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Aspirin reduces cardiovascular events in patients with pneumonia: a prior event rate ratio analysis in a large primary care database.

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Abstract

Background

Ischaemic stroke and myocardial infarction (MI) are common after pneumonia and are associated with long-term mortality. Aspirin may attenuate this risk and should be explored as a therapeutic option.

Methods

We extracted all patients with pneumonia, aged over 50, from the Clinical Practice Research Datalink (CPRD), a large UK primary care database, from inception until January 2019. We then performed a prior event rate ratio analysis (PERR) with propensity score matching, an approach that allows for control of measured and unmeasured confounding, with aspirin usage as the exposure, and ischaemic events as the outcome. The primary outcome was the combined outcome of ischaemic stroke and myocardial infarction. Secondary outcomes were ischaemic stroke and myocardial infarction individually. Relevant confounders were included in the analysis (smoking, comorbidities, age, gender).

Findings

48,743 patients were eligible for matching. 8,099 of these were aspirin users who were matched to 8,099 non-users. Aspirin users had a reduced risk of the primary outcome (adjusted hazard ratio, HR 0.64; 95% confidence interval 0.52 - 0.79) in the PERR analysis. For both secondary outcomes, aspirin use was also associated with a reduced risk HR 0.46 (0.30 – 0.72) and HR 0.70 (0.55 – 0.91) for myocardial infarction and stroke respectively).

Interpretation

This study provides supporting evidence that aspirin use is associated with reduced ischaemic events after pneumonia in a primary care setting. This drug may have a future clinical role in preventing this important complication.

Introduction:

It is well established that infections predispose to cardiovascular events, with data supporting this from both primary and secondary care. The risk appears to vary, but some reports suggest that the risk is as high as ten percent within patients who have hospitalised pneumococcal pneumonia.[1] These cardiovascular events are also associated with an increased short-term mortality.[2] The mechanism of this risk is not completely clear, although it appears to be mediated through a pro-inflammatory cascade. Given that pneumonia is very common, with around 100,000 cases in the UK alone each year,[3] any potential reduction of that risk is likely to lead to significant public health benefit.

Aspirin has been suggested as a potential therapeutic option to try and attenuate this risk. Aspirin has an excellent track record in secondary prevention of cardiovascular disease[4], although recent studies have confirmed the lack of benefit in primary prevention[5]. Because aspirin has both an anti-platelet and anti-inflammatory effect, it has been suggested this may reduce the risk of cardiovascular events.[5] Some limited secondary care evidence supports this, with small observational trials showing a reduction in cardiovascular events in patients taking aspirin when they are diagnosed with pneumonia, and a single, small RCT suggesting promise [6–8].

The aim of the current study was to establish whether aspirin reduced the risk of cardiovascular events in patients who had experienced a recent pneumonia, in a large observational cohort of UK primary care patients.

Methods:

Study design

This analysis was performed using data from the Clinical Practice Research Datalink (CPRD), a large database of routine coded primary care health records considered representative of the wider UK population. This includes all diagnoses coded by primary care clinicians. This also includes events occurring in hospital that are coded in the primary care record (e.g. via discharge summary), but this does not necessarily include all hospitalised events. We included all patients who had a coded diagnosis of pneumonia from inception of the database until January 2019. Primary care records were linked to Office for National Statistics (ONS) mortality data. If patients had multiple episodes of pneumonia, the first was taken, irrespective of time between events. The study period started 12 months prior to pneumonia diagnosis and lasted for 6 months after.

Outcomes

For all analyses, the primary outcome was the combined outcome of myocardial infarction or ischaemic stroke.

The two secondary outcomes were myocardial infarction and ischaemic stroke, individually.

Definitions

Codes for pneumonia were derived from previous literature[9] and were updated to ensure current validity. There has been extensive use of the CPRD for studying pneumonia, and coding in the CPRD is generally felt to be good quality.[9–13] Specific explicit codes for pneumonia rather than simple lower respiratory tract infection were included (see Appendix S1); these were again based on previous literature. As this is a primary care dataset, all presentations are those coded from primary care records.

Codes for outcomes and comorbidity were derived from the Manchester ClinicalCodes repository.[14] Code lists are also presented in Appendix S1. For myocardial infarction in particular, the codelist was edited to ensure that all events represented acute events, rather than chronic myocardial ischaemia. Mortality was based upon ONS mortality data, which is derived from death certificates. Timing of death was taken from ONS data rather than CPRD date, as this is more reliable.[15,16]

Patients who had outcomes on the same day as the pneumonia diagnosis were excluded. This was to ensure reliable data on which event happened first, and to limit reverse confounding (pneumonia as a consequence of myocardial infarctions or stroke).

Aspirin use was defined in relation to study entry (12 months prior to pneumonia diagnosis). Aspirin users were defined as patients who had received 2 or more prescriptions of aspirin at a daily dose of less than 100mg in the 6 months prior to study entry. This ensured chronic aspirin use at study entry use. This requirement was then repeated in the next two, six month blocks, to ensure a continued prescription of low dose aspirin over the whole 12-month period prior to pneumonia diagnosis.

Aspirin non-users were defined as patients who did not meet this criterion in all three six-month blocks. Patients who met the criteria in some, but not all of the three blocks, were censored, as explained below. Other drugs examined in secondary analyses (see below) were defined similarly. Age, gender, and index of multiple deprivation (IMD, an area-based measure of socioeconomic deprivation) were included as covariates in the analysis, alongside medical comorbidities.

Comorbidity data were collected on smoking status, hypertension, stroke, ischaemic heart disease, diabetes and peripheral vascular disease. All comorbidities were defined by codes derived from the ClinicalCodes repository and must have occurred prior to the whole study period (i.e. 12 months prior to the pneumonia diagnosis). The absence of a comorbidity was taken to mean the absence of that condition. Smoking was defined as a categorical variable based on the most recent smoking code (current, former, never, or missing).

Statistical methodology

Our primary analysis methodology was a propensity matched, prior event rate ratio (PERR) analysis.

In this analysis, confounding is taken account for in two ways; firstly by propensity score matching (PSM) aspirin users to non-aspirin users, to ensure similar baseline characteristics across both groups. Propensity matching was performed with 2:1 matching, using covariates that were likely to be relevant for aspirin prescription (age, smoking, gender, history of ischaemic heart disease, stroke, or peripheral vascular disease). An optimal, nearest neighbour approach was utilised, using the MatchIt package in R. Covariate imbalance was assessed using the standardised mean difference (SMD) using a detection threshold of 0.1.[17] Secondly, PERR analysis was used to account for

unmeasured confounders. Double adjustment was carried out for any covariates that remained imbalanced after PSM.[18]

PERR analysis uses a form of self-controlled design in which participants act as their own controls to reduce confounding. In a standard PERR analysis, the rate of events (in this case, cardiovascular events) prior to and after a discrete exposure are compared within the same population group, allowing for unmeasured confounders to be taken account of, and a calculation of a more reliable effect size. [19–21]

In this current analysis, the standard PERR methodology has been adapted to address the question of interest. Usually exposed and unexposed groups are defined based on incident exposure to a treatment at an index date (time origin). We define the index date as the date of pneumonia diagnosis. The incident exposure is defined to be experiencing the pneumonia diagnosis when a current aspirin user. The unexposed group are selected from non-aspirin users who also experience the pneumonia diagnosis. This allows calculation of an adjusted effect of aspirin use on post-pneumonia events.

For this analysis, patients were split into the two exposure groups (aspirin users and non-aspirin users), depending on their prescription records (defined above). For both groups, a prior period was identified, starting 12 months prior to the pneumonia date, and lasting for 6 months, and a posterior period, the 6 months directly after diagnosis of the pneumonia (Figure 1).

Cardiovascular events occurring during these periods were recorded and used to estimate a PERR ratio of hazards for prior events to posterior events. The hazards for the prior and study periods were calculated using a Cox proportional hazards model with group membership as the independent variable, adjusted for relevant covariates (see above). Bootstrapping was performed to generate confidence intervals. The resulting outcome then represents the estimated effect size of the aspirin use on post-pneumonia events after accounting for the effect of time-invariant confounding. Any patients who died in the posterior period were right-censored.

To avoid the possibility of patients switching from being non-aspirin users to aspirin users, which would violate the assumptions of the PERR methodology, patients were required to be either on or off aspirin throughout the whole reference period (12 months prior, until diagnosis of pneumonia). Patients who started aspirin between the prior period and diagnosis of pneumonia were censored.

The prior period deliberately ended 6 months prior to the pneumonia diagnosis. This was to ensure there was complete washout between periods. This was a pragmatic choice and aimed to reduce any concern of bias that pneumonia events could be as a consequence of myocardial infarction hospitalisation episodes.

Missing data for smoking status was coded as such, whereas other missing data was removed (complete case analysis), as this was rare (43 patients). We estimated a hazard ratio of 0.8, a prevalence of routine aspirin usage of 33%, and incidence of events at 6 months at 3%, with a crude sample size required of around 17,112 participants, which was easily achieved before propensity score matching.

Data were extracted from the CPRD and processed using Stata (StataCorp, TX, US), with the package *CPRDUTIL*, but all analyses were performed using R version 3.6.0 and 4.0.0 (R foundation for Statistical Computing, Vienna), using packages: *tidyverse, ggplot, matchit, broom, survival* and *rio*.

Sensitivity and secondary analyses

For the main analysis, it was possible for aspirin prescription not to overlap the pneumonia diagnosis index date (the precise timing of prescriptions can be subject to uncertainty in the CPRD). To determine whether findings were robust to the timing of aspirin use, a sensitivity analysis was performed restricting aspirin patients to those in receipt of the drug on the index date.

As participants might die in the posterior period and hence not have coded events, there is a potential for a survival bias (one group has fewer posterior events, as they have a higher mortality), which should be accounted for by right censoring. Death represents a competing risk and our chosen approach is to use a proportional cause-specific hazards model, as recommended for aetiological research in the presence of competing risks[22].

As a test for robustness, we also examined two alternative negative control outcomes: fracture (of any kind), and constipation, to ensure that any effect identified was specific to myocardial infarction/stroke, and to identify evidence of survival bias.

To look for possible evidence of residual confounding after PERR analysis, the analysis was replicated with four other drug classes, three of which were negative control exposures. Firstly, paracetamol and levothyroxine were chosen, as these have no known cardiovascular effect, and are not strongly correlated with aspirin prescription. NSAIDs were compared as another potential drug with anti-inflammatory effect, but known to have potential increased cardiovascular risk and which have been associated with increased events after pneumonia. Proton pump inhibitors were compared as a final, commonly prescribed agent, which is often co-prescribed with aspirin.

Standard Cox regression was undertaken as an analysis that accounts for measured confounders only, to compare with the PERR analysis, using the same outcome variables. This analysis was performed on the same population used in the PERR analysis, equivalent to simply performing the analysis on the posterior period only, without adjusting for the prior period events. These models were then tested for the proportional hazards assumption (using the Therneau and Grambsch approach), to look for evidence of a time varying-effect which might have impacted the PERR analysis.[23]

As coding in CPRD could be as a consequence of administrative activity (e.g. recording information from a hospital discharge summary or clinic letter) rather than direct clinical care provided by the GP, we undertook a subsequent sensitivity analysis only including consultations that were definitively performed by the primary care clinician, by limiting only to consultation types that were in the GP practice, at a home-visit, or over the telephone. This was achieved using the *constype* variable in CPRD.

Results:

Figure 2 describes the flow of patients through the study. Data for 66,004 patients, accounting for 85,911 episodes of pneumonia, were extracted from the CPRD. Patients with missing data, those who died on or before the index date (i.e. retrospective coding), and those where the primary outcome fell on the index date, were excluded, leaving 48,260 patients. Of those, 4,964 patients were intermittent aspirin users and excluded. Aspirin users were then matched one-to-one with non-aspirin users. Pre and post match group definitions are shown in Table 1.

Basic demographic details are in Table 1 showing differences between groups and the impact of propensity score matching. Before matching, aspirin users were older, more likely to be male, and more comorbid than non-aspirin users, and were imbalanced on many covariates. We considered matching to be successful as it limited baseline differences (SMD < 0.1) in all covariates except age (SMD = -0.1035), although aspirin users still had an increased history of hypertension and ischaemic heart disease . For all subsequent analysis, the matched cohort was used.

Characteristic	Aspirin users, N = 9,864	Matched non-aspirin users, N = 9,864	All non-aspirin users N = 35,197
Age[1]	81 (73, 87)	82 (75, 88)	74 (63, 84)
Female	4512 (46%)	4618 (47%)	18,489 (52.5%)
Diabetes	2245 (23%)	2175 (22%)	3,514 (10.0%)
PVD	1024 (10%)	802 (8.1%)	2,737 (7.8%)
Hypertension	5388 (55%)	4239 (43%)	11,350 (32.2%)
Previous IHD	2631 (27%)	2093 (21%)	2,737 (7.7%
Previous stroke	3425 (35%)	3448 (35%)	5,528 (15.7%)
Smoking status			
Former	4043 (41%)	3937 (40%)	3,358 (9.53%)
Current	1445 (15%)	1401 (14%)	12,029 (34.2%)
Bottom decile of IMD	969 (9.8%)	946 (9.6%)	3,005 (8.5%

1. Brackets represent interquartile range

Table 1: Demographics of study participants after propensity score matching

Numbers and rates of the primary outcome are presented in Table 2. Both groups had similar prior stroke events, although aspirin users had more prior myocardial infarction events. There was clear evidence for an increase in both outcomes after pneumonia ($p < 0.01$).

Table 2: Number of events (% of total in that group) in matched aspirin and non-aspirin users

Characteristic	Non-aspirin users (n = 9,468)	Aspirin users (n = 9,468)
Stroke in prior period:	175 (1.8%)	193 (2.0%)
Stroke in posterior period:	307 (3.1%)	234 (2.4%)
MI in prior period:	44 (0.4%)	81 (0.8%)
MI in posterior period:	182 (1.8%)	154 (1.6%)
Dead within 6 months:	2028 (21%)	2328 (24%)
Statistics presented: n (%), *MI = Myocardial Infarction*		

Results of the PERR analysis are shown in Table 3. Aspirin use was strongly associated with reduced MI and stroke, but had no effect on the two comparator outcomes (Appendix Table S2.1), with a hazard ratio of 0.64 (0.52 – 0.79) for the primary outcome, 0.70 (0.55 – 0.91) for ischaemic stroke, and 0.46 (0.30 – 0.72) for myocardial infarction.

Table 3: Hazard ratios for aspirin use vs. no aspirin use

	Hazard ratio (95% confidence interval)
Primary outcome (MI or ischaemic stroke)	0.64 (0.52 - 0.79)
Ischaemic stroke	0.70 (0.55 – 0.91)
Myocardial Infarction	0.47 (0.30 – 0.72)

Hazard ratio based on PERR analysis, adjusting for covariates in a Cox regression model. MI, myocardial infarction.

Sensitivity and secondary analyses

The PERR analysis for the other drugs is reported in the supplementary appendix (table S2.2). No significant association was found for paracetamol, levothyroxine or proton-pump inhibitors with either the primary, secondary or composite outcome. In comparison, NSAIDS were associated with an increased risk of the primary outcome with a HR of 1.88 (1.11 – 3.31).

The sensitivity analysis using a tighter definition of aspirin usage (Table S2.3) found similar relationships to the main analysis, with a HR of 0.64 (0.50-0.84) for aspirin users and the primary outcome. Again, no association was found with any other control drugs except NSAIDs, which were associated with increased hazard of the primary outcome, with a HR of 1.70 (0.95 – 3.21). When limiting consultations to those that were definitively primary care consultations(Table S2.4), the results remained similar, with a HR of 0.60 (0.42 – 0.87) for the primary outcome. However, due to the subsequent reduction in power, this did not meet significance for MI, with a HR of 0.63 (0.30 – 1.24)

The Cox regression analysis supported the PERR approach, with results in Table S3.1. In particular, aspirin was associated with a reduced hazard of the primary outcome (HR 0.84, 0.73 – 0.96) and stroke (HR 0.80, 0.68-0.96), with weaker evidence of a reduction in myocardial infarction (HR 0.82, 0.66 – 1.02).

Discussion

This is the first large-scale study to show that aspirin prescription is associated with a substantial reduction in risk of cardiovascular complications following pneumonia.

Strengths and limitations

This study has several important strengths. Firstly, a large observational dataset with high quality coding was used, comprising a significantly larger sample size than the previous study.[8] The analytical approach combining propensity score matching with a PERR approach helps strengthen causal inference, and a number of additional analyses were conducted which support the main findings. The analysis used data from primary care, where the majority of pneumonia is encountered; previous research has largely focused on secondary care.

There are several limitations of this study, most importantly with respect to confounding by indication and censoring. Although the PERR methodology aims to reduce confounding, the populations compared were still different across a range of demographics and had different absolute risks of myocardial infarction and stroke, although the propensity score matching substantially improved this. However, the limited (but generally supportive) empirical evidence, and statistical modelling are supportive that PERR can reduce bias in this setting.[19–21]

A second limitation regards censoring. One of the key requirements of PERR analysis is self-control of patients, so it was necessary to censor patients who were intermittent aspirin users and did not consistently use or not use aspirin over the whole study period. This censored population comprised around 10% of the whole population and was more similar to the aspirin user population than the non-aspirin user. Some of the censored patients may have started (or stopped) aspirin because they had ischaemic events across the study period, and the exclusion of these patients could bias the results. It is difficult to assess the direction of this bias, as the risk of post-pneumonia events in patients who switch aspirin is likely to be strongly related to the event that made them stop or start aspirin, rather than their underlying risk. This censoring bias is much less likely to occur in stroke (where aspirin is not commonly chronically prescribed, in the UK) than MI, and it is reassuring that the beneficial effect of aspirin was found in both groups, suggesting this bias did not fundamentally alter the results.

Thirdly, although the PERR method and Cox regression rely on time-invariant effects the risk of MI is felt to be highest in the few days just after pneumonia, so these assumptions may not apply. Also, the PERR approach requires hidden confounders not to vary with time, which may not be true after a significant medical event (e.g. lifestyle change after pneumonia).In our study, however, we found no evidence of time-varying effects of any agent, and all three Cox models did not violate the proportional hazards adjustment, supporting our statistical approach. As most events happened early, it is unlikely that change in hidden confounders such as lifestyle would substantially alter the risk of subsequent events.

A fourth limitation regards the lack of hospital linkage and coding accuracy. This study did not include individual hospital linkage, relying on accurate coding of hospital events in the primary care record. This has two implications. Firstly, pneumonia events could represent true primary care pneumonia events, or coded secondary care events (e.g. from discharge summaries). Importantly, in our sensitivity analyses restricting to definitive primary care events, the hazard ratios for the primary outcomes were similar in the main analysis (HR 0.64; 0.52 – 0.79) and the sensitivity analysis (HR 0.60; 0.42 – 0.87), suggesting that manner in which pneumonia was diagnosed and recorded did not alter risk estimates, or the effect of aspirin. Secondly, it is likely there is under-reporting of MI and stroke across the dataset, as these often present primarily to hospital. Previous research has found that although CPRD coding of MI is accurate, it does not pick up all hospitalised events, with underreporting compared to registry data.[24] However, we would not expect this to be biased with respect to aspirin use, and therefore this would not alter the relative risk of events between aspirin users and non-aspirin users, which is our reported outcome.

A final limitation is potential survival bias, with patients in the aspirin group dying more frequently, and therefore having an apparent reduced effect rate of ischaemic events. This was managed by death censoring in both the PERR and Cox analysis, which is supported by the literature.[22,25]

Comparison with previous work

There have been two previous studies on this specific topic, one observational and one randomised. In the randomised controlled trial (n = 185) from Turkey, aspirin showed some promise (1 event in the aspirin group, 10 in the control group), but the numbers were too small to draw firm conclusions; and 90% of potential participants were excluded, raising concern of bias or appropriate inclusion criteria, and some key information was not reported.[7] The observational study was performed in a single centre, and showed a two-fifths reduction in the rate of cardiovascular events (4.9% vs 8.3%) with aspirin usage, a similar effect size to ours.[6] Other observational data has identified a reduced mortality with aspirin usage, and one study has shown reduced mortality with clopidogrel usage.[8,26]

Implications for practice and research

Our study provides supporting evidence of an association between aspirin usage in community acquired pneumonia and preventing cardiovascular complications, and sets the foundation for a prospective, randomised trial. However, it is important to note this study enrolled patients on aspirin already, and any randomised trial would initiate therapy at diagnosis.

Future research should thus focus on the potential initiation of aspirin in patients with newly diagnosed pneumonia, and whether the risk-benefit balance is shifted in the short-term in favour of aspirin prophylaxis. Inflammation may be apparent early in the disease process, so the importance of the timeliness of aspirin initiation in preventing ischaemic complications must also be established.

The potential benefits of aspirin prescription in pneumonia are significant. Given approximately 100,000 cases of pneumonia occur every year in the U.K. alone,[3] and based on our own findings of an absolute risk of around 2% of MI or stroke, our observed 30% reduction in ischaemic events would lead to 600 fewer cases a year in primary care. In secondary care, with the absolute risk of MI and stroke approaching 10% in some studies, there could be even more benefit.

Conclusion

Aspirin usage is associated with reduced short-term ischaemic stroke and myocardial infarction, in primary care participants who develop pneumonia. Further work should explore this promising approach to preventing cardiovascular complications after pneumonia, in a prospective, randomised fashion.

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Competing Interests

FH, DA, and RP have nothing to declare. WH has previously received conference fees from Eisai, and grant funding from IQVIA, unrelated to this work.

Ethics:

Ethical approval for this study was given by the CPRD, who safeguard patient information in this database (https://www.cprd.com/safeguarding-patient-data), application ISAC 18_310R.

Data sharing and dissemination:

Unfortunately, CPRD does not allow direct data-sharing due to patient confidentiality issues. The lead author would welcome informal and formal contact if required. It is not feasible to disseminate results back to individual patients within the CPRD.

Contributions

FH and DA conceived of the idea. FH designed the study, did the majority of the analysis, and wrote the first draft. DA helped with the analysis, editing, and methodology. WH did some analysis, and provided methodological support and editing. RP was the senior supervisor, conceptualised the work, and performed editing

Transparency declaration

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

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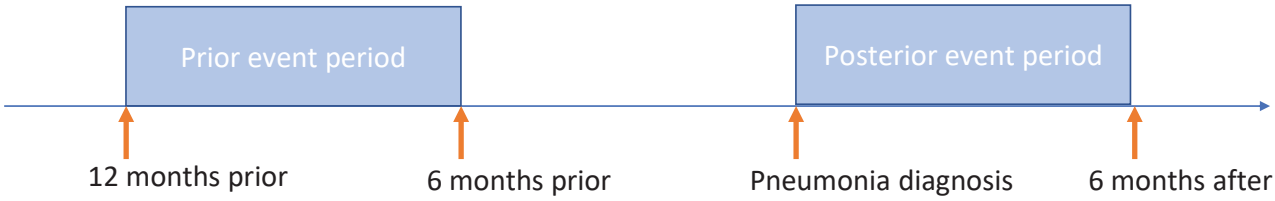
Figure 1: Schematic of the PERR analysis.

Figure 2: Flow of patients through the study.

Aspirin group: aspirin use over whole study:



Non-aspirin group: no aspirin use over whole study:

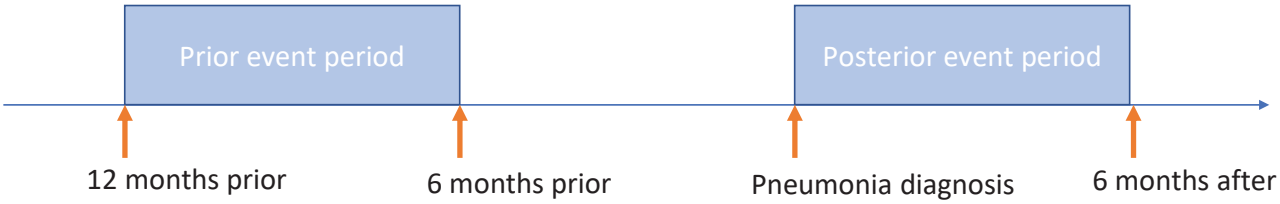
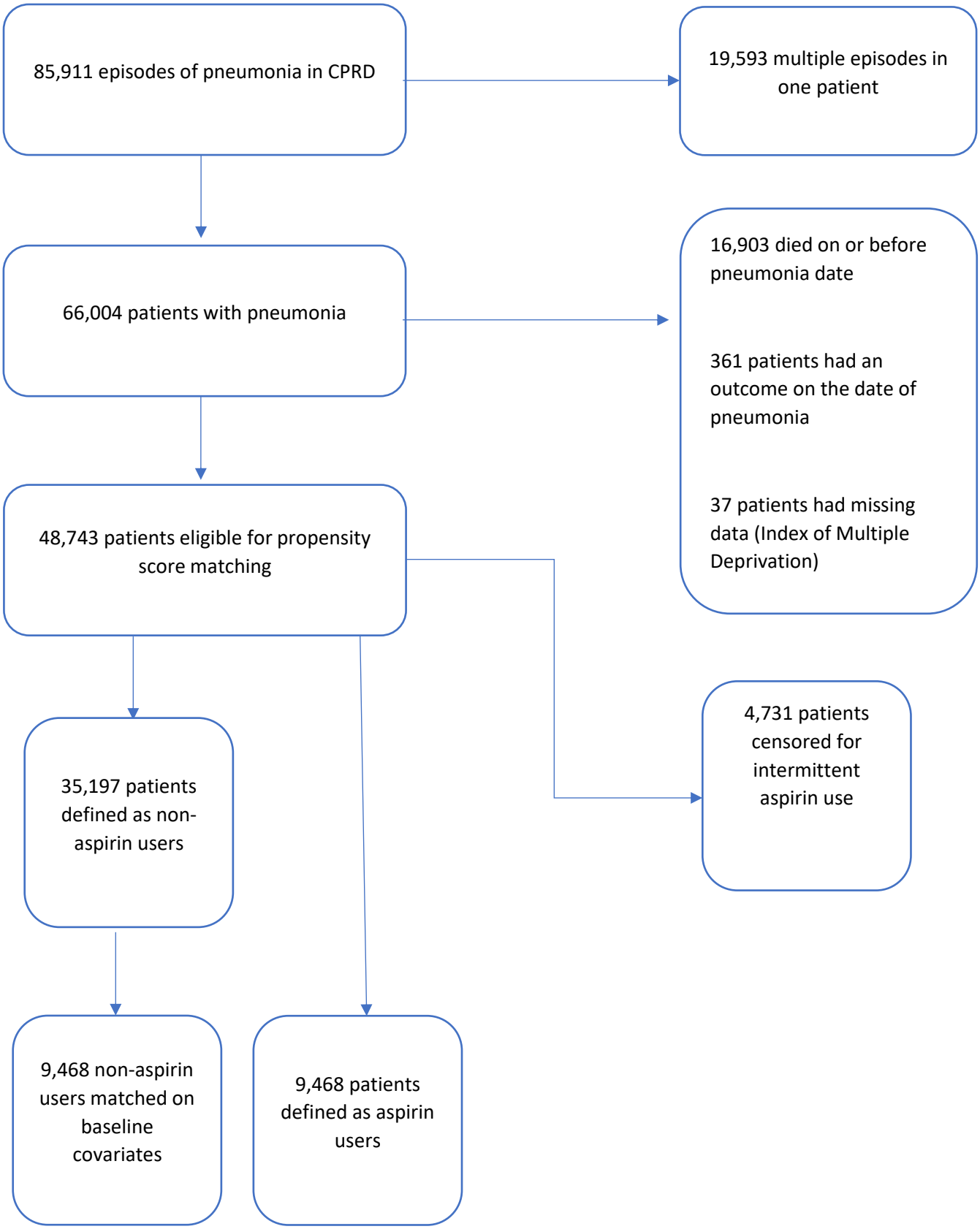


Figure 2: Flow of patients through the study



Supplementary appendices:

Appendix 1 – diagnostic and prescribing code lists

Pneumonia:

medcode	readterm
572	Pneumonia due to unspecified organism
886	Bronchopneumonia due to unspecified organism
1849	Lobar (pneumococcal) pneumonia
6094	Pneumonia or influenza NOS
10086	Pneumonia and influenza
9639	Lobar pneumonia due to unspecified organism
3683	Basal pneumonia due to unspecified organism
5324	Atypical pneumonia
5202	Viral pneumonia
8318	Lung consolidation
1576	Pneumonia due to mycoplasma pneumoniae
23095	Bacterial pneumonia NOS
14976	Viral pneumonia NOS
28634	Other bacterial pneumonia
25694	Pneumonia due to other specified organisms
16287	Chest infection - unspecified bronchopneumonia
12423	Pneumonia due to streptococcus
23333	Hypostatic pneumonia
19400	Chest infection - pnemonia due to unspecified organism
12061	Pneumonia - Legionella
13573	Influenza with bronchopneumonia
24356	Hypostatic bronchopneumonia
15912	Influenza with pneumonia
25462	Varicella pneumonitis
22795	Chest infection - other bacterial pneumonia
5612	Pneumonia due to staphylococcus
34251	Pneumonia due to specified organism NOS
43884	Pneumonia due to bacteria NOS
9389	Chest infection - viral pneumonia
23546	Pneumonia due to klebsiella pneumoniae
31269	Pneumonia due to respiratory syncytial virus
33478	Viral pneumonia NEC
29457	Chest infection - influenza with pneumonia
40299	Pneumonia - candidal
27641	HIV disease resulting in Pneumocystis carinii pneumonia
34300	Postoperative pneumonia
22835	Bronchiolitis obliterans organising pneumonia

30591	Pneumonia due to pseudomonas
27519	Pneumonia with pneumocystis carinii
41034	Pneumonia with measles
53753	[X]Other pneumonia, organism unspecified
35220	Pneumocystosis
37881	Pneumonia due to haemophilus influenzae
23726	Pneumonia with varicella
32172	Postmeasles pneumonia
17025	Chlamydial pneumonia
30437	Pneumonia with whooping cough
29166	Chest infection - pneumococcal pneumonia
40498	Pneumonia with infectious diseases EC
35082	Pneumonia with pertussis
50867	Pneumonia due to other specified bacteria
30653	Chest infection - pneumonia organism OS
35189	Abscess of lung with pneumonia
35745	Influenza with pneumonia NOS
34274	Pneumonia with aspergillosis
36675	Pneumonia due to parainfluenza virus
61623	Pneumonia with actinomycosis
45072	Cytomegaloviral pneumonitis
67836	Pneumonia due to adenovirus
52520	[X]Other viral pneumonia
63763	[X]Other bacterial pneumonia
48804	Pneumonia due to haemophilus influenzae
63858	Pneumonia due to streptococcus, group B
98381	[X]Pneumonia due to other specified infectious organisms
50408	Ornithosis with pneumonia
62632	Influenza with pneumonia, influenza virus identified
58896	Salmonella pneumonia
106300	Pneumonia due to human metapneumovirus
66362	Pneumonia with infectious diseases EC NOS
47973	Herpes simplex pneumonia
56762	Toxoplasma pneumonitis
65419	Pneumonia due to escherichia coli
69782	Pneumonia with other infectious diseases EC
47295	Pneumonic plague, unspecified
60299	E.coli pneumonia
46052	Severe acute respiratory syndrome
43286	Pneumonia with cytomegalic inclusion disease
62623	Pneumonia with ornithosis
52071	Pneumonia with candidiasis
60482	Pneumonia with Q-fever
72182	Pneumonia with salmonellosis
73735	Pneumonia due to pleuropneumonia like organisms

49398	Pneumonia with typhoid fever
70559	Pneumonia with other infectious diseases EC NOS
52384	Pneumonia due to other aerobic gram-negative bacteria
67901	Pneumonia with nocardiasis
70710	Primary pneumonic plague
57667	Gangrenous pneumonia
101507	Histoplasma capsulatum with pneumonia
101292	Histoplasma duboisii with pneumonia
45425	Pneumonia due to proteus
60119	Pneumonia due to Eaton's agent
53969	Pneumonia with systemic mycosis NOS
53947	[X]Pneumonia in viral diseases classified elsewhere
98782	Pneumonia with toxoplasmosis
106908	Pneumonia with tularaemia
110440	Pneumonia with other systemic mycoses
103404	Pneumonia with coccidioidomycosis

Myocardial infarction

medcode	Description
241	Acute myocardial infarction
1204	Heart attack
1677	MI - acute myocardial infarction
1678	Inferior myocardial infarction NOS
2491	Coronary thrombosis
3704	Acute subendocardial infarction
5387	Other specified anterior myocardial infarction
8568	Cardiac syndrome X
8935	Acute inferolateral infarction
9507	Acute non-Q wave infarction
9555	Post infarct angina
10562	Acute non-ST segment elevation myocardial infarction
12139	Acute anterolateral infarction
12229	Acute ST segment elevation myocardial infarction
13566	Attack - heart
13571	Thrombosis - coronary
14658	Acute myocardial infarction NOS
14897	Anterior myocardial infarction NOS
14898	Lateral myocardial infarction NOS
16408	Healed myocardial infarction
17133	Mural thrombosis
17689	Silent myocardial infarction
17872	Acute anteroseptal infarction
18842	Subsequent myocardial infarction
23579	Postmyocardial infarction syndrome

23708	Atrial septal defect/curr comp folow acut myocardal infarct
23892	Posterior myocardial infarction NOS
24126	Haemopericardium/current comp folow acut myocard infarct
28736	Acute atrial infarction
29553	Thrombosis atrium,auric append&vent/curr comp foll acute MI
29643	Acute inferoposterior infarction
29758	Acute transmural myocardial infarction of unspecif site
30330	Acute Q-wave infarct
30421	Cardiac rupture following myocardial infarction (MI)
32272	Postoperative myocardial infarction
32854	Acute posterolateral myocardial infarction
34803	Other acute myocardial infarction
36423	Certain current complication follow acute myocardial infarct
37657	Ventric septal defect/curr comp fol acut myocardal infarctn
38609	Subsequent myocardial infarction of inferior wall
40429	Acute anteroapical infarction
41221	Acute septal infarction
41835	Postoperative subendocardial myocardial infarction
45809	Subsequent myocardial infarction of anterior wall
46017	Other acute myocardial infarction NOS
46112	Postoperative transmural myocardial infarction anterior wall
46166	Subsequent myocardial infarction of unspecified site
46276	Postoperative transmural myocardial infarction inferior wall
59189	Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI
59940	Ruptur chordae tendinae/curr comp fol acute myocard infarct
62626	Acute papillary muscle infarction
63467	True posterior myocardial infarction
68748	Postoperative myocardial infarction, unspecified
69474	Rupture papillary muscle/curr comp fol acute myocard infarct
72562	Subsequent myocardial infarction of other sites
96838	[X]Acute transmural myocardial infarction of unspecif site
99991	[X]Subsequent myocardial infarction of unspecified site
106812	Postoperative transmural myocardial infarction unspec site
109035	[X]Subsequent myocardial infarction of other sites

Ischaemic Stroke

medcode	Description
504	Transient cerebral ischaemia
569	Infarction - cerebral
1298	CVA unspecified
1433	Transient ischaemic attack
1469	Stroke and cerebrovascular accident unspecified
1895	Transient cerebral ischaemia NOS
2418	Cerebrovascular disease
3149	Cerebral infarction NOS

5185	Lateral medullary syndrome
5363	CVA - cerebral artery occlusion
5602	Cerebellar infarction
6116	CVA - Cerebrovascular accident unspecified
6155	Stroke due to cerebral arterial occlusion
6253	Stroke unspecified
6960	CVA - cerebrovascular accid due to intracerebral haemorrhage
7780	Left sided CVA
8443	Brain stem stroke syndrome
8837	Cerebral arterial occlusion
9985	Left sided cerebral infarction
10504	Right sided cerebral infarction
12833	Right sided CVA
15019	Cerebral embolism
15252	Brainstem infarction NOS
15788	Transient cerebral ischaemia NOS
16507	Intermittent cerebral ischaemia
16517	Cerebral thrombosis
16956	Cerebral palsy, not congenital or infantile, acute
17322	Cerebellar stroke syndrome
18689	Middle cerebral artery syndrome
19201	Right sided intracerebral haemorrhage, unspecified
19260	Posterior cerebral artery syndrome
19280	Anterior cerebral artery syndrome
19354	Other transient cerebral ischaemia
23671	Cerebral infarct due to thrombosis of precerebral arteries
24446	Cerebral infarction due to embolism of precerebral arteries
25615	Brainstem infarction
26424	Infarction of basal ganglia
27975	Cerebral infarction due to embolism of cerebral arteries
33499	Pure motor lacunar syndrome
33543	Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artrs
34758	Cerebral embolus
36717	Cerebral infarction due to thrombosis of cerebral arteries
39344	Cereb infarct due cerebral venous thrombosis, nonpyogenic
40758	Cereb infarct due unsp occlus/stenos precerebr arteries
44765	Carotid artery syndrome hemispheric
47642	Wallenberg syndrome
50594	Multiple and bilateral precerebral artery syndromes
51767	Pure sensory lacunar syndrome
53745	[X]Other cerebral infarction
55247	Impending cerebral ischaemia
90572	[X]Occlusion and stenosis of other precerebral arteries
91627	[X]Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artrs
92036	[X]Occlusion and stenosis of other cerebral arteries

94482	[X]Cereb infarct due unsp occlus/stenos precerebr arteries
94482	[X]Cereb infarct due unsp occlus/stenos precerebr arteries

Aspirin codes:

prodcode	productname
52280	Aspirin 300mg Tablet (Wockhardt UK Ltd)
36543	Aspirin 100mg effervescent tablets
68752	Aspirin 75mg tablets (Sigma Pharmaceuticals Plc)
52905	Aspirin 300mg tablets (Lloyds Pharmacy Ltd)
29759	Aspro Tablet (Roche Consumer Health)
18261	Aspirin 500mg with Papaveretum 7.71mg dispersible tablets
53622	Aspirin 300mg Tablet (M & A Pharmachem Ltd)
43709	Aspirin 75mg gastro-resistant tablets (Almus Pharmaceuticals Ltd)
34434	Aspirin 75mg dispersible tablets (Thornton & Ross Ltd)
393	Disprin 300mg dispersible tablets (Reckitt Benckiser Healthcare (UK) Ltd)
53804	Aspirin 300mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd)
43434	Aspirin 300mg gastro-resistant tablets (A A H Pharmaceuticals Ltd)
48165	Aspirin 300mg tablets (Aspar Pharmaceuticals Ltd)
377	Aspirin 300mg dispersible tablets
54284	Aspirin 75mg dispersible tablets (Almus Pharmaceuticals Ltd)
10310	Aspirin powder
37541	Aspirin 227mg medicated chewing-gum
254	Aspirin 300mg tablets
31954	Aspirin 75mg dispersible tablets (Teva UK Ltd)
45851	Aspirin 300mg Soluble tablet (Ranbaxy (UK) Ltd)
50166	Generic Anadin Extra tablets
12964	Aspirin 600mg / Caffeine 50mg oral powder sachets sugar free
56007	Aspirin 300mg dispersible tablets (Sigma Pharmaceuticals Plc)
25718	Angettes 75 tablets (Bristol-Myers Squibb Pharmaceuticals Ltd)
25211	Anadin Original tablets (Pfizer Consumer Healthcare Ltd)
10305	Aspirin 162.5mg capsules
49685	Aspirin 75mg dispersible tablets (Sigma Pharmaceuticals Plc)
31001	Cullens headache powders Sachets (Cullen and Davidson)
22232	Disprin Direct 300mg orodispersible tablets (Reckitt Benckiser Healthcare (UK) Ltd)
59253	Aspirin 75mg gastro-resistant tablets (Waymade Healthcare Plc)
32036	Aspirin 75mg dispersible tablets (Actavis UK Ltd)
34386	Aspirin 300mg tablets (Actavis UK Ltd)
15364	Aspirin 150mg suppositories
1902	Aspirn 600mg gastro-resistant tablets
67160	Aspirin 300mg dispersible tablets (Lloyds Pharmacy Ltd)
1049	Nu-seals aspirin 600mg Tablet (Eli Lilly and Company Ltd)
52044	Aspirin 300mg caplets (The Boots Company Plc)
59244	Aspirin 100mg capsules
9044	Codis 500 dispersible tablets (Reckitt Benckiser Healthcare (UK) Ltd)

18329 Enprin 75mg gastro-resistant tablets (Galpharm International Ltd)
8186 Aspirin 300mg modified-release tablets
45840 Aspirin 300mg Dispersible tablet (Numark Management Ltd)
34385 Aspirin 75mg Soluble tablet (Co-operative)
60694 Aspirin 25mg/5ml oral solution
7539 Beechams Powders oral powder sachets (GlaxoSmithKline Consumer Healthcare)
32992 Aspirin 75mg gastro-resistant tablets (Mylan)
24025 Caprin 300mg gastro-resistant tablets (Pinewood Healthcare)
41512 Aspirin 75mg gastro-resistant tablets (Teva UK Ltd)
34 Aspirin 75mg gastro-resistant tablets
53178 Aspirin 75mg gastro-resistant tablets (Wockhardt UK Ltd)
18217 Aspirin 300mg orodispersible tablets sugar free
9144 Caprin 75mg gastro-resistant tablets (Wockhardt UK Ltd)
55230 Aspirin 300mg dispersible tablets (Kent Pharmaceuticals Ltd)
56995 Aspirin 75mg dispersible tablets (Phoenix Healthcare Distribution Ltd)
50555 Aspirin 300mg dispersible tablets (DE Pharmaceuticals)
22138 Aspirin 324mg modified-release tablets
41569 Aspirin 300mg tablets (A A H Pharmaceuticals Ltd)
31858 Caspac xl 162.5mg Capsule (Pharmacia Ltd)
67521 Aspirin 15mg/5ml oral suspension
8645 Aspirin 300mg effervescent tablets
34485 Aspirin 75mg gastro-resistant tablets (IVAX Pharmaceuticals UK Ltd)
67754 Aspirin 300mg dispersible tablets (Almus Pharmaceuticals Ltd)
60127 Aspirin 75mg tablets (DE Pharmaceuticals)
48000 Aspirin 300mg tablets (Sigma Pharmaceuticals Plc)
645 Aspirin 300mg suppositories
52618 Aspirin 75mg dispersible tablets (Bristol Laboratories Ltd)
33293 Aspirin 75mg gastro-resistant tablets (Sterwin Medicines)
12992 Aspirin 500mg / Codeine 8mg dispersible tablets sugar free
32210 Aspirin 300mg dispersible tablets (Actavis UK Ltd)
73994 Aspirin 75mg gastro-resistant tablets (Greenfield Pharmaceuticals Ltd)
70549 Danamep 75mg dispersible tablets (Ecogen Europe Ltd)
2628 Nu-seals aspirin ec 75mg Gastro-resistant tablet (Eli Lilly and Company Ltd)
34309 Aspirin 300mg dispersible tablets (A A H Pharmaceuticals Ltd)
30920 Aspirin 300mg Dispersible tablet (M & A Pharmachem Ltd)
57057 Aspirin 75mg dispersible tablets (Wockhardt UK Ltd)
74096 Aspirin 50mg/5ml oral suspension
67362 Aspirin 300mg suppositories (Alliance Healthcare (Distribution) Ltd)
33668 Aspirin 300mg Dispersible tablet (Rusco Ltd)
54997 Aspirin 75mg dispersible tablets (Dowelhurst Ltd)
53711 Aspirin 300mg Tablet (Nucare Plc)
50949 Aspirin 75mg tablets (A A H Pharmaceuticals Ltd)
74302 Aspirin 75mg/5ml oral suspension
20650 Aspirin 300mg / Paracetamol 200mg dispersible tablets sugar free
54526 Aspirin 300mg tablets (Alliance Healthcare (Distribution) Ltd)

43679 Flamasacard 162.5mg Modified-release capsule (Abbey Pharmaceuticals Ltd)
33676 Aspirin 75mg dispersible tablets (Kent Pharmaceuticals Ltd)
54734 Aspirin 300mg tablets (Wockhardt UK Ltd)
17704 Platet 100mg Effervescent tablet (Roche Products Ltd)
9939 Aspirin 500mg effervescent tablets sugar free
8185 Disprin CV 300mg modified-release tablets (Reckitt Benckiser Healthcare (UK) Ltd)
49799 Aspirin 150mg suppositories (A A H Pharmaceuticals Ltd)
71192 Aspirin 75mg tablets (Kent Pharmaceuticals Ltd)
67858 Aspirin 25mg capsules
49060 Aspirin 75mg dispersible tablets (Alliance Healthcare (Distribution) Ltd)
1137 Nu-seals aspirin ec 300mg Gastro-resistant tablet (Eli Lilly and Company Ltd)
59021 Aspirin 75mg gastro-resistant tablets (Bristol Laboratories Ltd)
71078 Aspirin 300mg dispersible tablets (Mawdsley-Brooks & Company Ltd)
34942 Aspirin 75mg Dispersible tablet (Nucare Plc)
16611 Anadin Tablet (Wyeth Consumer Healthcare)
18030 Imazin XL forte tablets (Napp Pharmaceuticals Ltd)
2105 Solprin 300mg Tablet (Reckitt Benckiser Healthcare (UK) Ltd)
60777 Aspirin 75mg gastro-resistant tablets (DE Pharmaceuticals)
58112 Alka-Seltzer effervescent tablets original (Bayer Plc)
685 Aspav dispersible tablets (Actavis UK Ltd)
24960 Aspirin 300mg tablets (Vantage)
59728 Aspirin 75mg tablets (Alissa Healthcare Research Ltd)
381 Anadin Tablet (Wyeth Consumer Healthcare)
31953 Aspirin 75mg dispersible tablets (IVAX Pharmaceuticals UK Ltd)
40144 Aspirin 300mg Dispersible tablet (Thornton & Ross Ltd)
54353 Generic Anadin Extra soluble tablets sugar free
66563 Aspirin 75mg gastro-resistant tablets (Phoenix Healthcare Distribution Ltd)
34762 Aspirin 300mg Gastro-resistant tablet (Galen Ltd)
62430 Aspirin 300mg suppositories (A A H Pharmaceuticals Ltd)
39738 Aspirin 162.5mg modified-release capsules
11951 Original Phensic Aspirin tablets (Merck Consumer Health Products)
28810 Aspirin 300mg with Glycine 133mg soluble tablets
55579 Aspirin 300mg tablets (Almus Pharmaceuticals Ltd)
22618 Solprin 75mg Tablet (Reckitt Benckiser Healthcare (UK) Ltd)
15367 Anadin Extra tablets (Pfizer Consumer Healthcare Ltd)
54430 Aspirin 75mg tablets (Alliance Healthcare (Distribution) Ltd)
33656 Aspirin 75mg dispersible tablets (A A H Pharmaceuticals Ltd)
44639 Aspirin 300mg Dispersible tablet (Nucare Plc)
19189 Micropirin 75mg Gastro-resistant tablet (Ratiopharm UK Ltd)
53791 Aspirin 150mg suppositories (Alliance Healthcare (Distribution) Ltd)
41594 Aspirin 300mg Dispersible tablet (Teva UK Ltd)
62334 Aspirin 300mg caplets (Wockhardt UK Ltd)
66546 Aspirin 75mg dispersible tablets (Numark Ltd)
16 Aspirin 75mg tablets
34796 Aspirin 75mg Gastro-resistant tablet (Galen Ltd)

60278 Aspirin 300mg tablets (DE Pharmaceuticals)
66345 Aspirin 75mg dispersible tablets (DE Pharmaceuticals)
68051 Aspirin 150mg suppositories (Colorama Pharmaceuticals Ltd)
59791 Aspirin 75mg dispersible tablets (Aspar Pharmaceuticals Ltd)
31210 Aspirin 300mg Tablet (Co-operative)
17920 Disprin cv 100mg Modified-release tablet (Reckitt Benckiser Healthcare (UK) Ltd)
6007 Nu-Seals 300 gastro-resistant tablets (Alliance Pharmaceuticals Ltd)
54565 Aspirin 75mg dispersible tablets (Lloyds Pharmacy Ltd)
2607 Paynocil Tablet (Beecham Research Laboratories)
36521 Aspirin 500mg modified-release tablets
11326 Meprobamate with ethoheptazine citrate and aspirin Tablet
33320 Aspirin 75mg Dispersible tablet (Sovereign Medical Ltd)
34666 Aspirin ec 300mg Gastro-resistant tablet (A A H Pharmaceuticals Ltd)
11977 Aspro clear maximum strength tablets
43060 Aspirin 300mg Soluble tablet (Celltech Pharma Europe Ltd)
21382 Aspirin 150mg / Isosorbide mononitrate 60mg modified-release tablets
24622 Aspirin 325mg / Caffeine 22mg tablets
25335 PostMI 75 EC tablets (Ashbourne Pharmaceuticals Ltd)
64071 Aspirin powder (J M Loveridge Ltd)
56996 Aspirin 75mg dispersible tablets (Waymade Healthcare Plc)
20840 Acetylsalicylic acid mix
49220 Aspirin 300mg tablets (Kent Pharmaceuticals Ltd)
22305 Disprin Extra dispersible tablets (Reckitt Benckiser Healthcare (UK) Ltd)
9301 Aspirin 100mg modified-release tablets
484 Equagesic Tablet (Wyeth Pharmaceuticals)
31938 Aspirin 75mg gastro-resistant tablets (Sandoz Ltd)
33662 Aspirin 300mg Dispersible tablet (A A H Pharmaceuticals Ltd)
47992 Aspirin 75mg gastro-resistant tablets (A A H Pharmaceuticals Ltd)
56883 Aspirin 75mg tablets (Waymade Healthcare Plc)
35967 Paramed Extra Power Pain Control tablets (Galpharm International Ltd)
29848 Aspirin 300mg with Glycine 150mg chewable tablets
6006 Nu-Seals 75 gastro-resistant tablets (Alliance Pharmaceuticals Ltd)
34797 Aspirin 75mg gastro-resistant tablets (Actavis UK Ltd)
50926 Aspirin 75mg dispersible tablets (The Boots Company Plc)
40381 Aspirin 75mg Soluble tablet (C P Pharmaceuticals Ltd)
6226 Aspirin 500mg / Papaveretum 7.71mg dispersible tablets sugar free
48974 Aspirin 75mg tablets (Phoenix Healthcare Distribution Ltd)
34611 Aspirin 75mg gastro-resistant tablets (C P Pharmaceuticals Ltd)
71821 Aspirin 300mg Tablet (Numark Management Ltd)
31870 Aspirin 320mg tablets
74786 Aspirin 75mg gastro-resistant tablets (Alliance Healthcare (Distribution) Ltd)
56736 Aspirin 300mg tablets (Waymade Healthcare Plc)
6696 Micropirin 75mg gastro-resistant tablets (Dexcel-Pharma Ltd)
31211 Aspirin 75mg Dispersible tablet (A A H Pharmaceuticals Ltd)
58331 Aspirin 300mg gastro-resistant tablets (Mylan)

70841 Aspirin 300mg Dispersible tablet (Family Health)
63603 Laboprin Tablet (Laboratories For Applied Biology Ltd)
41766 Maximum Strength Aspro Clear 500mg effervescent tablets (Bayer Plc)
73478 Lloydspharmacy Extra Power Pain Reliever tablets (Lloyds Pharmacy Ltd)
3309 Aspirin 325mg / Caffeine 15mg tablets
71676 Aspirin 75mg dispersible tablets (Mawdsley-Brooks & Company Ltd)
66171 Aspirin 150mg Suppository (Distriphar (UK))
395 Aspirin mixture
657 Aspirin 500mg granules sachets sugar free
71663 Aspirin 75mg tablets (Actavis UK Ltd)
3 Aspirin 75mg dispersible tablets
23878 Nu-seals cardio ec 75mg Gastro-resistant tablet (Genus Pharmaceuticals Ltd)
66861 Aspirin 75mg effervescent tablets
21921 Postmi ec 300mg Gastro-resistant tablet (Ashbourne Pharmaceuticals Ltd)
51474 Aspirin 150mg suppositories (Martindale Pharmaceuticals Ltd)
48021 Aspirin 75mg Tablet (Hillcross Pharmaceuticals Ltd)
434 Aspirin 300mg gastro-resistant tablets
7516 Aspirin 300mg effervescent tablets sugar free
31956 Aspirin 75mg gastro-resistant tablets (Kent Pharmaceuticals Ltd)
53816 Aspirin 300mg dispersible tablets (Alliance Healthcare (Distribution) Ltd)
47937 Aspirin 75mg dispersible tablets (Wockhardt UK Ltd)
23932 Aspro Clear 300mg effervescent tablets (Bayer Plc)
51561 Aspirin 75mg gastro-resistant tablets (Zanza Specials International Ltd)
60693 Aspirin 15mg/5ml oral solution
45643 Aspirin 75mg Soluble tablet (Celltech Pharma Europe Ltd)
7520 Anadin Extra soluble tablets (Pfizer Consumer Healthcare Ltd)
43806 Aspirin 300mg gastro-resistant tablets (Sandoz Ltd)
23488 Claradin 300mg Tablet (Nicholas Laboratories Ltd)
23593 PostMI 75 dispersible tablets (Ashbourne Pharmaceuticals Ltd)
32728 Askit oral powder sachets (Bayer Plc)
23491 ASPIRIN 500 MG SUP
40191 ASPIRIN /CAFFEINE /QUININE SULPHATE 325 MG TAB
430 Aspirin 500mg / Caffeine 32mg capsules
11941 ASPIRIN SACHETS 30 MG
9027 ASPIRIN disp 150 MG TAB
22863 ASPIRIN S/R 500 MG TAB
4523 ASPIRIN 50 MG CAP
8381 ASPIRIN /CAMPHOR /MENTHOL /METHYL SALICY 1.2 % LIN
20206 ASPIRIN 50 MG SUP
15447 ASPIRIN SOLUBLE 600 MG TAB
7944 ASPIRIN SOLUBLE 40 MG CAP
15044 ASPIRIN disp 500 MG TAB
22450 ASPIRIN & CODEINE 75 MG TAB
19724 ASPIRIN & CODEINE paed 75 MG TAB
12605 ASPIRIN & CAFFEINE disp 300 MG TAB
2754 ASPIRIN SOLUBLE 150 MG TAB

7770	ASPIRIN/CODEINE PHOSPHATE/PARACETAMOL 250 MG TAB
306	Aspirin with codeine phosphate and caffeine tablets
15517	ASPIRIN 100 MG SUP
28238	ASPIRIN 300MG/LYSINE 245MG 300 MG TAB
7486	ASPIRIN 37.5 MG TAB
28707	ASPIRIN M/F 324 MG TAB
42061	ASPIRIN 65 MG SUP
67984	Aspire Hayfever Relief 2% eye drops (Aspire Pharma Ltd)
33075	ASPIRIN 600MG/GLYCINE 300MG 600 MG TAB
13598	ASPIRIN & CODEINE 500 MG TAB
4557	ASPIRIN & PAPAVERUTUM 10 MG TAB
26424	ASPIRIN 200 MG SUP
7417	ASPIRIN 40 MG TAB
30432	ASPIRIN & DOVER'S pwdr TAB
22864	ASPIRIN PAED MIX
21380	Aspirin 75mg / Isosorbide mononitrate 60mg modified-release tablets
23495	ASPIRIN
12102	ASPIRIN SOLUBLE 100 MG TAB
111	ASPIRIN 40 MG CAP
25959	ASPIRIN/CAFFEINE/DEXTROPROPOXYPHENE NAPS PUL
383	ASPIRIN 60 MG TAB
17926	Aspirin 400mg with Codeine 8mg tablets
15397	ASPIRIN SOLUBLE 50 MG TAB
24857	ASPIRIN 250 MG SUP
33317	Aspirin with Sodium bicarbonate with Citric acid effervescent tablets
26099	ASPIRIN 175 MG SUP
7915	ASPIRIN SR 100 MG TAB
8734	ASPIRIN disp 37.5 MG TAB
9432	Aspirin 500mg / Codeine 8mg soluble tablets
30695	ASPIRIN 120 MG SUP
26792	ASPIRIN 125 MG SUP
28606	ASPIRIN/CAFFEINE/CODEINE PHOSPHATE 300 MG TAB
2924	ASPIRIN 150 MG TAB
34233	Aspirin with aloxiprin and caffeine capsules
27467	ASPIRIN SOLUBLE 400 MG TAB
7665	ASPIRIN SR 300 MG TAB
19813	ASPIRIN SOLUBLE
32314	Aspirin with aloxiprin and caffeine powder
63683	Aspirin with codeine Dispersible tablet (Actavis UK Ltd)
8424	ASPIRIN PAED 81 MG TAB
22107	ASPIRIN disp 200 MG TAB
24498	ASPIRIN/CODEINE PHOSPHATE/PARACETAMOL 300 MG TAB
12976	Aspirin 900mg / Metoclopramide 10mg oral powder sachets sugar free
23250	ASPIRIN /ETHOHEPTAZINE CITRATE /MEPROBAM 250 MG TAB
26582	ASPIRIN PAED 100 MG SUP
7518	Aspirin 400mg with Codeine 8mg dispersible tablets

31498	ASPIRIN / CAFFEINE CIT./ CODEINE PHOS./ 200 MG TAB
7769	ASPIRIN/PARACETAMOL TAB
8843	ASPIRIN 325 MG TAB
1486	ASPIRIN 75 MG SUP
10031	Aspirin 25mg with Dipyridamole 200mg modified-release capsules
22776	Aspirin 500mg with Cyclizine 25mg effervescent tablets
15352	ASPIRIN & PARACETAMOL TAB
8920	ASPIRIN SOLUBLE 500 MG TAB
216	ASPIRIN 70 MG TAB
4271	ASPIRIN SOLUBLE 200 MG TAB
22824	ASPIRIN disp 600 MG TAB
7462	ASPIRIN 325 MG CAP
22253	ASPIRIN paed 150 MG SUP
19674	ASPIRIN DISPERSIBLE

Appendix 2 –Additional PERR analyses

Table S2.1: Other outcomes for the Propensity Score Matched PERR analysis

	Hazard ratio (95% confidence interval)
Composite outcome (primary outcome and mortality)	0.61 (0.51 – 0.73)
Fracture	1.23 (0.82 – 1.73)
Constipation	0.92 (0.80 - 1.16)

Values presented are based on prior-event rate ratio analysis adjusted for smoking status, age, sex, diabetes, hypertension. NSAID, non-steroidal anti-inflammatory drug; MI, myocardial infarction.

Table S2.2: Association between different drugs and post-pneumonia cardiovascular outcomes

Drugs:	Primary (MI + Stroke)	Stroke	MI
Aspirin	0.64 (0.52 – 0.79)	0.70 (0.55 – 0.91)	0.46 (0.30 – 0.72)
Levothyroxine	1.10 (0.73-1.63)	1.33 (0.83 -2.19)	0.70 (0.31-1.41)
Proton Pump Inhibitors	0.98 (0.76 – 1.30)	0.98 (0.73 – 1.33)	0.87 (0.57 – 1.32)
Paracetamol	0.96 (0.69 – 1.33)	1.12 (0.72 – 1.63)	0.68 (0.36 – 1.28)
NSAIDS	1.88 (1.10 – 3.31)	1.57 (0.86 – 3.11)	4.87 (1.60-37.2)

Values presented are based on prior-event rate ratio analysis adjusted for smoking status, age, sex, diabetes, hypertension. NSAID, non-steroidal anti-inflammatory drug; MI, myocardial infarction.

Table S2.3: Association between different drugs and post-pneumonia cardiovascular outcomes (sensitivity analysis to drug definition)

Drugs:	Primary (MI + Stroke)	Stroke	MI
Aspirin	0.64 (0.50 – 0.84)	0.70 (0.52 – 0.95)	0.55 (0.33-0.89)
Levothyroxine	0.81 (0.51 – 1.29)	1.16 (0.68 – 2.07)	0.61 (0.24 – 1.47)
Proton Pump Inhibitors	0.90 (0.67 -1.21)	1.08 (0.75 – 1.54)	0.60 (0.34 – 1.05)
Paracetamol	1.47 (0.78 – 2.71)	1.54 (0.74- 3.38)	1.45 (0.43 – 6.45)
NSAIDS	1.70 (0.95 – 3.21)	1.24 (0.55 – 2.84)	4.14 (1.31 – 26.52)

Values presented are based on prior-event rate ratio analysis adjusted for smoking status, age, sex, diabetes, hypertension. NSAID, non-steroidal anti-inflammatory drug; MI, myocardial infarction.

Table S2.4: Association between different drugs and post-pneumonia cardiovascular outcomes (sensitivity analysis to only confirmed primary care consultations)

Drugs:	Primary (MI + Stroke)	Stroke	MI	Composite (MI + Stroke + Mortality
Aspirin	0.60 (0.42 – 0.87)	0.63 (0.41 – 0.97)	0.63 (0.30 – 1.24)	0.80 (0.60 – 1.08)
Levothyroxine	1.40 (0.77 – 2.71)	1.29 (00.59 – 2.77)	1.55 (0.33 – 7.74)	1.47 (0.94 – 2.34)
Proton Pump Inhibitors	0.96 (0.57 – 1.51)	0.78 (0.43 – 1.35)	1.22 (0.53 – 2.59)	1.25 (0.82 – 1.78)
Paracetamol	1.47 (0.85 – 2.45)	1.54 (0.74 – 2.83)	1.24 (0.34 – 4.15)	1.55 (1.02 – 2.33)
NSAIDS	1.21 (0.56 – 2.62)	0.69 (0.28 – 1.62)	9.35 (1.78 –	1.60 (0.84 – 3.22)

Values presented are based on prior-event rate ratio analysis adjusted for smoking status, age, sex, diabetes, hypertension. NSAID, non-steroidal anti-inflammatory drug; MI, myocardial infarction.

Appendix 3 – Cox regression model outputs

Table S3.1. Cox regression for primary outcome (combined MI and Stroke)

	Hazard ratio (95% confidence interval)		
	Primary (MI or stroke)	Stroke	MI
Aspirin user	0.84 (0.73-0.96)	0.80 (0.68-0.96)	0.82 (0.66-1.02)
Age (years)	1.01 (1.00-1.02)	1.02 (1.01-1.03)	1.00 (0.99-1.01)
Female gender	0.89 (0.77-1.02)	0.97 (0.81-1.16)	0.68 (0.54-0.86)
Previous stroke	4.75 (4.09-5.51)	2.76 (1.88-4.04)	0.64 (0.5-0.82)
Previous IHD	2.12 (1.17-3.85)	0.59 (0.14-2.40)	4.59 (2.36 – 8.92)
Hypertension	0.95 (0.82-1.08)	0.95 (0.81-1.13)	1.15 (0.92-1.43)
PVD	1.05 (0.84-1.32)	0.96 (0.71-1.32)	1.25 (0.89-1.76)
IMD	1.03 (1.00-1.05)	1.03 (1.01-1.06)	1.02 (0.98-1.06)
Diabetes	1.00 (0.85-1.19)	0.89 (0.72-1.11)	0.92 (0.89-1.76)
Smoking (ref=non-smoker)			
ex-smoker	0.97 (0.82-1.08)	0.80 (0.63-1.00)	0.85 (0.64-1.14)
current smoker	1.05 (0.83-1.33)	0.82 (0.60-1.11)	1.09 (0.76-1.55)
unknown smoking status	1.24 (1.03-1.50)	0.89 (0.99-1.11)	1.13 (0.82-1.56)

MI, myocardial infarction; IHD, ischaemic heart disease; CKD, chronic kidney disease; IMD, Index of Multiple Deprivation