharmaceuticals ltd)
37022	arpimycin 500mg/5ml liquid (rosemont pharmaceuticals ltd)
415	augmentin 125/31 sf oral suspension (glaxosmithkline uk ltd)
50595	augmentin 125/31 sf oral suspension (mawdsley-brooks & company ltd)
51164	augmentin 125/31 sf oral suspension (waymade healthcare plc)
569	augmentin 250/62 sf oral suspension (glaxosmithkline uk ltd)

52666 augmentin 250/62 sf oral suspension (sigma pharmaceuticals plc)
2507 augmentin 375mg dispersible tablets (glaxosmithkline uk ltd)
49063 augmentin 375mg tablets (doncaster pharmaceuticals ltd)
399 augmentin 375mg tablets (glaxosmithkline uk ltd)
48683 augmentin 375mg tablets (lexon (uk) ltd)
49374 augmentin 375mg tablets (mawdsley-brooks & company ltd)
49048 augmentin 375mg tablets (waymade healthcare plc)
50279 augmentin 625mg tablets (doncaster pharmaceuticals ltd)
509 augmentin 625mg tablets (glaxosmithkline uk ltd)
49656 augmentin 625mg tablets (lexon (uk) ltd)
52207 augmentin 625mg tablets (mawdsley-brooks & company ltd)
49321 augmentin 625mg tablets (sigma pharmaceuticals plc)
49683 augmentin 625mg tablets (waymade healthcare plc)
5341 augmentin-duo 400/57 oral suspension (glaxosmithkline uk ltd)
56591 augmentin-duo 400/57 oral suspension (lexon (uk) ltd)
51194 augmentin-duo 400/57 oral suspension (sigma pharmaceuticals plc)
31007 aureomycin powder (wyeth pharmaceuticals)
25127 avelox 400mg tablets (bayer plc)
26289 bacticlor mr 375mg tablets (ranbaxy (uk) ltd)
4895 benzoyl peroxide 5% / erythromycin 3% gel
21802 berkmycen 250mg tablet (berk pharmaceuticals ltd)
17093 bisolvomycin capsule (boehringer ingelheim ltd)
27016 ciprofloxacin
498 ciprofloxacin 100mg tablets
42507 ciprofloxacin 100mg tablets (a a h pharmaceuticals ltd)
48031 ciprofloxacin 100mg tablets (almus pharmaceuticals ltd)
54555 ciprofloxacin 100mg tablets (doncaster pharmaceuticals ltd)
54674 ciprofloxacin 100mg tablets (phoenix healthcare distribution ltd)
39913 ciprofloxacin 100mg tablets (sandoz ltd)
52309 ciprofloxacin 100mg tablets (sigma pharmaceuticals plc)

52945 ciprofloxacin 200mg/100ml solution for infusion vials
56439 ciprofloxacin 200mg/100ml solution for infusion vials (a a h pharmaceuticals ltd)
34647 ciprofloxacin 250mg tablet (neo laboratories ltd)
281 ciprofloxacin 250mg tablets
29343 ciprofloxacin 250mg tablets (a a h pharmaceuticals ltd)
50601 ciprofloxacin 250mg tablets (accord healthcare ltd)
34308 ciprofloxacin 250mg tablets (actavis uk ltd)
51537 ciprofloxacin 250mg tablets (alliance healthcare (distribution) ltd)
54393 ciprofloxacin 250mg tablets (arrow generics ltd)
54701 ciprofloxacin 250mg tablets (bristol laboratories ltd)
56381 ciprofloxacin 250mg tablets (co-pharma ltd)
43814 ciprofloxacin 250mg tablets (dr reddy's laboratories (uk) ltd)
33989 ciprofloxacin 250mg tablets (generics (uk) ltd)
41561 ciprofloxacin 250mg tablets (ivax pharmaceuticals uk ltd)
54302 ciprofloxacin 250mg tablets (medreich plc)
34448 ciprofloxacin 250mg tablets (niche generics ltd)
34694 ciprofloxacin 250mg tablets (pliva pharma ltd)
34559 ciprofloxacin 250mg tablets (sandoz ltd)
34478 ciprofloxacin 250mg tablets (teva uk ltd)
34655 ciprofloxacin 250mg tablets (wockhardt uk ltd)
4091 ciprofloxacin 250mg/5ml oral suspension
10304 ciprofloxacin 2mg/ml infusion
45341 ciprofloxacin 500mg tablet (neo laboratories ltd)
34322 ciprofloxacin 500mg tablet (niche generics ltd)
583 ciprofloxacin 500mg tablets
29458 ciprofloxacin 500mg tablets (a a h pharmaceuticals ltd)
52501 ciprofloxacin 500mg tablets (accord healthcare ltd)
34605 ciprofloxacin 500mg tablets (actavis uk ltd)
49445 ciprofloxacin 500mg tablets (almus pharmaceuticals ltd)
56789 ciprofloxacin 500mg tablets (apc pharmaceuticals & chemicals (europe) ltd)

52616 ciprofloxacin 500mg tablets (arrow generics ltd)
53641 ciprofloxacin 500mg tablets (co-pharma ltd)
50055 ciprofloxacin 500mg tablets (doncaster pharmaceuticals ltd)
53088 ciprofloxacin 500mg tablets (dr reddy's laboratories (uk) ltd)
30707 ciprofloxacin 500mg tablets (generics (uk) ltd)
42174 ciprofloxacin 500mg tablets (ivax pharmaceuticals uk ltd)
55917 ciprofloxacin 500mg tablets (medreich plc)
43557 ciprofloxacin 500mg tablets (pliva pharma ltd)
53878 ciprofloxacin 500mg tablets (ranbaxy (uk) ltd)
43797 ciprofloxacin 500mg tablets (sandoz ltd)
45285 ciprofloxacin 500mg tablets (teva uk ltd)
34494 ciprofloxacin 500mg tablets (wockhardt uk ltd)
34973 ciprofloxacin 750mg tablet (niche generics ltd)
1837 ciprofloxacin 750mg tablets
29472 ciprofloxacin 750mg tablets (a a h pharmaceuticals ltd)
43517 ciprofloxacin 750mg tablets (actavis uk ltd)
52099 ciprofloxacin 750mg tablets (bristol laboratories ltd)
56856 ciprofloxacin 750mg tablets (ranbaxy (uk) ltd)
28544 ciprofloxaxin 400mg/200ml in glucose 5% infusion
9154 ciproxin 100mg tablets (bayer plc)
1202 ciproxin 250mg tablets (bayer plc)
52353 ciproxin 250mg tablets (doncaster pharmaceuticals ltd)
53519 ciproxin 250mg tablets (lexon (uk) ltd)
163 ciproxin 250mg/5ml oral suspension (bayer plc)
728 ciproxin 500mg tablets (bayer plc)
52807 ciproxin 500mg tablets (mawdsley-brooks & company ltd)
52177 ciproxin 500mg tablets (sigma pharmaceuticals plc)
49839 ciproxin 500mg tablets (waymade healthcare plc)
7752 ciproxin 750mg tablets (bayer plc)
45591 clarie xl 500mg tablets (teva uk ltd)

10326	clarithromycin 125mg granules straws
331	clarithromycin 125mg/5ml oral suspension
45795	clarithromycin 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
54903	clarithromycin 125mg/5ml oral suspension (alliance healthcare (distribution) ltd)
51831	clarithromycin 125mg/5ml oral suspension (phoenix healthcare distribution ltd)
41453	clarithromycin 125mg/5ml oral suspension (ranbaxy (uk) ltd)
53168	clarithromycin 125mg/5ml oral suspension (sandoz ltd)
26059	clarithromycin 187.5mg granules straws
765	clarithromycin 250mg granules sachets
17645	clarithromycin 250mg granules straws
537	clarithromycin 250mg tablets
34650	clarithromycin 250mg tablets (a a h pharmaceuticals ltd)
54472	clarithromycin 250mg tablets (accord healthcare ltd)
48163	clarithromycin 250mg tablets (actavis uk ltd)
52158	clarithromycin 250mg tablets (alliance healthcare (distribution) ltd)
54882	clarithromycin 250mg tablets (almus pharmaceuticals ltd)
52719	clarithromycin 250mg tablets (apotex uk ltd)
53086	clarithromycin 250mg tablets (doncaster pharmaceuticals ltd)
34394	clarithromycin 250mg tablets (generics (uk) ltd)
51154	clarithromycin 250mg tablets (kent pharmaceuticals ltd)
53153	clarithromycin 250mg tablets (phoenix healthcare distribution ltd)
53688	clarithromycin 250mg tablets (ranbaxy (uk) ltd)
47582	clarithromycin 250mg tablets (sandoz ltd)
50946	clarithromycin 250mg tablets (sigma pharmaceuticals plc)
54269	clarithromycin 250mg tablets (somex pharma)
34533	clarithromycin 250mg tablets (teva uk ltd)
54897	clarithromycin 250mg tablets (tillomed laboratories ltd)
53144	clarithromycin 250mg tablets (wockhardt uk ltd)
5357	clarithromycin 250mg/5ml oral suspension
54241	clarithromycin 250mg/5ml oral suspension (a a h pharmaceuticals ltd)

55148 clarithromycin 250mg/5ml oral suspension (alliance healthcare (distribution) ltd)
34811 clarithromycin 250mg/5ml oral suspension (ranbaxy (uk) ltd)
53179 clarithromycin 250mg/5ml oral suspension (sandoz ltd)
54208 clarithromycin 250mg/5ml oral suspension (sigma pharmaceuticals plc)
55428 clarithromycin 250mg/5ml oral suspension (waymade healthcare plc)
54529 clarithromycin 500mg modified-release tablet (hillcross pharmaceuticals ltd)
6803 clarithromycin 500mg modified-release tablets
681 clarithromycin 500mg tablets
38163 clarithromycin 500mg tablets (a a h pharmaceuticals ltd)
51426 clarithromycin 500mg tablets (accord healthcare ltd)
48023 clarithromycin 500mg tablets (actavis uk ltd)
49939 clarithromycin 500mg tablets (alliance healthcare (distribution) ltd)
53715 clarithromycin 500mg tablets (almus pharmaceuticals ltd)
53776 clarithromycin 500mg tablets (doncaster pharmaceuticals ltd)
34608 clarithromycin 500mg tablets (generics (uk) ltd)
53703 clarithromycin 500mg tablets (kent pharmaceuticals ltd)
46488 clarithromycin 500mg tablets (ranbaxy (uk) ltd)
40784 clarithromycin 500mg tablets (sandoz ltd)
53109 clarithromycin 500mg tablets (somex pharma)
34974 clarithromycin 500mg tablets (teva uk ltd)
53875 clarithromycin 500mg tablets (tillomed laboratories ltd)
11433 clarithromycin 500mg with lansoprazole 30mg and amoxicillin 500mg triple pack
6497 clarithromycin 500mg with metronidazole 400mg with lansoprazole 30mg triple pack
28349 clarosip 125mg granules for oral suspension straws (grunenthal ltd)
31689 clarosip 187.5mg granules for oral suspension straws (grunenthal ltd)
31690 clarosip 250mg granules for oral suspension straws (grunenthal ltd)
9925 clavulanic acid 125mg with amoxicillin 250mg tablets
13239 clavulanic acid 125mg with amoxicillin 500mg tablets
24006 clavulanic acid 31mg with amoxcillin 125mg/5ml oral suspension
21775 clavulanic acid 31mg with amoxicillin 125mg/5ml sugar free oral suspension

20432	clavulanic acid 57mg with amoxicillin 400mg/5ml sugar free suspension
42485	clavulanic acid 62mg with amoxicillin 250mg/5ml oral suspension
16612	clavulanic acid 62mg with amoxicillin 250mg/5ml sugar free suspension
24093	clavulanic acid with amoxicillin dispersible tablets
12504	clomocycline 170mg capsules
10200	co-amoxiclav 125mg/31mg/5ml oral suspension
54052	co-amoxiclav 125mg/31mg/5ml oral suspension (a a h pharmaceuticals ltd)
54732	co-amoxiclav 125mg/31mg/5ml oral suspension (generics (uk) ltd)
1638	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free
43548	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
54324	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (actavis uk ltd)
54452	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
54808	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
28874	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
56884	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (phoenix healthcare distribution ltd)
34680	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (ranbaxy (uk) ltd)
34972	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (sandoz ltd)
829	co-amoxiclav 250mg/125mg dispersible tablets sugar free
545	co-amoxiclav 250mg/125mg tablets
30786	co-amoxiclav 250mg/125mg tablets (a a h pharmaceuticals ltd)
19209	co-amoxiclav 250mg/125mg tablets (actavis uk ltd)
51623	co-amoxiclav 250mg/125mg tablets (alliance healthcare (distribution) ltd)
48147	co-amoxiclav 250mg/125mg tablets (almus pharmaceuticals ltd)
34297	co-amoxiclav 250mg/125mg tablets (generics (uk) ltd)
28871	co-amoxiclav 250mg/125mg tablets (ivax pharmaceuticals uk ltd)
33693	co-amoxiclav 250mg/125mg tablets (kent pharmaceuticals ltd)
50446	co-amoxiclav 250mg/125mg tablets (phoenix healthcare distribution ltd)
30783	co-amoxiclav 250mg/125mg tablets (ranbaxy (uk) ltd)

19414 co-amoxiclav 250mg/125mg tablets (sandoz ltd)
34734 co-amoxiclav 250mg/125mg tablets (teva uk ltd)
55312 co-amoxiclav 250mg/125mg tablets (waymade healthcare plc)
46915 co-amoxiclav 250mg/125mg tablets (zentiva)
7364 co-amoxiclav 250mg/62mg/5ml oral suspension
54708 co-amoxiclav 250mg/62mg/5ml oral suspension (a a h pharmaceuticals ltd)
54780 co-amoxiclav 250mg/62mg/5ml oral suspension (generics (uk) ltd)
524 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free
42227 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
51678 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
37304 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
40320 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (ranbaxy (uk) ltd)
46918 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (sandoz ltd)
34234 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (teva uk ltd)
56578 co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (waymade healthcare plc)
6687 co-amoxiclav 400mg/57mg/5ml oral suspension sugar free
51637 co-amoxiclav 400mg/57mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
641 co-amoxiclav 500mg/125mg tablets
33701 co-amoxiclav 500mg/125mg tablets (a a h pharmaceuticals ltd)
50742 co-amoxiclav 500mg/125mg tablets (actavis uk ltd)
50341 co-amoxiclav 500mg/125mg tablets (alliance healthcare (distribution) ltd)
53609 co-amoxiclav 500mg/125mg tablets (apc pharmaceuticals & chemicals (europe) ltd)
53996 co-amoxiclav 500mg/125mg tablets (aurobindo pharma ltd)
30705 co-amoxiclav 500mg/125mg tablets (generics (uk) ltd)
29356 co-amoxiclav 500mg/125mg tablets (ivax pharmaceuticals uk ltd)
40148 co-amoxiclav 500mg/125mg tablets (kent pharmaceuticals ltd)
49610 co-amoxiclav 500mg/125mg tablets (medreich plc)
54591 co-amoxiclav 500mg/125mg tablets (phoenix healthcare distribution ltd)
34493 co-amoxiclav 500mg/125mg tablets (ranbaxy (uk) ltd)
32910 co-amoxiclav 500mg/125mg tablets (sandoz ltd)

29353 co-amoxiclav 500mg/125mg tablets (teva uk ltd)
44154 co-amoxiclav 500mg/125mg tablets (zentiva)
21860 cyclodox 100mg capsule (berk pharmaceuticals ltd)
21878 demix 100 capsules (ashbourne pharmaceuticals ltd)
21828 demix 50 capsules (ashbourne pharmaceuticals ltd)
2428 distaclor 125mg/5ml liquid (dista products ltd)
25384 distaclor 125mg/5ml oral suspension (flynn pharma ltd)
4576 distaclor 250mg capsule (dista products ltd)
9219 distaclor 250mg/5ml liquid (dista products ltd)
22042 distaclor 250mg/5ml oral suspension (flynn pharma ltd)
7889 distaclor 375mg modified-release tablet (dista products ltd)
319 distaclor 500mg capsule (dista products ltd)
18243 distaclor 500mg capsules (flynn pharma ltd)
3523 distaclor 500mg modified-release tablet (dista products ltd)
20992 distaclor mr 375mg tablets (flynn pharma ltd)
21038 doxatet 100mg tablet (manufacturer unknown)
2884 doxycycline (as hyclate) 100mg dispersible tablets
970 doxycycline (as hyclate) 100mg tablets
12987 doxycycline (as hyclate) 50mg capsules with microgranules
23819 doxycycline (as hyclate) 50mg capsules with microgranules
8724 doxycycline (as hyclate) 50mg/5ml oral solution
41560 doxycycline 100mg capsule (ivax pharmaceuticals uk ltd)
34594 doxycycline 100mg capsule (neo laboratories ltd)
34423 doxycycline 100mg capsule (pliva pharma ltd)
41605 doxycycline 100mg capsule (sandoz ltd)
1046 doxycycline 100mg capsules
24149 doxycycline 100mg capsules (a a h pharmaceuticals ltd)
34300 doxycycline 100mg capsules (actavis uk ltd)
49737 doxycycline 100mg capsules (alliance healthcare (distribution) ltd)
46807 doxycycline 100mg capsules (almus pharmaceuticals ltd)

32066 doxycycline 100mg capsules (generics (uk) ltd)
24126 doxycycline 100mg capsules (ivax pharmaceuticals uk ltd)
33671 doxycycline 100mg capsules (kent pharmaceuticals ltd)
53310 doxycycline 100mg capsules (sigma pharmaceuticals plc)
30739 doxycycline 100mg capsules (teva uk ltd)
55519 doxycycline 100mg capsules (waymade healthcare plc)
6396 doxycycline 100mg dispersible tablets sugar free
26747 doxycycline 100mg tablet (neo laboratories ltd)
40796 doxycycline 40mg modified-release capsules
264 doxycycline 50mg capsules
34175 doxycycline 50mg capsules (a a h pharmaceuticals ltd)
48095 doxycycline 50mg capsules (actavis uk ltd)
53973 doxycycline 50mg capsules (alliance healthcare (distribution) ltd)
34765 doxycycline 50mg capsules (generics (uk) ltd)
40391 doxycycline 50mg capsules (ivax pharmaceuticals uk ltd)
32419 doxycycline 50mg capsules (teva uk ltd)
23405 doxylar 100mg capsules (sandoz ltd)
23432 doxylar 50mg capsules (sandoz ltd)
17226 economycin 250mg capsule (ddsa pharmaceuticals ltd)
26111 economycin 250mg tablet (ddsa pharmaceuticals ltd)
40980 efracea 40mg modified-release capsules (galderma (uk) ltd)
4489 erycen 250mg tablet (berk pharmaceuticals ltd)
23017 erycen 500mg tablet (berk pharmaceuticals ltd)
318 erymax 250mg capsule (elan pharma)
10190 erymax 250mg gastro-resistant capsules (teva uk ltd)
14511 erymax sprinkle 125mg capsule (elan pharma)
9434 erymin 250mg/5ml oral suspension (elan pharma)
48017 erythoden 125mg/5ml liquid (stevenden healthcare)
41389 erythoden 250mg/5ml liquid (stevenden healthcare)
39616 erythrocin 250 tablets (amdipharm plc)

480 erythrocin 250mg tablet (abbott laboratories ltd)
1072 erythrocin 500 500mg tablet (abbott laboratories ltd)
39613 erythrocin 500 tablets (amdipharm plc)
53449 erythrocin 500 tablets (lexon (uk) ltd)
51984 erythrocin 500 tablets (mawdsley-brooks & company ltd)
53004 erythrocin 500 tablets (necessity supplies ltd)
50693 erythrocin 500 tablets (sigma pharmaceuticals plc)
50223 erythrocin 500 tablets (stephar (u.k.) ltd)
27768 erythrolar 250mg tablet (lagap)
50205 erythrolar 250mg tablets (ennogen pharma ltd)
4153 erythrolar 250mg/5ml liquid (lagap)
23954 erythrolar 500mg tablet (lagap)
49301 erythrolar 500mg tablets (ennogen pharma ltd)
3209 erythromid 250mg tablet (abbott laboratories ltd)
9148 erythromid ds 500mg tablet (abbott laboratories ltd)
1376 erythromycin 100 mg syr
7792 erythromycin 12 mg syr
14429 erythromycin 125mg sprinkle capsules
34231 erythromycin 125mg/5ml liquid (berk pharmaceuticals ltd)
33248 erythromycin 125mg/5ml liquid (ivax pharmaceuticals uk ltd)
397 erythromycin 125mg/5ml oral suspension
9656 erythromycin 2% gel
1969 erythromycin 250 mg mix
29154 erythromycin 250mg capsule (actavis uk ltd)
103 erythromycin 250mg gastro-resistant capsules
33686 erythromycin 250mg gastro-resistant capsules (a a h pharmaceuticals ltd)
50580 erythromycin 250mg gastro-resistant capsules (actavis uk ltd)
50694 erythromycin 250mg gastro-resistant capsules (alliance healthcare (distribution) ltd)
55133 erythromycin 250mg gastro-resistant capsules (kent pharmaceuticals ltd)
49952 erythromycin 250mg gastro-resistant capsules (phoenix healthcare distribution ltd)

34512 erythromycin 250mg gastro-resistant capsules (teva uk ltd)
55397 erythromycin 250mg gastro-resistant capsules (waymade healthcare plc)
34837 erythromycin 250mg gastro-resistant tablet (co-pharma ltd)
63 erythromycin 250mg gastro-resistant tablets
24127 erythromycin 250mg gastro-resistant tablets (a a h pharmaceuticals ltd)
33703 erythromycin 250mg gastro-resistant tablets (abbott laboratories ltd)
29344 erythromycin 250mg gastro-resistant tablets (actavis uk ltd)
52906 erythromycin 250mg gastro-resistant tablets (alliance healthcare (distribution) ltd)
42661 erythromycin 250mg gastro-resistant tablets (almus pharmaceuticals ltd)
52952 erythromycin 250mg gastro-resistant tablets (co-pharma ltd)
42296 erythromycin 250mg gastro-resistant tablets (dr reddy's laboratories (uk) ltd)
34334 erythromycin 250mg gastro-resistant tablets (generics (uk) ltd)
24129 erythromycin 250mg gastro-resistant tablets (ivax pharmaceuticals uk ltd)
53986 erythromycin 250mg gastro-resistant tablets (medreich plc)
55483 erythromycin 250mg gastro-resistant tablets (milpharm ltd)
52428 erythromycin 250mg gastro-resistant tablets (phoenix healthcare distribution ltd)
31530 erythromycin 250mg gastro-resistant tablets (ranbaxy (uk) ltd)
34479 erythromycin 250mg gastro-resistant tablets (sovereign medical ltd)
33685 erythromycin 250mg gastro-resistant tablets (teva uk ltd)
34873 erythromycin 250mg tablet (berk pharmaceuticals ltd)
34189 erythromycin 250mg tablet (c p pharmaceuticals ltd)
553 erythromycin 250mg.5ml oral suspension
47242 erythromycin 250mg/5ml liquid (c p pharmaceuticals ltd)
41584 erythromycin 250mg/5ml liquid (ivax pharmaceuticals uk ltd)
3408 erythromycin 500 mg cap
401 erythromycin 500mg ec gastro-resistant tablets
34869 erythromycin 500mg tablet (c p pharmaceuticals ltd)
41604 erythromycin 500mg tablet (hillcross pharmaceuticals ltd)
26365 erythromycin 500mg tablet (ivax pharmaceuticals uk ltd)
55300 erythromycin 500mg tablet (teva uk ltd)

47676	erythromycin 500mg/5ml liquid (c p pharmaceuticals ltd)
2326	erythromycin 500mg/5ml oral suspension
37796	erythromycin estolate 125mg/5ml suspension
9903	erythromycin estolate 250mg capsules
40073	erythromycin estolate 250mg/5ml suspension
37694	erythromycin estolate 500mg tablets
2429	erythromycin ethyl succinate 125mg/5ml oral suspension
13167	erythromycin ethyl succinate 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
49978	erythromycin ethyl succinate 125mg/5ml oral suspension (focus pharmaceuticals ltd)
50948	erythromycin ethyl succinate 125mg/5ml oral suspension (phoenix healthcare distribution ltd)
47126	erythromycin ethyl succinate 125mg/5ml oral suspension (pinewood healthcare)
34779	erythromycin ethyl succinate 125mg/5ml oral suspension (sandoz ltd)
4672	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free
33697	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
42659	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (abbott laboratories ltd)
55589	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
48101	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (focus pharmaceuticals ltd)
33695	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (generics (uk) ltd)
34795	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
45870	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (pinewood healthcare)
33705	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (teva uk ltd)
2376	erythromycin ethyl succinate 250mg/5ml oral suspension
13120	erythromycin ethyl succinate 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
32902	erythromycin ethyl succinate 250mg/5ml oral suspension (kent pharmaceuticals ltd)

46696	erythromycin ethyl succinate 250mg/5ml oral suspension (sandoz ltd)
2225	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free
32898	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
46154	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (abbott laboratories ltd)
52860	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
33694	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (generics (uk) ltd)
30177	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34853	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (teva uk ltd)
733	erythromycin ethyl succinate 500mg tablets
2226	erythromycin ethyl succinate 500mg/5ml oral suspension
30980	erythromycin ethyl succinate 500mg/5ml oral suspension (kent pharmaceuticals ltd)
14171	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free
31514	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (abbott laboratories ltd)
25595	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
27203	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (teva uk ltd)
25751	erythromycin ethylsuccinate (coated) 250mg/5ml oral suspension sugar free
30234	erythromycin ethylsuccinate 125mg sachets
12330	erythromycin ethylsuccinate 1g sachets
13635	erythromycin ethylsuccinate 250mg sachets
15713	erythromycin ethylsuccinate 500mg sachets
1037	erythromycin ethylsuccinate sf 125 mg/5ml sus
3907	erythromycin sf sach 250 mg
438	erythromycin stearate 250mg tablets
2350	erythromycin stearate 500mg tablets
3572	erythroped 250mg powder (abbott laboratories ltd)

16747 erythroped 250mg sachets (abbott laboratories ltd)
105 erythroped 250mg/5ml liquid (abbott laboratories ltd)
532 erythroped 250mg/5ml oral suspension (abbott laboratories ltd)
4596 erythroped a 1g sachets (abbott laboratories ltd)
327 erythroped a 500mg tablet (abbott laboratories ltd)
39632 erythroped a 500mg tablets (amdipharm plc)
54098 erythroped a 500mg tablets (lexon (uk) ltd)
56203 erythroped a 500mg tablets (sigma pharmaceuticals plc)
4372 erythroped forte 500mg sachets (abbott laboratories ltd)
993 erythroped forte 500mg/5ml liquid (abbott laboratories ltd)
4610 erythroped forte 500mg/5ml oral suspension (abbott laboratories ltd)
39642 erythroped forte sf 500mg/5ml oral suspension (amdipharm plc)
3042 erythroped pi 125mg sachets (abbott laboratories ltd)
997 erythroped pi 125mg/5ml liquid (abbott laboratories ltd)
825 erythroped pi 125mg/5ml oral suspension (abbott laboratories ltd)
39623 erythroped pi sf 125mg/5ml oral suspension (amdipharm plc)
39669 erythroped sf 250mg/5ml oral suspension (amdipharm plc)
18930 flemoxin 375mg soluble tablet (paines & byrne ltd)
24396 flemoxin 750mg soluble tablet (paines & byrne ltd)
14386 galenamox 125mg/5ml oral suspension (galen ltd)
14371 galenamox 250mg capsules (galen ltd)
14407 galenamox 250mg/5ml oral suspension (galen ltd)
14396 galenamox 500mg capsules (galen ltd)
18682 ilosone 125mg/5ml liquid (dista products ltd)
17207 ilosone 250mg capsule (dista products ltd)
19330 ilosone 250mg/5ml liquid (dista products ltd)
18643 ilosone 500mg tablet (dista products ltd)
23244 ilotycin 250mg tablet (eli lilly and company ltd)
12541 imperacin 250mg tablet (astrazeneca uk ltd)
7485 keflex 125mg/5ml liquid (eli lilly and company ltd)

27072 keflex 125mg/5ml oral suspension (flynn pharma ltd)
7430 keflex 250mg capsule (eli lilly and company ltd)
11989 keflex 250mg capsules (flynn pharma ltd)
9157 keflex 250mg tablet (eli lilly and company ltd)
830 keflex 250mg tablets (flynn pharma ltd)
10455 keflex 250mg/5ml liquid (eli lilly and company ltd)
28722 keflex 250mg/5ml oral suspension (flynn pharma ltd)
12276 keflex 500mg capsule (eli lilly and company ltd)
24618 keflex 500mg capsules (flynn pharma ltd)
9603 keflex 500mg tablet (eli lilly and company ltd)
31110 keflex 500mg tablets (flynn pharma ltd)
26233 keftid 125mg/5ml oral suspension (co-pharma ltd)
26207 keftid 250mg capsules (co-pharma ltd)
41853 keftid 250mg/5ml oral suspension (co-pharma ltd)
26236 keftid 500mg capsules (co-pharma ltd)
33304 kerymax 250mg gastro-resistant capsules (kent pharmaceuticals ltd)
26989 kiflone 125mg/5ml oral solution (berk pharmaceuticals ltd)
21835 kiflone 250mg capsule (berk pharmaceuticals ltd)
21979 kiflone 250mg/5ml oral solution (berk pharmaceuticals ltd)
27017 kiflone 500mg capsule (berk pharmaceuticals ltd)
26992 kiflone 500mg tablet (berk pharmaceuticals ltd)
3736 klaricid 125mg/5ml oral suspension (abbott laboratories ltd)
2719 klaricid 250mg tablets (abbott laboratories ltd)
52411 klaricid 250mg tablets (necessity supplies ltd)
9583 klaricid 250mg/5ml oral suspension (abbott laboratories ltd)
6623 klaricid 500 tablets (abbott laboratories ltd)
14816 klaricid adult 250mg granules sachets (abbott laboratories ltd)
38997 klaricid paediatric 125mg/5ml oral suspension (abbott laboratories ltd)
39010 klaricid paediatric 250mg/5ml oral suspension (abbott laboratories ltd)
6121 klaricid xl 500mg tablets (abbott laboratories ltd)

15290	lansoprazole with amoxicillin and clarithromycin 30mg + 500mg + 500mg triple pack
7439	ledermycin 150mg capsule (wyeth pharmaceuticals)
16613	ledermycin 150mg capsules (mercury pharma group ltd)
22076	ledermycin 300mg tablet (wyeth pharmaceuticals)
6295	levofloxacin 250mg tablets
55708	levofloxacin 250mg tablets (actavis uk ltd)
56012	levofloxacin 250mg tablets (dr reddy's laboratories (uk) ltd)
5238	levofloxacin 500mg tablets
53673	levofloxacin 500mg/100ml infusion bags
19001	megaclor 170mg capsule (pharmax ltd)
6306	moxifloxacin 400mg tablets
17222	mysteclin oral solution (bristol-myers squibb pharmaceuticals ltd)
15071	nordox 100mg capsule (sankyo pharma uk ltd)
8393	novobiocin/tetracycline 125 mg cap
25752	nystatin with tetracycline hc capsule
9361	oxymycin 250mg tablets (dr reddy's laboratories (uk) ltd)
2458	oxytetracycline 100 mg tab
9034	oxytetracycline 125mg/5ml syrup
8285	oxytetracycline 250 mg syr
132	oxytetracycline 250mg capsules
34888	oxytetracycline 250mg tablet (c p pharmaceuticals ltd)
77	oxytetracycline 250mg tablets
34044	oxytetracycline 250mg tablets (a a h pharmaceuticals ltd)
34040	oxytetracycline 250mg tablets (actavis uk ltd)
34336	oxytetracycline 250mg tablets (ivax pharmaceuticals uk ltd)
40483	oxytetracycline 250mg tablets (sandoz ltd)
34141	oxytetracycline 250mg tablets (teva uk ltd)
28291	oxytetracycline 3%/hydrocortisone 1%
10542	oxytetracycline hcl/hydrocortisone .5 % ear
17703	oxytetramix 250 tablets (ashbourne pharmaceuticals ltd)

30520 primacine 125mg/5ml liquid (pinewood healthcare)
39118 primacine 250mg/5ml liquid (pinewood healthcare)
27504 primacine 500mg/5ml liquid (pinewood healthcare)
27681 ranclav 125mg/31mg/5ml sf oral suspension (ranbaxy (uk) ltd)
25370 ranclav 375mg tablets (ranbaxy (uk) ltd)
22017 respillin 125mg/5ml oral solution (opd pharm)
22015 respillin 125mg/5ml oral solution (opd pharm)
24203 respillin 250mg capsule (opd pharm)
24200 respillin 500mg capsule (opd pharm)
31428 retcin 250mg tablet (ddsa pharmaceuticals ltd)
21808 rommix 125mg/5ml oral suspension sugar free (ashbourne pharmaceuticals ltd)
11611 rommix 250 ec tablets (ashbourne pharmaceuticals ltd)
25278 rommix 500mg tablet (ashbourne pharmaceuticals ltd)
24097 rondomycin 150mg capsule (pfizer ltd)
18109 sebomin mr 100mg capsules (actavis uk ltd)
37440 sebren mr 100mg capsules (teva uk ltd)
19693 sustamycin 250mg capsule (boehringer mannheim uk ltd)
17693 tavanic 250mg tablets (sanofi)
6206 tavanic 500mg tablets (sanofi)
27254 tenkorex 500mg capsule (opd pharm)
7455 terramycin 250mg capsule (pfizer ltd)
17467 terramycin 250mg tablets (pfizer ltd)
9014 tetrabid-organon 250mg capsule (organon laboratories ltd)
8219 tetrachel 250mg capsule (berk pharmaceuticals ltd)
3816 tetrachel 250mg tablet (berk pharmaceuticals ltd)
25017 tetracycline
56044 tetracycline 125mg/5ml oral solution
8284 tetracycline 125mg/5ml syrup
21804 tetracycline 125mg/5ml syrup
41547 tetracycline 250mg capsule (berk pharmaceuticals ltd)

121	tetracycline 250mg capsules
34011	tetracycline 250mg capsules
56181	tetracycline 250mg tablet (celltech pharma europe ltd)
45271	tetracycline 250mg tablet (numark management ltd)
386	tetracycline 250mg tablets
43538	tetracycline 250mg tablets (a a h pharmaceuticals ltd)
41636	tetracycline 250mg tablets (actavis uk ltd)
54214	tetracycline 250mg tablets (alliance healthcare (distribution) ltd)
53117	tetracycline 250mg tablets (almus pharmaceuticals ltd)
48100	tetracycline 250mg tablets (teva uk ltd)
2922	tetracycline 250mg with nystatin 250000units tablets
2636	tetracycline 500 mg cap
3528	tetracycline 500 mg tab
21654	tetracycline ear/eye
21629	tetracycline eye
31425	tetracycline hcl/pancreatic concentrate cap
28736	tetracycline hydrochloride/amphotericin syr
15355	tetracycline with chlortetracycline & demeclocycline tablets
25071	tetracycline with nystatin capsules
4951	tetralysal 300 capsules (galderma (uk) ltd)
20054	tetralysal 408mg capsule (pharmacia ltd)
25280	tiloryth 250mg gastro-resistant capsules (tillomed laboratories ltd)
268	vibramycin 100mg capsules (pfizer ltd)
3152	vibramycin 100mg dispersible tablet (pfizer ltd)
10454	vibramycin 50mg/5ml oral solution (pfizer ltd)
9267	vibramycin acne pack 50mg capsules (pfizer ltd)
56198	vibramycin-d 100mg dispersible tablets (mawdsley-brooks & company ltd)
14904	vibramycin-d 100mg dispersible tablets (pfizer ltd)
52967	vibramycin-d 100mg dispersible tablets (stephar (u.k.) ltd)
53135	vibramycin-d 100mg dispersible tablets (waymade healthcare plc)

26392	vibrox 100mg capsules (kent pharmaceuticals ltd)
21829	zoxycil 250mg capsule (trinity pharmaceuticals ltd)
26262	zoxycil 500mg capsule (trinity pharmaceuticals ltd)

E: NHS Wellness check

Medcode	Readcode	Readterm
1547	69D2.13	Well man health check
49460	9OQA.00	Well man monitor. check done
61066	9OQ1.00	Attends well man monitoring
8211	69D2.14	Well man health examination
56237	9OQ3.00	Well man monitoring default
1087	69D2.15	Well woman health check
52723	9OP3.00	Well woman monitoring default
61926	9OP1.00	Attends well woman monitoring
830	69D2.16	Well woman health examination
52816	9OPA.00	Well woman monitor.check done
13286	9N0R.00	Seen in well person clinic
20579	ZV7..00	[V]Well persons examination, investigation and screening
7061	ZV7..11	[V]Well person screening
44970	ZV7z.00	[V]Unspecified well person screening

Table S2: Time between the diagnosis of immune mediated inflammatory disease (IMID) and pneumococcal vaccination[1]

	LRTI treated with antibiotics		**Hospitalisation for pneumonia**		**Death due to pneumonia**	
	Cases	Controls	Cases	Controls	Cases	Controls
Diagnosis of IMID recorded in the CPRD before the vaccination date.						
Number (%)	2,450 (46.7)	13,743 (62.6)	532 (42.7)	3,829 (60.8)	246 (42.3)	1,990 (59.0)
Time between date of first record of IMID diagnosis in the CPRD and vaccination; median (IQR) years	2.01 (0.71,4.45)	3.38 (1.35,6.26)	2.70 (1.06,5.13)	3.85 (1.69,6.44)	3.28 (1.36,5.81)	3.73 (1.71,5.81)
Diagnosis of IMID recorded in the CPRD after the vaccination date.						
Number (%)	2,800 (53.3)	8,203 (37.4)	713 (57.3)	2,465 (39.2)	335 (57.7)	1,382 (41.0)
Time between vaccination and date of first recorded diagnosis of IMID in CPRD; median (IQR) years	4.16 (1.80,7.70)	3.46 (1.50,6.31)	4.49 (2.12,7.61)	3.18 (1.45,5.83)	3.93 (1.82,6.76)	3.13 (1.42,5.69)

[1]among those that received a single pneumococcal vaccination.

Table S3: Effectiveness of a single dose of pneumococcal vaccine (model-3)

Outcomes		Cases n (%)	Controls n (%)	Adjusted OR (95% CI)
LRTI treated with antibiotics in primary-care				
	Unvaccinated	5,299 (52.2)	22,035 (52.1)	1
	Vaccinated	4,860 (47.8)	20,237 (47.9)	0.77 (0.73,0.81)
Hospitalisation for pneumonia				
	Unvaccinated	639 (36.1)	4,182 (41.7)	1
	Vaccinated	1,133 (63.9)	5,839 (58.3)	0.70 (0.60,0.81)
Death due to pneumonia				
	Unvaccinated	200 (27.4)	1,168 (27.3)	1
	Vaccinated	529 (72.6)	3,372 (72.7)	0.61 (0.48,0.78)

OR: odds ratio; CI, confidence interval; adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to index date, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory) drug, at-risk conditions for pneumococcal vaccination (chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia outcome), corticosteroid prescription within 30 days of index date.

Table S4: Pneumococcal vaccine effectiveness: subgroup analyses (model-3)

	LRTI treated with antibiotics			Hospitalisation for pneumonia			Death due to pneumonia		
Subgroup	Cases, n (%)	Controls, n (%)	aOR*(95% CI)	Cases, n (%)	Controls, n (%)	aOR*(95% CI)	Cases, n (%)	Controls, n (%)	aOR*(95% CI)
Any immunosuppressant prescribed within 30-days									
Vaccinated, No	3,026 (57.5)	13,354 (57.3)	1	349 (36.9)	2,453 (43.9)	1	92 (24.4)	670 (27.9)	1
Vaccinated, Yes	2,234 (42.5)	9,945 (42.7)	0.78 (0.73,0.84)[1]	597 (63.1)	3,135 (56.1)	0.69 (0.57,0.85)[1]	285 (75.6)	1,732 (72.1)	0.56 (0.40,0.77)[1]
Methotrexate prescribed within 30-days									
Vaccinated, No	1,530 (41.1)	5,484 (38.9)	1	1,201 (33.1)	192 (28.7)	1	75 (26.9)	381 (22.9)	1
Vaccinated, Yes	2,195 (58.9)	8,600 (61.1)	0.77 (0.71,0.84)[1]	2,429 (66.9)	476 (71.3)	0.64 (0.50,0.82)[1]	204 (73.1)	1,285 (77.1)	0.51 (0.35,0.75)[1]
Data restricted to cases with outcome in the year 2012 or later and matched controls									
Vaccinated, No	2,327 (41.3)	13,481 (44.7)	1	265 (28.7)	2,184 (35)	1	61 (18.4)	499 (20.5)	1
Vaccinated, Yes	3,307 (58.7)	16,662 (55.3)	0.78 (0.73,0.84)	660 (71.4)	4,052 (65)	0.63 (0.51,0.78)	270 (81.6)	1,938 (79.5)	0.63 (0.42,0.95)
Data restricted to cases with outcome before 2012 and matched controls									
Vaccinated, No	2,972 (60.5)	8,554 (61.8)	1	374 (39)	1,998 (47.1)	1	139 (30.9)	669 (31.8)	1
Vaccinated, Yes	1,943 (39.5)	5,284 (38.2)	0.95 (0.87,1.04)	585 (61)	2,242 (52.9)	0.87 (0.70,1.07)	311 (69.1)	1,434 (68.2)	0.66 (0.49,0.89)
Men									
Vaccinated, No	1,993 (50.4)	8,658 (51)	1	262 (33.3)	1,678 (39.5)	1	82 (24.3)	484 (25.9)	1
Vaccinated, Yes	1,959 49.6)	8,315 (49)	0.72 (0.66,0.79)	526 (66.8)	2,568 (60.5)	0.70 (0.55,0.89)	256 (75.7)	1,387 (74.1)	0.55 (0.37,0.80)
Women									
Vaccinated, No	3,306 (50.1)	13,377 (49.5)	1	377 (34.4)	2,504 (40.2)	1	118 (26.6)	684 (25.6)	1
Vaccinated, Yes	3,291 (49.9)	13,631 (50.5)	0.79 (0.74,0.84)	719 (65.6)	3,726 (59.8)	0.70 (0.58,0.84)	325 (73.4)	1,985 (74.4)	0.63 (0.47,0.86)

*adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to index date, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date, deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory), chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia), corticosteroid prescription within 30 days of index date. [1]Excluded corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory) as a covariate.

Table 5. Results of complete case analysis.

Outcomes		Cases n (%)	Controls n (%)	Adjusted OR (95% CI)
LRTI treated with antibiotics in primary-care				
	Unvaccinated	4,256 (47.2)	17,882 (47.4)	1
	Vaccinated	4,753 (52.8)	19,827 (52.6)	0.77 (0.73,0.82)
Hospitalisation for pneumonia				
	Unvaccinated	463 (30.0)	3,336 (37.3)	1
	Vaccinated	1,082 (70.0)	5,609 (62.7)	0.75 (0.63,0.88)
Death due to pneumonia				
	Unvaccinated	140 (22.3)	918 (23.6)	1
	Vaccinated	488 (77.7)	2,972 (76.4)	0.70 (0.53,0.91)

OR: odds ratio; CI, confidence interval; adjusted for age, sex, body mass index, alcohol, smoking, Charlson comorbidity index, number of primary care consultations in 12 months prior to index date, number of hospital admission in 12 months prior to index date, influenza vaccination in 12 months prior to index date, shingles vaccination in 12 months prior to index date deprivation score, inflammatory condition type, corticosteroid sparing drug prescription within 30-days (immune suppressing vs. immunomodulatory) drug, at-risk conditions for pneumococcal vaccination (chronic heart disease, diabetes immunosuppression, chronic liver disease, chronic kidney disease, chronic respiratory disease, asplenia (except for death due to pneumonia outcome), corticosteroid prescription within 30 days of index date.