Non-Interventional Study

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Assessment of 13-valent pneumococcal conjugate vaccine effectiveness among people with HIV in the United States

Statistical Analysis Plan

(SAP)

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1. AMENDMENTS FROM PREVIOUS VERSION(S)

Version	Date	Changes	Rationale
1.3	07-Dec-2023	Added 'in the United States' to the title	Reflect protocol amendment
1.3	07-Dec-2023	Added age group and PPSV23 number of doses as potential stratification variables	Reflect protocol amendment
1.3	07-Dec-2023	Updated potential negative control outcomes	Reflect protocol amendment
1.3	07-Dec-2023	Updated opportunistic infections list	Reflect protocol amendment
1.3	07-Dec-2023	Study follow-up now begins six months after the first HIV-related ICD-9-CM or ICD-10-CM code	Reflect protocol amendment
1.3	07-Dec-2023	Removed requirement for six months of continuous enrollment before members' first HIV-related ICD-9-CM or ICD-10-CM code, updated inclusion start date and removed exclusion for individuals with evidence of ART therapy during baseline period	Reflect protocol amendment
1.2	10-Aug-2023	Updated to SOP template version 3.0	
1.2	10-Aug-2023	Added alternate definition of outpatient	Reflect protocol amendment

		candidiasis infection and NDC table	
1.2	10-Aug-2023	Added time-varying covariates for annual HIV viral load testing and annual CD4 cell count testing and their CPT codes. Added time-varying covariates for respiratory virus season.	Reflect protocol amendment
1.2	10-Aug-2023	Study follow-up now begins 90 days after index and at least 90 days of continuous enrolment in medical plans is added to the inclusion criteria	Reflect protocol amendment
1.2	10-Aug-2023	The two outpatient HIV-related codes are now no more than 730 days apart	Reflect protocol amendment
1.2	10-Aug-2023	90 instead of 30-day intervals now used for the analysis of RZV	Needed due to low numbers of patients vaccinated with RZV overall and in each interval
1.2	10-Aug-2023	Updated person-time exclusion in Incidence Rates subsection of 7.1 from 29 to 89 days	Needed to reflect the previous update to the number of days separating recurrent events from 30 to 90 days
1.2	10-Aug-2023	Added a definition of overall SMD	Needed for reporting in output table
1.2	10-Aug-2023	Specified cluster robust standard errors for the 95% confidence intervals for the incidence rates based on recurrent events and updated R code	Needed to account for multiple events per patient

1.2	10-Aug-2023	Updated Payor categories in Table 5.2	Previous categories did not accurately represent the values in the database
1.2	10-Aug-2023	Added text and reference to potentially correct main results for any bias identified from the negative control outcome	Needed to clarify the potential calculation that will be used
1.1	2-Jun-2023	The number of days used to separate pneumonia and candidiasis episodes to identify independent events was increased from 30 to 90 days.	Unrealistically high numbers of recurrent events were generated for several patients when using 30 days. It was therefore decided that 30 days may be insufficient time to recover from these infections in a HIV population. This decision was taken prior to generating incidence rates by vaccination status and prior to generating vaccine effectiveness results using recurrent events.
1.1	2-Jun-2023	Included the reporting of incidence rates annually and during the time periods of interest.	Added to explore potential changes over time.
1.1	2-Jun-2023	Specified that covariates imbalanced after weighting may be included in final weighted models.	Added to clarify the purpose of the assessment of covariate balance.
1.1	2-Jun-2023	Updated example code for standardized differences	Fixed error in code to match description.
1.0	20-Mar-2023	N/A. First version	N/A

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AG	Andersen-Gill
ART	Antiretroviral therapy
ATE	Average treatment effect
CI	Confidence interval
Cox-MSM	Marginal structural Cox models
CPT	Current procedural terminology®
CSF	Cerebrospinal fluid
HIV	Human immunodeficiency virus
HR	Hazard ratio
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
ICD-9-PCS	International Classification of Diseases, Ninth Revision, Procedure Coding System
ICD-10-PCS	International Classification of Diseases, Tenth Revision, Procedure Coding System
IPCW	Inverse probability of censoring weighting
IPD	Invasive pneumococcal disease
IPTW	Inverse probability of treatment weighting
NDC	National Drug Code
NI	Non-interventional

PCV	Pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PPSV23	23-valent pneumococcal polysaccharide vaccine
PLWH	People living with HIV
RZV	Recombinant zoster vaccine
SMD	Standardized mean differences
SVI	Social Vulnerability Index
VE	Vaccine effectiveness

Note: in this document, any text taken directly from the non-interventional (NI) study protocol is ***italicized***.

3. RATIONALE AND BACKGROUND

People living with HIV (PLWH) are at increased risk of pneumococcal infections, but there is a lack of data on 13-valent pneumococcal conjugate vaccine (PCV13) vaccine effectiveness (VE) in PLWH.

The purpose of this study is to estimate PCV13 VE against pneumococcal disease in PLWH aged ≥18 years, overall and, if feasible, at 3, 5, and 7 years of follow-up. The primary outcomes of interest are invasive pneumococcal disease (IPD), pneumococcal pneumonia and all-cause pneumonia.

4. STUDY OBJECTIVES AND HYPOTHESES

4.1. Primary Objectives

The primary objectives of this study are:

1. *Estimate vaccine effectiveness (VE) of PCV13 for invasive pneumococcal disease (IPD) among people living with HIV (PLWH) ≥18 years of age, overall and, if feasible, at 3, 5, and 7 years of follow-up*

2. *Estimate VE of PCV13 for pneumococcal pneumonia among PLWH ≥18 years of age, overall and, if feasible, at 3, 5, and 7 years of follow-up*

3. *Estimate VE of PCV13 for all-cause pneumonia among PLWH ≥18 years of age, overall and, if feasible, at 3, 5, and 7 years of follow-up.*

4.2. Secondary Objectives

The secondary objectives of this study are:

1. *Estimate VE of PCV13 for pneumococcal pneumonia or pneumonia with unspecified causes among PLWH ≥18 years of age, overall and, if feasible, at 3, 5, and 7 years of follow-up*

2. *Estimate VE of PCV13 for pneumonia with unspecified causes among PLWH ≥18 years of age, overall and, if feasible, at 3, 5, and 7 years of follow-up.*

5. RESEARCH METHODS

5.1. Study Design

The VE study will be a retrospective cohort study using health care administrative claims and laboratory data.

PLWH will be identified using administrative claims and include individuals with at least one inpatient International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code related to HIV (Appendix Table 7.1) or at least 2 outpatient ICD-9-CM or ICD-10-CM codes at least 30 days, but no more than 730 days, apart during January 1, 2014 and December 31, 2021. PLWH are required to have at least six months of continuous enrollment in one or more health plans and pharmacy benefits after their first HIV-related ICD-9-CM or ICD-10-CM code. These six months of continuous enrollment will be considered the baseline period, during which baseline covariates including demographics, comorbidities, and preventative care will be measured. The baseline period was also selected to minimize the number of outcome events that existing prior to or triggered an HIV diagnosis.

The date following the last date of the baseline period will be defined as the index date. The end of the study will occur on the last date that administrative claims data will be available, September 30, 2022.

5.2. Study Population

PLWH will be identified by ICD-9-CM or ICD-10-CM diagnosis codes (Appendix Table 7.1). Information provided by Komodo Health indicated that approximately 175,000 individuals meet the eligibility criteria.

All PLWH in the provided Komodo Health who meet the following criteria will be included in the analysis.

5.2.1. Inclusion Criteria

1. *HIV infection defined as at least one inpatient International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code related to HIV (*Appendix Table 7.1*) or ≥2 outpatient ICD-9-CM or ICD-10-CM codes at least 30 days, but no more than 730 days, apart during January 1, 2014 and December 31, 2021*

AND

2. *At least 18 years of age at the time of the first recording of HIV-related ICD-9-CM or ICD-10-CM code*

AND

3. *At least six months of continuous enrollment in medical and pharmacy plans after the first HIV-related ICD-9-CM or ICD-10-CM code between January 1, 2014 and December 31, 2021. A gap of 30 days or less in enrollment will be allowed during this six month period.*

5.2.2. Exclusion Criteria

Patients meeting the following criterion will not be included in the study:

1. *Evidence of PCV13 vaccination before the first HIV-related ICD-9-CM or ICD-10-CM code*

All available data prior to first HIV-related ICD-9-CM or ICD-10-CM code will be used to assess evidence of PCV13 vaccination, however there is no minimum time requirement.

5.2.3. Subgroups and Stratification

Several stratified analyses will be conducted. PPSV23 is recommended for PLWH and feasibility data provided by Komodo suggest that one in four PWLH who received PCV13 during 2014-2015 also received PPSV23 within two years. Rather than censor or exclude individuals who receive PPSV23, we will calculate PCV13 VE among PWLH who have/have not received PPSV23 before and during the study period. The analysis may also be stratified by the number of PPSV23 doses, e.g. 0, 1, 2+.

Feasibility assessments from Komodo indicate that approximately 25% of PWLH have at least one CD4 cell count or percentage laboratory result available. Therefore, we will calculate PCV13 VE among the subset of PWLH who have a CD4 cell count during the baseline period or follow-up, and potentially stratify by CD4 category using the patient's lowest value during the study.

Additional VE stratifications by ART adherence during follow-up, year of HIV diagnosis, and age will be assessed for feasibility as well, as these affect patients' immune status and immune reconstitution. Due to possible waning of the VE and different lengths of follow-up by index year, VE stratification by year of HIV diagnosis will be restricted to the first 3 years of follow-up (0 to 1079 days).

The above subgroup analyses will be conducted if there are sufficient numbers of patients/ events to maintain patient de-identification (Section 5.8.3) and where the 95% confidence intervals (CI) for the VE estimates can be expected to exclude zero in the best case scenarios for the analyses, i.e. the highest expected VE estimate, the lowest expected censoring rate and at the maximum follow-up time. Table 5.1 provides precision estimates for IPD and all-cause pneumonia under different numbers of individuals available for the analysis. The following assumptions were used for the estimates:

- 32% of individuals received PCV13
- IPD incidence among PLWH is 183 cases per 100,000 population [1]
- All-cause pneumonia incidence among PLWH is 5,487 cases per 100,000 population
- VE for IPD due to any serotype is 22.5% [2, 3]
- VE for all-cause pneumonia is 15% [4]

- Annual censoring of individuals due to loss to follow-up or death is 4%
- Up to 97 months of follow-up

Survival and censoring times were simulated assuming exponential distributions. Vaccination status was modelled as a time-varying covariate [5]. Hazard ratios were assumed as 1-(VE/100). Simulations were run 100 to 200 times per scenario. Cox regression models were run on each simulated dataset to estimate the 95% CIs for the log HRs. Means were generated and exponentiated to obtain the 95% CIs for the VEs using (1- HR) x 100 and used to describe VE precision.

Table 5.1 Precision of PCV13 Vaccine Effectiveness Estimates for Invasive Pneumococcal Disease and All-Cause Pneumonia Subgroup Analyses

Number of individuals	IPD VE: 22.5%		All-cause pneumonia VE: 15%	
	Lower 95% confidence interval estimate	Upper 95% confidence interval estimate	Lower 95% confidence interval estimate	Upper 95% confidence interval estimate
87,000 (N/2)	6%	37%	11%	18%
58,000 (N/3)	1%	40%	11%	19%
43,000 (N/4)	-5%	41%	10%	20%
35,000 (N/5)	-6%	44%	9%	20%
29,000 (N/6)	-9%	46%	9%	20%
22,000 (N/8)	-16%	49%	8%	21%

Table 5.1 shows that, under the current assumptions, 95% CIs for the IPD VE would still be expected to exclude 0% in subgroups with 58,000 individuals. For all-cause pneumonia the 95% CIs for the VE would still be expected to exclude 0 in subgroups with fewer than 22,000 individuals. Therefore, the study should have sufficient precision to address the study the objectives in several of the planned subgroups.

5.3. Variables

5.3.1. Effectiveness Endpoints

The outcomes of interest for the primary and secondary objectives are listed in Table 5.2.

Episodes separated by at least 90 days will be considered independent events. For claims that include pneumonia that are separated by <90 days, those claims will be collapsed into a single episode with a date of the initial diagnosis.

Table 5.2 Outcomes of Interest

Outcome Type	Outcome	Definition
Primary outcomes	IPD	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.4
	Pneumococcal pneumonia	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.4
	All-cause pneumonia	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.4
Secondary outcomes	Pneumococcal pneumonia or pneumonia with unspecified causes	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.5
	Pneumonia with unspecified causes	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.5
Sensitivity analysis outcome	All-cause pneumonia not associated with HIV	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.6

For combination diagnosis codes, (e.g., bacteremia + pneumococcus) for diagnoses in an inpatient setting patients must have all codes within the same admission. The latest date of the combination of diagnoses will be used as the diagnosis date. For diagnoses in an outpatient setting patients must have all codes within the same date.

5.3.2. Covariates

The list of demographic and clinical characteristics considered for descriptive reporting, subgroups and inclusion as covariates in models for generating the propensity scores are provided in Table 5.3. The Komodo Health database will be source of all variables.

Patients will be considered to have a comorbidity or hospitalization during baseline if there was evidence of a diagnosis at any time during the baseline period. Evidence of comorbidities or hospitalization during follow-up will be considered as new diagnoses. Once diagnosed, patients will be considered diagnosed for the remainder of their follow-up. ART adherence during baseline and follow-up will be updated every 6 months (180 days) based on the data collected in that previous timeframe. For baseline annual physical exam and annual influenza vaccine, patients will be considered adherent (coded as 'Yes') if there was evidence of these events at any time during the baseline period. During the follow-up, patients will be considered adherent up to 365 days after the last event date.

For annual CD4 and viral load laboratory tests during baseline and follow-up, patients will be coded as 'Yes' up to 365 days after the last event date. For respiratory virus season during follow-up, patients will be coded as 'Yes' if the observation time is in October, November, December, January, February, March or April.

The baseline period for the assessment of covariates is the six months prior to the index date, i.e., no data prior to six months will be included.

Covariates used at baseline only will be considered time-fixed confounders. Covariates additionally or only used during follow-up will be considered time-varying confounders.

Categories may be collapsed, or covariates may be excluded from the propensity scores if models fail to converge.

Table 5.3 List of Covariates

Variable	Operational Definition	Role	Time of Use
Age in years	Calculated as [year individual meets HIV criteria] – [birth year] Categorized as: 18-49, 50-64, 65-74, and ≥75 years As a subgroup, age will be categorized as 18-49, 50-64 and 65+ years	Descriptive (continuous and categorical) Covariate (categorical) Subgroup (categorical)	Baseline
Sex	Male, Female, Other/ Unknown	Descriptive, covariate	Baseline
Social Vulnerability Index (SVI)	SVI characterizes resiliency of a community when faced by external pressures and stresses[6, 7]. SVI ranges from 0 to 100, where a value of 100 indicates the most vulnerable population. 3-digit zip codes will be translated to 3-digit zip code tabulation areas, and SVI will be calculated at the 3-digit zip code tabulation area. Categorized as: low (lowest quartile), average (middle two quartiles) and high (highest quartile).	Descriptive, covariate	Baseline
US region	Northeast, North Central, South, West, Unknown	Descriptive, covariate	Baseline

Payor	Commercial, Dually eligible, Medicaid/CHIP, Medicare, Missing, Other	Descriptive, covariate	Baseline
Year of HIV diagnosis	Calendar year of first HIV diagnosis code 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021. When used as a subgroup year will be categorized as 2014, 2015-2016, 2017-2018, 2019-2021.	Descriptive, covariate, subgroup	Baseline
Alcoholism	ICD-9-CM or ICD-10-CM codes listed in Appendix Protocol Annex Table 1.1 Yes, No	Descriptive, covariate	Baseline and follow-up
Asplenia	CPT/Healthcare Common Procedure Coding System (HCPCS), ICD-10-Procedure Coding System (ICD-10-PCS), ICD-9-Procedure Coding System (ICD-9-PCS), ICD-9-CM, or ICD-10-CM codes listed in Protocol Annex Table 1.2	Descriptive, covariate	Baseline and follow-up
Chronic heart disease	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, ICD-9-CM, or ICD-10-CM codes listed in Protocol Annex Table 1.4 Yes, No	Descriptive, covariate	Baseline and follow-up
Chronic kidney disease and renal failure	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, ICD-9-CM, or ICD-10-CM codes listed in Protocol Annex Table 1.5 Yes, No	Descriptive, covariate	Baseline and follow-up
Chronic liver disease	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, ICD-9-CM, or ICD-10-CM codes listed in Protocol Annex Table 1.6 Yes, No	Descriptive, covariate	Baseline and follow-up
Chronic lung disease	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.7 Yes, No	Descriptive, covariate	Baseline and follow-up
Asthma	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.3 Yes, No	Descriptive, covariate	Baseline and follow-up
Diabetes mellitus	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.9 Yes, No	Descriptive, covariate	Baseline and follow-up
Generalized malignancy	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, ICD-9-CM or ICD-10-CM codes listed in Annex Table 1.10	Descriptive, covariate	Baseline and follow-up
Immunosuppressive medications	PLWH will be considered on immunosuppressive medications if: 1) ≥1 NDC, HCPCS, or ICD-10-PCS code in Appendix Table 7.7	Descriptive, covariate	Baseline and follow-up

	2) ≥ 1 NDC (using orals only) in Appendix Table 7.7 where the daily dose is ≥ 20mg or prednisone or prednisone equivalent for a duration of ≥14 consecutive days Yes, No		
Leukemia	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.12	Descriptive, covariate	Baseline and follow-up
Multiple myeloma	ICD-9-CM or ICD-10-CM codes listed in Annex Table 1.13	Descriptive, covariate	Baseline and follow-up
Nephrotic syndrome	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.14 Yes, No	Descriptive, covariate	Baseline and follow-up
Non-Hodgkin's lymphoma	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.15	Descriptive, covariate	Baseline and follow-up
Organ transplant	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.16	Descriptive, covariate	Baseline and follow-up
Sickle cell disease or other hemoglobinopathies	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.17 Yes, No	Descriptive, covariate	Baseline and follow-up
Hepatitis B	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 2.1 Yes, No	Descriptive, covariate	Baseline and follow-up
Hepatitis C	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 2.2 Yes, No	Descriptive, covariate	Baseline and follow-up
Cigarette smoking	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 1.7 Yes, No	Descriptive, covariate	Baseline and follow-up
Annual physical exam	CPT/HCPCS codes listed in Protocol Annex Table 3.1 Yes, No	Descriptive, covariate	Baseline and follow-up
Annual influenza vaccine	CPT/HCPCS, ICD-10-PCS, ICD-9-PCS, or NDC codes listed in Appendix Table 7.8 Yes, No	Descriptive, covariate	Baseline and follow-up
Any pneumonia infection	ICD-9-CM or ICD-10-CM codes listed in Appendix Table 7.4 Yes, No	Descriptive, covariate	Baseline
Any hospitalization	Evidence of inpatient claim(s) Yes, No	Descriptive, covariate	Baseline and follow-up
Hodgkin's lymphoma	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex 1.11 Yes, No	Descriptive, covariate	Baseline and follow-up
Opportunistic infections	ICD-9-CM or ICD-10-CM codes listed in Protocol Annex Table 14	Descriptive, covariate	Baseline and follow-up

	Yes, No Note: In the analysis of all-cause pneumonia, pneumocystis jirovecii pneumonia codes are excluded from the follow-up. In the analysis of candidiasis negative control outcomes, candidiasis infection codes are excluded from the follow-up.		
Antiretroviral treatment (ART) adherence	ART use will be identified by NDC codes listed in Appendix Table 7.2 Adherence will be measured as 'Proportion of days covered = (Number of days covered by any ART, excluding ritonavir and cobicistat) ÷ (total days)*100'[8] every six months Individuals with >80% of days covered will be classified as 'adherent' and individuals with ≤80% of days covered will be classified as 'non-adherent'[8]. Individuals without ART information will be classified as Missing. As a subgroup, ART adherence will calculated using the information over the entire follow-up.	Descriptive, covariate, subgroup	Baseline and follow-up
CD4 cell count	Categorized as <200, 200-499, ≥500 cells/mm^3	Descriptive, subgroup	Baseline and follow-up
PPSV23 vaccination	NDC and CPT codes listed in Appendix Table 7.9 Yes, No. 0, 1, 2+ doses	Descriptive, subgroup	Before first HIV diagnosis, baseline and follow-up
Annual CD4 laboratory test	CD4 laboratory tests will be identified by CPT codes listed in Appendix Table 7.11 Individuals who have at least one CD4 laboratory test performed during each year of follow-up Yes, No	Covariate	Baseline and follow-up
Annual viral load laboratory test	Viral load laboratory tests will be identified by CPT codes listed in Appendix Table 7.12 Individuals who have at least one viral load laboratory test performed during each year of follow-up Yes, No	Covariate	Baseline and follow-up

Respiratory virus season	Respiratory virus season occurs between October 1 and April 30 Yes, No	Covariate	Follow-up

5.3.3. Negative Controls

Table 5.4 List of Negative Control Variables

Variable	Operational Definition	Role	Time of Use
Recombinant zoster vaccine (RZV; Shingrix, GlaxoSmithKline)	NDC and CPT codes listed in Appendix Table 7.10	Negative control exposure	Follow-up
May include, but not limited to, candidiasis infection, all-cause diarrhea and accidental injury	ICD-9-CM and ICD-10-CM codes listed in Protocol Annex Table 4.1 Candidiasis infection: evidence of an antifungal treatment within 7 days of outpatient candidiasis ICD-9-CM or ICD-10-CM codes will be explored. NDC and CPT codes listed in Appendix Table 7.13	Negative control outcomes	Follow-up

5.4. Data Sources

The source of data for the VE study will be health care administrative claims and HIV-laboratory data provided by Komodo Health. Komodo Health uses artificial intelligence and data analytics to combine and link patient-level information from more than 150 payers in the United States, including Medicare, Medicaid, and Commercial plans. Currently, Komodo Health has patient-level data on approximately 325 million individuals and these data include inpatient and outpatient claims, pharmacy dispensing claims, provider specialty claims, and mortality information.

Komodo Health will provide administrative claims available during January 1, 2014 through September 30, 2022 for individuals who have at least one ICD-9-CM or ICD-10-CM code related to HIV (Appendix Table 7.1) or at least one antiretroviral (ART) medication dispensed (Appendix Table 7.2).

5.5. Treatment Labels

Information on PCV13 vaccination status will continue to be collected on and after index date and will therefore be treated as a time-varying exposure. PLWH in the study will be assigned to 'PCV13 Vaccinated' or 'PCV13 Unvaccinated' according to their vaccination status by each person-time record during the follow-up. Individuals will be considered vaccinated from 14 days after their PCV13 vaccination date till the remainder of their follow-up.

National Drug Codes (NDC) and Current Procedural Terminology® (CPT) codes used to identify PCV13 receipt are listed in Appendix Table 7.3.

5.6. Sample Size and Power Calculations

The planned analyses do not involve hypothesis testing and sample size calculations are not applicable. However, we examined the precision of PCV13 vaccine effectiveness for IPD and all-cause pneumonia among people living with HIV at 36 months and 97 months (which was the maximum follow-up time available from feasibility assessments) after index. This was conducted for the 175,000 individuals expected in the overall analysis (Protocol Section 9.5) and for varying potential subgroup sizes (Section 5.2.3).

5.7. Missing Data

No imputation for missing values will be performed. Subject to patient counts (Section 5.8.3), missing or 'unknown' values will be reported and analyzed as separate categories and included in the totals.

5.8. Statistical Methodology and Analyses

5.8.1. General Considerations

Descriptive statistics will be used to summarize variables. For categorical variables, the frequency and percentage of patients in each category will be presented. Percentages will be based on the total number of relevant patients, including those with 'unknown' or missing values. For continuous variables, data will be presented as means, standard deviations, medians, 25th and 75th percentiles, minimums and maximums. Continuous variables may be additionally categorized and analyzed as categorical variables.

No statistical hypotheses are specified and there will be no correction for multiple comparisons.

Time in years between two dates will be calculated as (end date – start date) + 1, divided by 365.25, unless otherwise specified.

All data analysis will be conducted in R, version 4.1.3 or later (R Foundation for Statistical Computing, Vienna, Austria).

5.8.2. Index Date and Follow-up

The date following the last date of the baseline period will be defined as the index date. The end of the study will occur on the last date that administrative claims data will be available, September 30, 2022.

For PLWH who receive PCV13 after their index date, we will include the time between their index date and the 13 days after their PCV13 vaccination date as unvaccinated follow-up time. Any outcomes occurring during this time will be counted as events in the unvaccinated

cohort. Follow-up that occurs 14 days after PCV13 vaccination will be defined as vaccinated follow-up time.

Unvaccinated (no PCV13) PLWH will be followed from their index date until the earliest occurrence of the following: 13 days after PCV13 vaccination, death, end of health plan enrollment, or end of study period. Vaccinated PLWH will be followed from 14 days after their PCV13 vaccination date or index date if they were vaccinated during the baseline period, until the earliest occurrence of the following: death, end of health plan enrollment, or end of study period.

5.8.3. Minimum Sample Size Requirements

In order to maintain patient de-identification, outcomes, covariates and subgroups will have at least 10 patients/ events in each category for inclusion in outputs.

5.8.4. Inverse Probability of Treatment Weighting for Time-Varying Exposures

Except for patients vaccinated more than 13 days before the end of the baseline period, exposure (vaccination) status will not be fixed at start of follow-up, with patients able to receive PCV13 during follow-up. Therefore, PCV13 will be considered a time-varying exposure. The values for some clinical characteristics may also change during the study period and values during baseline may be poor proxies for covariate values at the various points during the follow-up. Therefore, some covariates will be treated as time-varying confounders (Section 5.3.2).

Inverse probability of treatment weighting (IPTW) will be generated from predicted probabilities of vaccination status (propensity scores) to create pseudo-populations where any imbalances in the potential confounders by vaccination status are reduced. For the analyses of first events, stabilized weights will be generated for each patient for the baseline period and every 30 days from index during the follow-up until the earliest of the following: outcome, death, end of health plan enrollment or end of study period. For the analyses of recurrent events, stabilized weights will be generated for each patient for the baseline period and every 30 days from index during the follow-up until the earliest of the following: death, end of health plan enrollment or end of study period. This aims to make vaccination status independent of the measured confounders at each of the follow-up timepoints [9]. The weights will be used to estimate the average treatment effect (ATE). For the analysis of RZV, stabilized weights will be generated every 90 days instead of 30, due to the expected lower numbers of patients vaccinated with RZV overall and in each interval.

The numerators for the stabilized weights will be the estimated probability of a patient's observed vaccination status at timepoint given their prior vaccination status and time-fixed covariates. The denominators will be the estimated probability of a patient's observed vaccination status at the given timepoint given their prior vaccination status, time-fixed covariates and time-varying covariates. Numerators and denominators after vaccination will be set to 1 and the cumulative product of these ratios will be calculated, therefore IPT

weights after vaccination will be constant. Time-varying covariates will be lagged, i.e., within each 30-day (or 90-day for RZV) interval the vaccination status will be the status at the end of the interval, whereas the values for the covariates will be from the end of the previous interval. Cox proportional hazards models will be used to model the associations between vaccination status and the numerators and denominators.

It is possible that censoring may be informative, with patient characteristics associated with loss to follow-up. Therefore, patients who are censored may have different risks of the study outcomes than patients who are not censored. Inverse probability of censoring weighting (IPCW) will also be generated during the follow-up using the above methods for IPTW. These weights will be multiplied by the IPT weights to produce a new set of weights [9].

Distributions of the IPT, IPC and IPT*IPC weights will be summarized by vaccination status. In the presence of extreme/outlier weights, stabilized weights may be truncated at the 1st and 99th percentiles for use in the Cox models for the outcomes. Although there is no formal definition of an extreme weight, the need for truncation will be judged based on the distributions and the potential effect on the interpretation of results [9].

Weights for first and recurrent events will be generated separately in datasets created for each study outcome; however, all weights will be derived without assessing their impact on the VE estimates. Weights will also be generated again in each of the subgroups. The weights will generated using the *ipwtm* function within the *ipw* R package [10]. Example R code is provided in Appendix 7.2.

5.8.5. Assessment of Covariate Balance

Standardized mean differences (SMD) will be calculated for the baseline period and every 30 days (or 90 days for RZV) since index for each of the covariates up to any PCV13 vaccination before and after the IPTW. Overall SMDs will be presented for each covariate before and after the IPTW (such as median and maximum values across the intervals with at least 100 patients vaccinated), as well as those at the end of each year of follow-up (at 360, 720, 1080, 1440, 1800, 2190, 2550, 2910 days). SMDs $\leq$0.1 will be considered as evidence of negligible imbalance. Variables with SMDs >0.1 after IPTW may be added to final weighted outcome models.

5.8.6. Incidence Rates

Incidence rates will be reported using first episodes only and again after including recurrent episodes of the same type. Crude incidence rates and 95% CIs will be presented as episodes per 100,000 person-years by PCV13 vaccination status for each outcome overall as well as annually and during time periods of interest (0-3, 3-5 and 5-7 years).

For incidence rates based on first episodes only, the total unvaccinated person-time will be calculated as time from index date to the earliest of the following: outcome, 13 days after their PCV13 vaccination, death, end of health plan enrolment or end of study period. The

total vaccinated person-time will be calculated as time from 14 days after their PCV13 vaccination date or index date, if they were vaccinated more than 13 days before the end of the baseline period, to the earliest of the following: outcome, death, end of health plan enrolment or end of study period.

For incidence rates including recurrent episodes of the same type (separated by at least 90 days), the total unvaccinated person-time will be calculated as time from index date to the earliest of the following: 13 days after their PCV13 vaccination, death, end of health plan enrolment or end of study period. The total vaccinated person-time will be calculated as time from 14 days after their PCV13 vaccination date or index date, if they were vaccinated more than 13 days before the end of the baseline period ,to the earliest of the following: death, end of health plan enrolment or end of study period. Person-time will exclude any time the patient is not at risk, i.e. the first 89 days after an episode. Cluster robust standard errors will be used in the calculation of 95% confidence intervals to account for multiple events per patient.

5.8.7. Vaccine Effectiveness

Crude PCV13 VE percentages will be estimated based on (1-HR) x 100, where HR is obtained from unadjusted Cox models for first episodes for each outcome. VE percentages will also be obtained from marginal structural Cox models (Cox-MSM) after applying the IPT and the IPT*IPC weights. As the numerators for the stabilized weights will include the index-fixed covariates, those covariates will also be included in the Cox-MSM for the outcomes [9]. Cluster robust standard errors will be used to account for the multiple records per patient. The proportional hazards assumption will be assessed graphically with the inspection of Schoenfeld residuals.

To explore potential changes in VE over time, HRs may also be generated during specific time periods using piecewise Cox models. The time periods will be 0-3 years (0 to 1079 days), 3-5 years (1080 to 1799 days), 5-7 years (1800 to 2549 days).

VE may also be assessed for recurrent events using the Andersen-Gill (AG) model [11]. For each outcome, subsequent events will be of the same type, e.g., in the analysis of IPD it will be assumed that a patient is only at risk for future IPD events. The VE is assumed constant across the recurrent events.

5.8.8. Assessment of Residual Confounding

Residual confounding of our VE estimates due to inadequate control for health care seeking behavior and immune status in our analyses will be explored. To do so, we will employ a negative control exposure and a negative control outcome. Potential negative control exposures include vaccinations that are recommended for PLWH but would not be expected to have any protective effect against the pneumonia outcomes of interest. We plan to use recombinant zoster vaccine (RZV) as the negative control exposure. Current US clinical guidelines recommend that PLWH be offered RZV vaccination. Therefore, we will develop a

model for our study population in which the exposure is at least one dose of RZV and the outcomes are our primary outcomes of interest. If residual confounding does not exist, RZV would not have an effect on the pneumonia outcomes. However, if the analysis demonstrates that RZV protects against these outcomes, this suggests the presence of residual confounding. Patients who have evidence of RZV during the six-month baseline period will be excluded from the negative control exposure analysis.

Similarly, potential negative control outcomes are outcomes that share the same sources of biases as the primary outcomes in our study population but are not causally-related to PCV13 vaccination. For example, immune status is an important predictor of pneumonia outcomes among PLWH, but we will be missing CD4 laboratory values for most of our study population. In order to detect potential residual confounding by lack of control for immune status, a potential negative control outcome could include a more common AIDS defining illness such as candidiasis. Again, if no residual confounding exists, PCV13 vaccination would have no effect on the occurrence of the negative control outcomes. However, if the results suggest that PCV13 vaccination prevents the negative control outcomes, residual confounding may exist.

If the negative control outcome analysis indicates residual confounding, the results of the main outcomes may be additionally reported after correcting for the bias [12].

5.8.9. Eligibility, Demographic, Clinical and Exposure Characteristics

The number and percentage of patients meeting the eligibility criteria will be reported in a subject evaluation table overall and by index calendar year.

Descriptive statistics will be used to summarize patient demographics and clinical characteristics of all PLWH using values at index date by vaccination status by the end of the baseline period. Overall SMDs will be presented before and after IPTW. SMDs at the end of each year since follow-up will also be tabulated.

Summaries of the overall follow-up time will be presented and calculated as time from index date to the earliest of death, end of health plan enrollment, or end of study period.

The number of patients who receive PCV13 by the end of the overall follow-up will be reported. Kaplan-Meier analysis will be used to summarize the percentage of persons who receive PCV13 by the end of each year of follow-up from index date. Patients will be censored at the earliest of the following: death, end of health plan enrollment, or end of study period.

The overall distributions of the IPT, IPC and IPT*IPC weights will be summarized by vaccination status. To graphically assess the IPT weights over time a plot of the distributions of the log-transformed stabilized weights may also be presented at regular (e.g. six-monthly) intervals during the follow-up.

The above analysis will be repeated by the subgroups stated in Section 5.2.3.

5.8.10. Summaries of Study Outcomes

The number of patients with each study outcome will be presented by vaccination status at the time of infection (Table 5.2). Length of follow-up by PCV13 vaccination status will be presented by summarizing person-time before and after any PCV13 vaccine. Crude incidence rates and 95% CIs will be presented PCV13 vaccination status for each outcome for first episodes and again including recurrent episodes of the same type.

The above analysis will be repeated by the subgroups stated in Section **Error! Reference source not found.**.

5.8.11. Analysis of Study Objectives

Crude HRs for PCV13 vaccination and the corresponding VE percentages will be presented together with 95% CIs for each study outcome overall and again during specific time periods (0-3, 3-5, 5-7 years). This will be done for first events and again including recurrent events. Analysis will be repeated using Cox-MSM after applying IPT and the IPT*IPC weights.

The above analysis will be repeated by the subgroups stated in Section **Error! Reference source not found.**.

5.8.12. Analysis of Negative Control Outcomes and Exposure

The number of patients with the negative control outcome(s) will be presented by PCV13 vaccination status at the time of occurrence. Crude incidence rates and 95% CIs will be presented by PCV13 status for first and recurrent (separated by at least 90 days) episodes. Unadjusted and Cox-MSM will be used to obtain crude and weighted VE estimates and 95% CIs of PCV13 on candidiasis.

The number of patients who receive at least one dose of RZV by the end of the overall follow-up will be reported. Patients will be considered vaccinated with RZV 14 days after their vaccination date. Unadjusted and Cox-MSM will be used to obtain crude and weighted VE estimates and 95% CIs of RZV on each of the study outcomes of interest. Cox-MSM will additionally adjust for the main exposure of PCV13 as a time-varying covariate. Patients who have evidence of RZV before the six-month baseline period will be excluded from the negative control exposure analysis.

Weighted 95% CIs for the VEs that exclude 0% would suggest the presence of residual confounding in the weighted models between PCV13 and the study outcomes. If so, the results for the main outcomes may be corrected for bias identified from the negative control outcome.

6. REFERENCES

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7. APPENDICES

7.1. Appendix A: Table shells

The list of planned outputs and table shells will be presented in a separate document.

7.2. Appendix B: R Example Code

7.2.1. Example Data Formats for First Event and Recurrent Events

Example dataset for time to first outcome:

ptid	tstart	tstop	pcv13	ipd	x1	x2	xt1	xt2	censor	endfu
1001	-1	0	0	0	1	0	0	0	0	87
1001	0	30	0	0	1	0	0	0	0	87
1001	30	60	1	0	1	0	1	0	0	87
1001	60	87	1	0	1	0	1	0	1	87
1002	-1	0	0	0	0	0	0	0	0	45
1002	0	30	0	0	0	0	0	1	0	45
1002	30	45	0	1	0	0	1	1	0	45

Example dataset including any subsequent outcomes:

ptid	tstart	tstop	pcv13	ipd	x1	x2	xt1	xt2	censor	endfu2
1001	-1	0	0	0	1	0	0	0	0	87
1001	0	30	0	0	1	0	0	0	0	87
1001	30	60	1	0	1	0	1	0	0	87
1001	60	87	1	0	1	0	1	0	1	87
1002	-1	0	0	0	0	0	0	0	0	106
1002	0	30	0	0	0	0	0	1	0	106
1002	30	45	0	1	0	0	1	1	0	106
1002	45	60	0	0	0	0	1	1	0	106
1002	60	84	0	1	0	0	1	1	0	106
1002	84	90	0	0	0	0	1	1	0	106
1002	90	106	0	0	0	0	1	1	0	106

Where:

- *ptid*: patient identifier
- *tstart*: first day of interval. -1 represents baseline period
- *tstop*: last day of interval
- *pcv13*: binary indicator for time-varying PCV13 vaccination status (exposure)
- *ipd*: binary indicator for IPD event (outcome)
- *x1, x2, ..., xn*: time-fixed confounders
- *xt1, xt2, ..., xtn*: time-varying confounders
- *censor*: binary indicator for censoring event

- *endfu*: last day of follow-up up to any first event
- *endfu2*: last day of follow-up

For binary variables, 1 indicates Yes, 0 indicates No. Note, all variables in dataset must be numeric for the *ipwtm* function.

7.2.2. Code for Generating IPTW and IPCW

```
library(ipw)
iptw <- ipwtm(exposure = pcv13, family = "survival",
numerator = ~ x1 + x2 + … + xn, denominator = ~ x1+ x2 + … + xn + xt1 + xt2 + … + xtn,
id = ptid, tstart = tstart, timevar = tstop, type = "first",
data = ipdfirst)
ipcw <- ipwtm(exposure = censor, family = "survival",
numerator = ~ x1 + x2 + … + xn, denominator = ~ x1+ x2 + … + xn + xt1 + xt2 + … + xtn,
          id = patient, tstart = tstart, timevar = tstop, type = "cens",
          data = ipdfirst)
iptw.stab<-iptw$ipw.weights
ipcw.stab<-ipcw$ipw.weights
ipdfirst<-cbind(ipdfirst, iptw.stab, ipcw.stab)
ipdfirst$comb.weights<- ipdfirst$ iptw.stab*ipdfirst$ ipcw.stab

#Plot of stabilized weights during follow-up in unvaccinated
ipwplot(weights = subset(ipdfirst$iptw, ipdifrst$pcv13==0),
        subset(timevar = ipdfirst$tstop, ipdifrst$pcv13==0),
        binwidth = 183, ylim = c(-1.5, 1.5), main = "Stabilized weights",
        xlab = "Years Since Index", ylab = "Logarithm of Stabilized IPTW",
xaxt = "n", yaxt = "n")
axis(side = 1, at = seq(0, 15,1),      labels = as.character(seq(0,15,1)*0.5))
axis(side = 2, at = c(-1.5, -1, -0.5, 0, 0.5, 1, 1.5),
   labels = as.character(c(-1.5, -1, -0.5, 0, 0.5, 1, 1.5)))
```

7.2.3. Code for Incidence Rates

```
#First events
ipdfirst$py <-ifelse(ipdfirst$tstart>=0,
                (ipdfirst$tstop - ipdfirst$tstart)/365.25,0)
ipdfirst$lnpy <-ifelse(ipdfirst$tstart>=0,log(ipdfirst$py),0)
#Rate in unvaccinated

fit_erate_unvac <- glm(event ~ pcv13 + offset(lnpy), family=poisson(link="log"),
            subset(ipdfirst[ipdfirst$tstart>=0, ]))
summary(fit_erate_unvac)
exp(coef(fit_erate_unvac)[1])
```

```
exp(confint(fit_erate_unvac))
#Rate in vaccinated (where pcv13 is factor)
fit_erate_vac <- glm(event ~ relevel(pcv13, ref= "1") + offset(lnpy),
    family= poisson(link="log"), subset(ipdfirst[ipdfirst$tstart>=0, ]))
summary(fit_erate_vac)
exp(coef(fit_erate_vac)[1])
exp(confint(fit_erate_vac))

#Recurrent events
library("sandwich")
library("lmtest")
#Rate in unvaccinated
fit_erate_rec_unvac <- glm(event ~ pcv13 + offset(lnpy), family=poisson(link="log"),
          subset(ipdrec[ipdrec$tstart>=0, ]))
fit_clust_rec_unvac <-coeftest(fit_erate_rec_unvac, vcov. = vcovCL(fit_erate_rec_unvac,
                              cluster = ipdrec$patid, type = "HC0"))
fit_clust_rec_unvac
exp(coef(fit_clust_rec_unvac)[1])
exp(confint(fit_clust_rec_unvac))

#Rate in vaccinated (where pcv13 is factor)
fit_erate_rec_vac <- glm(event ~ relevel(pcv13, ref= "1") + offset(lnpy),
    family=poisson(link="log"), subset(ipdrec[ipdrec$tstart>=0, ]))
fit_clust_rec_vac <-coeftest(fit_erate_rec_vac, vcov. = vcovCL(fit_erate_rec_vac,
                              cluster = ipdrec$patid, type = "HC0"))
fit_clust_rec_vac
exp(coef(fit_clust_rec_vac)[1])
exp(confint(fit_clust_rec_vac))
```

7.2.4. Code for Standardized Differences

```
library(cobalt)
smdDataY1<-subset(ipdfirst[ipdfirst$tstart==360 &
                (ipdfirst$tstart < ipdfirst$pcv13date14 | is.na(ipdfirst$ pcv13date14)),])
#Where pcv13date14 is 14 days after the PCV13 vaccination date
covs <- subset(smdDataY1, select = c(x1, x2, …))
#Before IPTW
smdsUn<-bal.tab(covs, treat = smdDataY1$pcv13,  continuous = "std",
        binary = "std", s.d.denom = "pooled")
x1SmdUn<-smdsUn$Balance[1,2]
x2SmdUn<-smdsUn$Balance[2,2]
…
#After IPTW
smdsWt<-bal.tab(covs, treat = smdDataY1$pcv13,  continuous = "std",
```

```
        binary = "std", s.d.denom = "pooled", weights=smdDataY1$iptw.stab)
x1SmdWt<-smdsWt$Balance[1,3]
x2SmdWt<-smdsWt$Balance[2,3]
...
```

7.2.5. Code for Cox Models

```
#Code is the same for first event and recurrent events (Andersen-Gill) models
#Crude overall
library(survival)
crude.cox<-coxph(Surv(tstart, tstop, ipd) ~ pcv13 + cluster(ptid), data = ipdfirst)

#IPT weighted overall
iptw.cox<-coxph(Surv(tstart, tstop, ipd) ~ pcv13 + x1 + x2 + cluster(ptid),
        data = ipdfirst),  weights = iptw.stab

# Schoenfeld residuals
plot(cox.zph(iptw.cox)[1])

#Piecewise IPT weighted
library(Publish)
ipdfirst$timestrata<-ifelse(ipdfirst$tstart<1080,"0-3",
        ifelse(ipdfirst$tstart<1800,"3-5", ifelse(ipdfirst$tstart<2550,"5-7","7+")))

iptw.cox.p<-coxph(Surv(tstart, tstop, ipd) ~ pcv13*strata(timestrata) + x1 + x2 +
        cluster(ptid), data = ipdfirst, weights = iptw.stab)
summary(iptw.cox.p)
publish(iptw.cox.p)
```

7.3. Appendix C: Diagnosis and Procedure Codes Used in the Study

Table 7.1 Diagnosis Codes for Identifying HIV Infection

Code	Type	Description
042	ICD-9-CM	HIV-1 infection
V08	ICD-9-CM	Asymptomatic HIV disease
B20	ICD-10-CM	HIV-1 infection
Z21	ICD-10-CM	Asymptomatic HIV disease

Table 7.2 National Drug Codes for Identifying HIV Antiretrovirals (see Excel)

Table 7.3 NDC and CPT Codes for Identifying PCV13 Vaccination

Code	Type	Description
50090194409	NDC	13-valent pneumococcal conjugate vaccine
54569661300	NDC	13-valent pneumococcal conjugate vaccine
50090194400	NDC	13-valent pneumococcal conjugate vaccine
00005197105	NDC	13-valent pneumococcal conjugate vaccine
00005197104	NDC	13-valent pneumococcal conjugate vaccine
00005197102	NDC	13-valent pneumococcal conjugate vaccine
00005197101	NDC	13-valent pneumococcal conjugate vaccine
90670	CPT	13-valent pneumococcal conjugate vaccine

Table 7.4 Diagnosis Codes for Identifying Invasive Pneumococcal Disease, All-Cause Pneumonia, and Pneumococcal Pneumonia

Condition	ICD-9-CM		ICD-10-CM	
	Codes	Description	Codes	Description
IPD				
Bacteremia	790.7 + 041.2 771.83 + 041.2	Bacteremia + pneumococcus	R78.81 + B95.3	Bacteremia + Streptococcus pneumoniae as the cause of diseases classified elsewhere (Streptococcus pneumoniae)
	038.2	Pneumococcal septicemia	A40.3	Sepsis due to Streptococcus pneumoniae
	038.9 + 041.2	Unspecified septicemia + pneumococcus	A41.9 + B95.3	Sepsis, unspecified organism + Streptococcus pneumoniae
Meningitis	320.1	Pneumococcal meningitis	G00.1	Pneumococcal meningitis
	320.9 + 041.2	Meningitis due to unspecified bacterium + pneumococcus	G00.9 + B95.3 G04.2 + B95.3	Bacterial meningitis, unspecified + Streptococcus pneumoniae Bacterial meningoencephalitis and meningomyelitis, not elsewhere classified + Streptococcus pneumoniae
	322.9 + 041.2	Meningitis, unspecified + pneumococcus	G03.9 + B95.3	Meningitis, unspecified + Streptococcus pneumoniae
Other	421.x + 041.2	Endocarditis + pneumococcus		
	421 + 041.2	Acute and subacute bacterial endocarditis + pneumococcus	I33.0 + B95.3	Acute and subacute infective endocarditis + Streptococcus pneumoniae
	421.1 + 041.2	Acute and subacute infective endocarditis in diseases classified elsewhere + pneumococcus	I39 + B95.3	Endocarditis and heart valve disorders in diseases classified elsewhere + Streptococcus pneumoniae

	421.9 + 041.2	Acute endocarditis, unspecified + pneumococcus	I33.9 + B95.3	Acute and subacute endocarditis, unspecified + Streptococcus pneumoniae
	711.0 + 041.2	Septic arthritis + pneumococcus	M00.00 + B95.3 M00.20 + B95.3 M00.80 + B95.3 M00.9 + B95.3 M00.10 + B95.3	Staphylococcal arthritis, unspecified joint + Streptococcus pneumoniae Other streptococcal arthritis, unspecified joint + Streptococcus pneumoniae Arthritis due to other bacteria, unspecified joint + Streptococcus pneumoniae Pyogenic arthritis, unspecified + Streptococcus pneumoniae Pneumococcal arthritis, unspecified joint + Streptococcus pneumoniae
	711.01 + 041.2	Pyogenic arthritis, shoulder region + pneumococcus	M00.011 + B95.3 M00.012 + B95.3 M00.019 + B95.3 M00.211 + B95.3 M00.212 + B95.3 M00.219 + B95.3 M00.811 + B95.3 M00.812 + B95.3 M00.819 + B95.3 M00.119 + B95.3 M00.111 + B95.3 M00.112 + B95.3	Staphylococcal arthritis, right shoulder + Streptococcus pneumoniae Staphylococcal arthritis, left shoulder + Streptococcus pneumoniae Staphylococcal arthritis, unspecified shoulder + Streptococcus pneumoniae Other streptococcal arthritis, right shoulder + Streptococcus pneumoniae Other streptococcal arthritis, left shoulder + Streptococcus pneumoniae Other streptococcal arthritis, unspecified shoulder + Streptococcus pneumoniae Arthritis due to other bacteria, right shoulder + Streptococcus pneumoniae Arthritis due to other bacteria, left shoulder + Streptococcus pneumoniae Arthritis due to other bacteria, unspecified shoulder + Streptococcus pneumoniae Pneumococcal arthritis, unspecified shoulder + Streptococcus pneumoniae Pneumococcal arthritis, right shoulder + Streptococcus pneumoniae Pneumococcal arthritis, left shoulder + Streptococcus pneumoniae
	711.02 + 041.2	Pyogenic arthritis, upper arm + pneumococcus	M00.021 + B95.3 M00.022 + B95.3 M00.029 + B95.3 M00.221 + B95.3 M00.222 + B95.3 M00.229 + B95.3 M00.821 + B95.3 M00.822 + B95.3 M00.829 + B95.3 M00.129 + B95.3 M00.121 + B95.3 M00.122 + B95.3	Staphylococcal arthritis, right elbow + Streptococcus pneumoniae Staphylococcal arthritis, left elbow + Streptococcus pneumoniae Staphylococcal arthritis, unspecified elbow + Streptococcus pneumoniae Other streptococcal arthritis, right elbow + Streptococcus pneumoniae Other streptococcal arthritis, left elbow + Streptococcus pneumoniae Other streptococcal arthritis, unspecified elbow + Streptococcus pneumoniae Arthritis due to other bacteria, right elbow + Streptococcus pneumoniae Arthritis due to other bacteria, left elbow + Streptococcus pneumoniae Arthritis due to other bacteria, unspecified elbow + Streptococcus pneumoniae Pneumococcal arthritis, unspecified elbow + Streptococcus pneumoniae Pneumococcal arthritis, right elbow + Streptococcus pneumoniae Pneumococcal arthritis, left elbow + Streptococcus pneumoniae
	711.03 + 041.2	Pyogenic arthritis, forearm + pneumococcus	M00.031 + B95.3 M00.032 + B95.3 M00.039 + B95.3 M00.231 + B95.3	Staphylococcal arthritis, right wrist + Streptococcus pneumoniae Staphylococcal arthritis, left wrist + Streptococcus pneumoniae Staphylococcal arthritis, unspecified wrist + Streptococcus pneumoniae Other streptococcal arthritis, right wrist + Streptococcus pneumoniae

			M00.232 + B95.3	Other streptococcal arthritis, left wrist + Streptococcus pneumoniae
			M00.239 + B95.3	Other streptococcal arthritis, unspecified wrist + Streptococcus pneumoniae
			M00.831 + B95.3	Arthritis due to other bacteria, right wrist + Streptococcus pneumoniae
			M00.832 + B95.3	Arthritis due to other bacteria, left wrist + Streptococcus pneumoniae
			M00.839 + B95.3	Arthritis due to other bacteria, unspecified wrist + Streptococcus pneumoniae
			M00.139 + B95.3	Pneumococcal arthritis, unspecified wrist + Streptococcus pneumoniae
			M00.131 + B95.3	Pneumococcal arthritis, right wrist + Streptococcus pneumoniae
			M00.132 + B95.3	Pneumococcal arthritis, left wrist + Streptococcus pneumoniae
	711.04 + 041.2	Pyogenic arthritis, hand + pneumococcus	M00.041 + B95.3	Staphylococcal arthritis, right hand + Streptococcus pneumoniae
			M00.042 + B95.3	Staphylococcal arthritis, left hand + Streptococcus pneumoniae
			M00.049 + B95.3	Staphylococcal arthritis, unspecified hand + Streptococcus pneumoniae
			M00.241 + B95.3	Other streptococcal arthritis, right hand + Streptococcus pneumoniae
			M00.242 + B95.3	Other streptococcal arthritis, left hand + Streptococcus pneumoniae
			M00.249 + B95.3	Other streptococcal arthritis, unspecified hand + Streptococcus pneumoniae
			M00.841 + B95.3	Arthritis due to other bacteria, right hand + Streptococcus pneumoniae
			M00.842 + B95.3	Arthritis due to other bacteria, left hand + Streptococcus pneumoniae
			M00.849 + B95.3	Arthritis due to other bacteria, unspecified hand + Streptococcus pneumoniae
			M00.149 + B95.3	Pneumococcal arthritis, unspecified hand + Streptococcus pneumoniae
			M00.141 + B95.3	Pneumococcal arthritis, right hand + Streptococcus pneumoniae
			M00.142 + B95.3	Pneumococcal arthritis, left hand + Streptococcus pneumoniae
	711.05 + 041.2	Pyogenic arthritis, pelvic region and thigh + pneumococcus	M00.051 + B95.3	Staphylococcal arthritis, right hip + Streptococcus pneumoniae
			M00.052 + B95.3	Staphylococcal arthritis, left hip + Streptococcus pneumoniae
			M00.059 + B95.3	Staphylococcal arthritis, unspecified hip + Streptococcus pneumoniae
			M00.251 + B95.3	Other streptococcal arthritis, right hip + Streptococcus pneumoniae
			M00.252 + B95.3	Other streptococcal arthritis, left hip + Streptococcus pneumoniae
			M00.259 + B95.3	Other streptococcal arthritis, unspecified hip + Streptococcus pneumoniae
			M00.851 + B95.3	Arthritis due to other bacteria, right hip + Streptococcus pneumoniae
			M00.852 + B95.3	Arthritis due to other bacteria, left hip + Streptococcus pneumoniae
			M00.859 + B95.3	Arthritis due to other bacteria, unspecified hip + Streptococcus pneumoniae
			M00.159 + B95.3	Pneumococcal arthritis, unspecified hip + Streptococcus pneumoniae
			M00.151 + B95.3	Pneumococcal arthritis, right hip + Streptococcus pneumoniae
			M00.152 + B95.3	Pneumococcal arthritis, left hip + Streptococcus pneumoniae

	711.06 + 041.2	Pyogenic arthritis, lower leg + pneumococcus	M00.061 + B95.3 M00.062 + B95.3 M00.069 + B95.3 M00.261 + B95.3 M00.262 + B95.3 M00.269 + B95.3 M00.861 + B95.3 M00.862 + B95.3 M00.869 + B95.3 M00.169 + B95.3 M00.161 + B95.3 M00.162 + B95.3	Staphylococcal arthritis, right knee + Streptococcus pneumoniae Staphylococcal arthritis, left knee + Streptococcus pneumoniae Staphylococcal arthritis, unspecified knee + Streptococcus pneumoniae Other streptococcal arthritis, right knee + Streptococcus pneumoniae Other streptococcal arthritis, left knee + Streptococcus pneumoniae Other streptococcal arthritis, unspecified knee + Streptococcus pneumoniae Arthritis due to other bacteria, right knee + Streptococcus pneumoniae Arthritis due to other bacteria, left knee + Streptococcus pneumoniae Arthritis due to other bacteria, unspecified knee + Streptococcus pneumoniae Pneumococcal arthritis, unspecified knee + Streptococcus pneumoniae Pneumococcal arthritis, right knee + Streptococcus pneumoniae Pneumococcal arthritis, left knee + Streptococcus pneumoniae
	711.07 + 041.2	Pyogenic arthritis, ankle and foot + pneumococcus	M00.071 + B95.3 M00.072 + B95.3 M00.079 + B95.3 M00.271 + B95.3 M00.272 + B95.3 M00.279 + B95.3 M00.871 + B95.3 M00.872 + B95.3 M00.879 + B95.3 M00.179 + B95.3 M00.171 + B95.3 M00.172 + B95.3	Staphylococcal arthritis, right ankle and foot + Streptococcus pneumoniae Staphylococcal arthritis, left ankle and foot + Streptococcus pneumoniae Staphylococcal arthritis, unspecified ankle and foot + Streptococcus pneumoniae Other streptococcal arthritis, right ankle and foot + Streptococcus pneumoniae Other streptococcal arthritis, left ankle and foot + Streptococcus pneumoniae Other streptococcal arthritis, unspecified ankle and foot + Streptococcus pneumoniae Arthritis due to other bacteria, right ankle and foot + Streptococcus pneumoniae Arthritis due to other bacteria, left ankle and foot + Streptococcus pneumoniae Arthritis due to other bacteria, unspecified ankle and foot + Streptococcus pneumoniae Pneumococcal arthritis, unspecified ankle and foot + Streptococcus pneumoniae Pneumococcal arthritis, right ankle and foot + Streptococcus pneumoniae Pneumococcal arthritis, left ankle and foot + Streptococcus pneumoniae
	711.08 + 041.2	Pyogenic arthritis, other specified sites + pneumococcus	M00.08 + B95.3 M00.28 + B95.3 M00.88 + B95.3 M00.9+ B95.3 M00.18 + B95.3	.Staphylococcal arthritis, vertebrae + Streptococcus pneumoniae Other streptococcal arthritis, vertebrae + Streptococcus pneumoniae Arthritis due to other bacteria, vertebrae + Streptococcus pneumoniae Pyogenic arthritis, unspecified + Streptococcus pneumoniae Pneumococcal arthritis, vertebrae + Streptococcus pneumoniae
	711.09 + 041.2	Pyogenic arthritis, multiple sites + pneumococcus	M00.09 + B95.3 M00.29 + B95.3 M00.89 + B95.3 M00.19 + B95.3	Staphylococcal polyarthritis + Streptococcus pneumoniae Other streptococcal polyarthritis + Streptococcus pneumoniae Polyarthritis due to other bacteria + Streptococcus pneumoniae Pneumococcal polyarthritis + Streptococcus pneumoniae

	730.0x + 041.2 730.2x + 041.2	Osteomyelitis + pneumococcus		
	730.00 + 041.2	Acute osteomyelitis, site unspecified + pneumococcus	M86.00 + B95.3 M86.10 + B95.3 M86.20 + B95.3	Acute hematogenous osteomyelitis, unspecified site + Streptococcus pneumoniae Other acute osteomyelitis, unspecified site + Streptococcus pneumoniae Subacute osteomyelitis, unspecified site + Streptococcus pneumoniae
	730.01 + 041.2	Acute osteomyelitis, shoulder region + pneumococcus	M86.011 + B95.3 M86.012 + B95.3 M86.019 + B95.3 M86.111 + B95.3 M86.112 + B95.3 M86.119 + B95.3 M86.211 + B95.3 M86.212 + B95.3 M86.219 + B95.3	Acute hematogenous osteomyelitis, right shoulder + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left shoulder + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified shoulder + Streptococcus pneumoniae Other acute osteomyelitis, right shoulder + Streptococcus pneumoniae Other acute osteomyelitis, left shoulder + Streptococcus pneumoniae Other acute osteomyelitis, unspecified shoulder + Streptococcus pneumoniae Subacute osteomyelitis, right shoulder + Streptococcus pneumoniae Subacute osteomyelitis, left shoulder + Streptococcus pneumoniae Subacute osteomyelitis, unspecified shoulder + Streptococcus pneumoniae
	730.02 + 041.2	Acute osteomyelitis, upper arm + pneumococcus	M86.021 + B95.3 M86.022 + B95.3 M86.029 + B95.3 M86.121 + B95.3 M86.122 + B95.3 M86.129 + B95.3 M86.221 + B95.3 M86.222 + B95.3 M86.229 + B95.3	Acute hematogenous osteomyelitis, right humerus + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left humerus + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified humerus + Streptococcus pneumoniae Other acute osteomyelitis, right humerus + Streptococcus pneumoniae Other acute osteomyelitis, left humerus + Streptococcus pneumoniae Other acute osteomyelitis, unspecified humerus + Streptococcus pneumoniae Subacute osteomyelitis, right humerus + Streptococcus pneumoniae Subacute osteomyelitis, left humerus + Streptococcus pneumoniae Subacute osteomyelitis, unspecified humerus + Streptococcus pneumoniae
	730.03 + 041.2	Acute osteomyelitis, forearm	M86.031 + B95.3 M86.032 + B95.3 M86.039 + B95.3 M86.131 + B95.3 M86.132 + B95.3 M86.139 + B95.3 M86.231 + B95.3	Acute hematogenous osteomyelitis, right radius and ulna + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left radius and ulna + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified radius and ulna + Streptococcus pneumoniae Other acute osteomyelitis, right radius and ulna + Streptococcus pneumoniae Other acute osteomyelitis, left radius and ulna + Streptococcus pneumoniae

			M86.232 + B95.3 M86.239 + B95.3	Other acute osteomyelitis, unspecified radius and ulna + Streptococcus pneumoniae Subacute osteomyelitis, right radius and ulna + Streptococcus pneumoniae Subacute osteomyelitis, left radius and ulna + Streptococcus pneumoniae Subacute osteomyelitis, unspecified radius and ulna + Streptococcus pneumoniae
	730.04 + 041.2	Acute osteomyelitis, hand + pneumococcus	M86.041 + B95.3 M86.042 + B95.3 M86.049 + B95.3 M86.141 + B95.3 M86.142 + B95.3 M86.149 + B95.3 M86.241 + B95.3 M86.242 + B95.3 M86.249 + B95.3	Acute hematogenous osteomyelitis, right hand + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left hand + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified hand + Streptococcus pneumoniae Other acute osteomyelitis, right hand + Streptococcus pneumoniae Other acute osteomyelitis, left hand + Streptococcus pneumoniae Other acute osteomyelitis, unspecified hand + Streptococcus pneumoniae Subacute osteomyelitis, right hand + Streptococcus pneumoniae Subacute osteomyelitis, left hand + Streptococcus pneumoniae Subacute osteomyelitis, unspecified hand + Streptococcus pneumoniae
	730.05 + 041.2	Acute osteomyelitis, pelvic region and thigh + pneumococcus	M86.051 + B95.3 M86.052 + B95.3 M86.059 + B95.3 M86.151 + B95.3 M86.152 + B95.3 M86.159 + B95.3 M86.251 + B95.3 M86.252 + B95.3 M86.259 + B95.3	Acute hematogenous osteomyelitis, right femur + Streptococcus pneumonia Acute hematogenous osteomyelitis, left femur + Streptococcus pneumonia Acute hematogenous osteomyelitis, unspecified femur + Streptococcus pneumonia Other acute osteomyelitis, right femur + Streptococcus pneumonia Other acute osteomyelitis, left femur + Streptococcus pneumonia Other acute osteomyelitis, unspecified femur + Streptococcus pneumonia Subacute osteomyelitis, right femur + Streptococcus pneumoniae Subacute osteomyelitis, left femur + Streptococcus pneumoniae Subacute osteomyelitis, unspecified femur + Streptococcus pneumoniae
	730.06 + 041.2	Acute osteomyelitis, lower leg + pneumococcus	M86.061 + B95.3 M86.062 + B95.3 M86.069 + B95.3 M86.161 + B95.3 M86.162 + B95.3 M86.169 + B95.3 M86.261 + B95.3 M86.262 + B95.3 M86.269 + B95.3	Acute hematogenous osteomyelitis, right tibia and fibula + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left tibia and fibula + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified tibia and fibula + Streptococcus pneumoniae Other acute osteomyelitis, right tibia and fibula + Streptococcus pneumoniae Other acute osteomyelitis, left tibia and fibula + Streptococcus pneumoniae Other acute osteomyelitis, unspecified tibia and fibula + Streptococcus pneumoniae Subacute osteomyelitis, right tibia and fibula + Streptococcus pneumoniae Subacute osteomyelitis, left tibia and fibula + Streptococcus pneumoniae Subacute osteomyelitis, unspecified tibia and fibula + Streptococcus pneumoniae

	730.07 + 041.2	Acute osteomyelitis, ankle and foot + pneumococcus	M86.071 + B95.3 M86.072 + B95.3 M86.079 + B95.3 M86.171 + B95.3 M86.172 + B95.3 M86.179 + B95.3 M86.271 + B95.3 M86.272 + B95.3 M86.279 + B95.3	Acute hematogenous osteomyelitis, right ankle and foot + Streptococcus pneumoniae Acute hematogenous osteomyelitis, left ankle and foot + Streptococcus pneumoniae Acute hematogenous osteomyelitis, unspecified ankle and foot + Streptococcus pneumoniae Other acute osteomyelitis, right ankle and foot + Streptococcus pneumoniae Other acute osteomyelitis, left ankle and foot + Streptococcus pneumoniae Other acute osteomyelitis, unspecified ankle and foot + Streptococcus pneumoniae Subacute osteomyelitis, right ankle and foot + Streptococcus pneumoniae Subacute osteomyelitis, left ankle and foot + Streptococcus pneumoniae Subacute osteomyelitis, unspecified ankle and foot + Streptococcus pneumoniae
	730.08 + 041.2	Acute osteomyelitis, other specified sites + pneumococcus	M86.08 + B95.3 M86.18 + B95.3 M86.28 + B95.3	Acute hematogenous osteomyelitis, other sites + Streptococcus pneumoniae Other acute osteomyelitis, other site + Streptococcus pneumoniae Subacute osteomyelitis, other site + Streptococcus pneumoniae
	730.09 + 041.2	Acute osteomyelitis, multiple sites + pneumococcus	M86.09 + B95.3 M86.19 + B95.3 M86.29 + B95.3	Acute hematogenous osteomyelitis, multiple sites + Streptococcus pneumoniae Other acute osteomyelitis, multiple sites + Streptococcus pneumoniae Subacute osteomyelitis, multiple sites + Streptococcus pneumoniae
	730.2 + 041.2 730.21 + 041.2 730.22 + 041.2 730.23 + 041.2 730.24 + 041.2 730.25 + 041.2 730.26 + 041.2 730.27 + 041.2 730.29 + 041.2	Unspecified osteomyelitis, site unspecified + pneumococcus Unspecified osteomyelitis, shoulder region + pneumococcus Unspecified osteomyelitis, upper arm + pneumococcus Unspecified osteomyelitis, forearm + pneumococcus Unspecified osteomyelitis, hand + pneumococcus Unspecified osteomyelitis, pelvic region and thigh + pneumococcus Unspecified osteomyelitis, lower leg + pneumococcus Unspecified osteomyelitis, ankle and foot + pneumococcus Unspecified osteomyelitis, multiple sites + pneumococcus	M86.9 + B95.3	Osteomyelitis, unspecified + Streptococcus pneumoniae

	730.28 + 041.2	Unspecified osteomyelitis, other specified sites + pneumococcus	M46.20 + B95.3 M46.21 + B95.3 M46.22 + B95.3 M46.23 + B95.3 M46.24 + B95.3 M46.25 + B95.3 M46.26 + B95.3 M46.27 + B95.3 M46.28 + B95.3	Osteomyelitis of vertebra, site unspecified + Streptococcus pneumoniae Osteomyelitis of vertebra, occipito-atlanto-axial region + Streptococcus pneumoniae Osteomyelitis of vertebra, cervical region + Streptococcus pneumoniae Osteomyelitis of vertebra, cervicothoracic region + Streptococcus pneumoniae Osteomyelitis of vertebra, thoracic region + Streptococcus pneumoniae Osteomyelitis of vertebra, thoracolumbar region + Streptococcus pneumoniae Osteomyelitis of vertebra, lumbar region + Streptococcus pneumoniae Osteomyelitis of vertebra, lumbosacral region + Streptococcus pneumoniae Osteomyelitis of vertebra, sacral and sacrococcygeal region + Streptococcus pneumoniae
Pneumonia				
All-Cause	480-486 487.0	Viral, bacterial, unspecified pneumonia		
	480	Pneumonia due to adenovirus	J12.0	Adenoviral pneumonia
	480.1	Pneumonia due to respiratory syncytial virus	J12.1	Respiratory syncytial virus pneumonia
	480.2	Pneumonia due to parainfluenza virus	J12.2	Parainfluenza virus pneumonia
	480.3	Pneumonia due to SARS-associated coronavirus	J12.81 J12.82	Pneumonia due to SARS-associated coronavirus Pneumonia due to coronavirus disease 2019
	480.8	Pneumonia due to other virus not elsewhere classified	J12.3 J12.89	Human metapneumovirus pneumonia Other viral pneumonia
	480.9	Viral pneumonia, unspecified	J12.9	Viral pneumonia, unspecified
	481	Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	J18.1 J13	Lobar pneumonia, unspecified organism Pneumonia due to Streptococcus pneumoniae

	482	Pneumonia due to Klebsiella pneumoniae	J15.0	Pneumonia due to Klebsiella pneumoniae
	482.1	Pneumonia due to Pseudomonas	J15.1	Pneumonia due to Pseudomonas
	482.2	Pneumonia due to Hemophilus influenzae [H. influenzae]	J14	Pneumonia due to Hemophilus influenzae
	482.3	Pneumonia due to Streptococcus, unspecified	J15.4	Pneumonia due to other streptococci
	482.31	Pneumonia due to Streptococcus, group A	J15.4	Pneumonia due to other streptococci
	482.32	Pneumonia due to Streptococcus, group B	J15.3	Pneumonia due to streptococcus, group B
	482.39	Pneumonia due to other Streptococcus	J15.4	Pneumonia due to other streptococci
	482.4	Pneumonia due to Staphylococcus, unspecified	J15.20	Pneumonia due to staphylococcus, unspecified
	482.41	Methicillin susceptible pneumonia due to Staphylococcus aureus	J15.211	Pneumonia due to Methicillin susceptible Staphylococcus aureus
	482.42	Methicillin resistant pneumonia due to Staphylococcus aureus	J15.212	Pneumonia due to Methicillin resistant Staphylococcus aureus
	482.49	Other Staphylococcus pneumonia	J15.29	Pneumonia due to other staphylococcus
	482.81	Pneumonia due to anaerobes	J15.8	Pneumonia due to other specified bacteria

	482.82	Pneumonia due to escherichia coli [E. coli]	J15.5	Pneumonia due to Escherichia coli
	482.83	Pneumonia due to other gram-negative bacteria	J15.6	Pneumonia due to other aerobic Gram-negative bacteria
	482.84	Pneumonia due to Legionnaires' disease	A48.1	Legionnaires' disease
	482.89	Pneumonia due to other specified bacteria	J15.8	Pneumonia due to other specified bacteria
	482.9	Bacterial pneumonia, unspecified	J15.9	Unspecified bacterial pneumonia
	483	Pneumonia due to mycoplasma pneumoniae	J15.7	Pneumonia due to Mycoplasma pneumoniae
	483.1	Pneumonia due to chlamydia	J16.0	Chlamydial pneumonia
	483.8	Pneumonia due to other specified organism	J16.8	Pneumonia due to other specified infectious organisms
	484.1	Pneumonia in cytomegalic inclusion disease	B25.0	Cytomegaloviral pneumonitis
	484.3	Pneumonia in whooping cough	A37.91 A37.01 A37.11 A37.81	Whooping cough, unspecified species with pneumonia Whooping cough due to Bordetella pertussis with pneumonia Whooping cough due to Bordetella parapertussis with pneumonia Whooping cough due to other Bordetella species with pneumonia
	484.5	Pneumonia in anthrax	A22.1	Pulmonary anthrax
	484.6	Pneumonia in aspergillosis	B44.0	Invasive pulmonary aspergillosis

	484.7	Pneumonia in other systemic mycoses	J17	Pneumonia in diseases classified elsewhere
	484.8	Pneumonia in other infectious diseases classified elsewhere	J17 B77.81	Pneumonia in diseases classified elsewhere Ascariasis pneumonia
	485	Bronchopneumonia, organism unspecified	J18.0	Bronchopneumonia, unspecified organism
	486	Pneumonia, organism unspecified	J18.8 J18.9	Other pneumonia, unspecified organism Pneumonia, unspecified organism
	487	Influenza with pneumonia	J10.00 J10.08 J11.00 J11.08 J12.9	Influenza due to other identified influenza virus with unspecified type of pneumonia Influenza due to other identified influenza virus with other specified pneumonia Influenza due to unidentified influenza virus with unspecified type of pneumonia Influenza due to unidentified influenza virus with specified pneumonia Viral pneumonia, unspecified
	510.x	Empyema		
	510	Empyema with fistula	J86.0	Pyothorax with fistula
	510.9	Empyema without mention of fistula	J86.9	Pyothorax without fistula
			J85.1	Abscess of lung with pneumonia
	136.3	Pneumocystosis	B59	Pneumocystosis
Pneumococcal	481	Pneumococcal pneumonia	J13	Pneumonia due to Streptococcus pneumoniae
	482.9 + 041.2	Bacterial pneumonia, unspecified + pneumococcus	J15.9 + B95.3	Unspecified bacterial pneumonia + Streptococcus pneumoniae
	485 + 041.2	Bronchopneumonia, organism unspecified + pneumococcus	J18.0 + B95.3	Bronchopneumonia, unspecified organism + Streptococcus pneumoniae

	486 + 041.2	Pneumonia, organism unspecified + pneumococcus	J18.8 + B95.3 J18.9 + B95.3	Other pneumonia, unspecified organism + Streptococcus pneumoniae Pneumonia, unspecified organism + Streptococcus pneumoniae
	510.x + 041.2	Empyema + pneumococcus		
	510 + 041.2	Empyema with fistula + pneumococcus	J86.0 + B95.3	Pyothorax with fistula + Streptococcus pneumoniae
	510.9 + 041.2	Empyema without mention of fistula + pneumococcus	J86.9 + B95.3	Pyothorax without fistula + Streptococcus pneumoniae

Table 7.5 Diagnosis Codes for Identifying Pneumococcal Pneumonia and Pneumonia with Unspecified Causes

Condition	ICD-9-CM		ICD-10-CM	
	Codes	Description	Codes	Description
Pneumococcal pneumonia	481	Pneumococcal pneumonia	J13	Pneumonia due to Streptococcus pneumoniae
	482.9 + 041.2	Bacterial pneumonia, unspecified + pneumococcus	J15.9 + B95.3	Unspecified bacterial pneumonia + Streptococcus pneumoniae
	485 + 041.2	Bronchopneumonia, organism unspecified + pneumococcus	J18.0 + B95.3	Bronchopneumonia, unspecified organism + Streptococcus pneumoniae
	486 + 041.2	Pneumonia, organism unspecified + pneumococcus	J18.8 + B95.3 J18.9 + B95.3	Other pneumonia, unspecified organism + Streptococcus pneumoniae Pneumonia, unspecified organism + Streptococcus pneumoniae
	510.x + 041.2	Empyema + pneumococcus		
	510 + 041.2	Empyema with fistula + pneumococcus	J86.0 + B95.3	Pyothorax with fistula + Streptococcus pneumoniae

	510.9 + 041.2	Empyema without mention of fistula + pneumococcus	J86.9 + B95.3	Pyothorax without fistula + Streptococcus pneumoniae
Pneumonia with unspecified causes	480-486 487.0	Viral, bacterial, unspecified pneumonia		
	480.9	Viral pneumonia, unspecified	J12.9	Viral pneumonia, unspecified
	482.9	Bacterial pneumonia, unspecified	J15.9	Unspecified bacterial pneumonia
	485	Bronchopneumonia, organism unspecified	J18.0	Bronchopneumonia, unspecified organism
	486	Pneumonia, organism unspecified	J18.8 J18.9	Other pneumonia, unspecified organism Pneumonia, unspecified organism

Table 7.6 Diagnosis Codes for Identifying All-Cause Pneumonia not due to HIV

Condition	ICD-9-CM		ICD-10-CM	
	Codes	Description	Codes	Description
All-Cause	480-486 487.0	Viral, bacterial, unspecified pneumonia		
	480	Pneumonia due to adenovirus	J12.0	Adenoviral pneumonia
	480.1	Pneumonia due to respiratory syncytial virus	J12.1	Respiratory syncytial virus pneumonia
	480.2	Pneumonia due to parainfluenza virus	J12.2	Parainfluenza virus pneumonia

	480.3	Pneumonia due to SARS-associated coronavirus	J12.81 J12.82	Pneumonia due to SARS-associated coronavirus Pneumonia due to coronavirus disease 2019
	480.8	Pneumonia due to other virus not elsewhere classified	J12.3 J12.89	Human metapneumovirus pneumonia Other viral pneumonia
	480.9	Viral pneumonia, unspecified	J12.9	Viral pneumonia, unspecified
	481	Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	J18.1 J13	Lobar pneumonia, unspecified organism Pneumonia due to Streptococcus pneumoniae
	482	Pneumonia due to Klebsiella pneumoniae	J15.0	Pneumonia due to Klebsiella pneumoniae
	482.1	Pneumonia due to Pseudomonas	J15.1	Pneumonia due to Pseudomonas
	482.2	Pneumonia due to Hemophilus influenzae [H. influenzae]	J14	Pneumonia due to Hemophilus influenzae
	482.3	Pneumonia due to Streptococcus, unspecified	J15.4	Pneumonia due to other streptococci
	482.31	Pneumonia due to Streptococcus, group A	J15.4	Pneumonia due to other streptococci
	482.32	Pneumonia due to Streptococcus, group B	J15.3	Pneumonia due to streptococcus, group B
	482.39	Pneumonia due to other Streptococcus	J15.4	Pneumonia due to other streptococci
	482.4	Pneumonia due to Staphylococcus, unspecified	J15.20	Pneumonia due to staphylococcus, unspecified

	482.41	Methicillin susceptible pneumonia due to Staphylococcus aureus	J15.211	Pneumonia due to Methicillin susceptible Staphylococcus aureus
	482.42	Methicillin resistant pneumonia due to Staphylococcus aureus	J15.212	Pneumonia due to Methicillin resistant Staphylococcus aureus
	482.49	Other Staphylococcus pneumonia	J15.29	Pneumonia due to other staphylococcus
	482.81	Pneumonia due to anaerobes	J15.8	Pneumonia due to other specified bacteria
	482.82	Pneumonia due to escherichia coli [E. coli]	J15.5	Pneumonia due to Escherichia coli
	482.83	Pneumonia due to other gram-negative bacteria	J15.6	Pneumonia due to other aerobic Gram-negative bacteria
	482.84	Pneumonia due to Legionnaires' disease	A48.1	Legionnaires' disease
	482.89	Pneumonia due to other specified bacteria	J15.8	Pneumonia due to other specified bacteria
	482.9	Bacterial pneumonia, unspecified	J15.9	Unspecified bacterial pneumonia
	483.1	Pneumonia due to chlamydia	J16.0	Chlamydial pneumonia
	483.8	Pneumonia due to other specified organism	J16.8	Pneumonia due to other specified infectious organisms
	484.3	Pneumonia in whooping cough	A37.91 A37.01 A37.11 A37.81	Whooping cough, unspecified species with pneumonia Whooping cough due to Bordetella pertussis with pneumonia Whooping cough due to Bordetella parapertussis with pneumonia Whooping cough due to other Bordetella species with pneumonia

	484.5	Pneumonia in anthrax	A22.1	Pulmonary anthrax
			J17	Pneumonia in diseases classified elsewhere
	484.8	Pneumonia in other infectious diseases classified elsewhere	J17 B77.81	Pneumonia in diseases classified elsewhere Ascariasis pneumonia
	485	Bronchopneumonia, organism unspecified	J18.0	Bronchopneumonia, unspecified organism
	486	Pneumonia, organism unspecified	J18.8 J18.9	Other pneumonia, unspecified organism Pneumonia, unspecified organism
	487	Influenza with pneumonia	J10.00 J10.08 J11.00 J11.08 J12.9	Influenza due to other identified influenza virus with unspecified type of pneumonia Influenza due to other identified influenza virus with other specified pneumonia Influenza due to unidentified influenza virus with unspecified type of pneumonia Influenza due to unidentified influenza virus with specified pneumonia Viral pneumonia, unspecified
	510.x	Empyema		
	510	Empyema with fistula	J86.0	Pyothorax with fistula
	510.9	Empyema without mention of fistula	J86.9	Pyothorax without fistula
			J85.1	Abscess of lung with pneumonia

Table 7.7 National Drug Codes and Procedure Codes for Identifying Immunosuppressive Medications (see Excel)

Table 7.8 National Drug Codes and Procedure Codes for Identifying Influenza Vaccinations (see Excel)

Table 7.9 National Drug Codes and CPT® Codes for Identifying PPSV23 Vaccination

Code	Type	Description
90732	CPT	Pneumovax 23
00006473900	NDC	Pneumovax 23
00006473901	NDC	Pneumovax 23
00006473950	NDC	Pneumovax 23
00006474100	NDC	Pneumovax 23
00006483701	NDC	Pneumovax 23
00006483702	NDC	Pneumovax 23
00006483703	NDC	Pneumovax 23
00006489400	NDC	Pneumovax 23
00006489400	NDC	Pneumovax 23
00006494300	NDC	Pneumovax 23
00006494301	NDC	Pneumovax 23
00247040201	NDC	Pneumovax 23
50090145200	NDC	Pneumovax 23
50090145209	NDC	Pneumovax 23
54569141200	NDC	Pneumovax 23
54569653800	NDC	Pneumovax 23
54868333901	NDC	Pneumovax 23
54868333909	NDC	Pneumovax 23
54868432000	NDC	Pneumovax 23
54868432009	NDC	Pneumovax 23
55045354202	NDC	Pneumovax 23
00005230931	NDC	Pnu-Imune 23
00005230933	NDC	Pnu-Imune 23
54868070700	NDC	Pnu-Imune 23

Table 7.10 National Drug Codes and CPT® Codes for Identifying Recombinant Zoster Vaccination

Code	Type	Description
58160082801	NDC	Shingrix
58160082803	NDC	Shingrix
50090514700	NDC	Shingrix
58160081912	NDC	Shingrix
58160082311	NDC	Shingrix

50090337200	NDC	Shingrix
90750	CPT	Zoster Vaccine Recombinant, Adjuvanted, Suspension for Intramuscular Injection

Table 7.11 CPT® Codes to Identify CD4 Laboratory Tests

Code	Type	Description
86361	CPT	Absolute CD4 count
86360	CPT	Absolute CD4 and CD8 counts with ratio

Table 7.12 CPT® Codes to identify Viral Load Laboratory Tests

Code	Type	Description
87534	CPT	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, direct probe technique
87535	CPT	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, amplified probe technique
87536	CPT	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, quantification

Table 7.13 National Drug Codes for Identifying Candidiasis Antifungals (see Excel)

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