NON-INTERVENTIONAL (NI) STUDY PROTOCOL

PASS information

Title	A Post-Authorization Safety Study of Guillain-Barré Syndrome (GBS) Following ABRYSVO™ Among Older Adults in the United States
Protocol number	C3671031
Protocol version identifier	Version 6.0
Date	15 April 2026
EU Post Authorization Study (PAS) register number	EUPAS1000000753
Active substance	ABRYSVO™ is a bivalent recombinant stabilized prefusion F protein subunit vaccine (Respiratory Syncytial Virus Vaccine). It consists of equal amounts of prefusion F antigens from the two major RSV subgroups: RSV subgroup A prefusion F (60 µg) and RSV subgroup B prefusion F (60 µg).
Medicinal product	Respiratory Syncytial Virus Bivalent Stabilized Prefusion F Subunit Vaccine (ABRYSVO™, Respiratory Syncytial Virus Vaccine)
Product reference	EU/1/23/1752/001-006 PLGB 00057/1722
Procedure number	EMEA/H/C/006027
Marketing Authorization Holder(s)	Pfizer Europe MA EEIG Boulevard de la Plaine 17 1050 Bruxelles Belgium
Joint PASS	No
Research question and objectives	Research question: What are the incidence rates of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among adults aged 60 years and older who are vaccinated with ABRYSVO as compared to expected rates of those events?

	Primary study objective: • To estimate the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO among adults 60 years of age and older *Secondary study objective:* • To assess whether adults 60 years of age and older experience an increased risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO
Country of study	United States
Author	Joanne (Juan) Wu, ScD, MS Director, Epidemiology Safety Surveillance Research Worldwide Medical and Safety Pfizer, Inc. New York, NY Mei Sheng Duh, ScD, MPH Managing Principal and Chief Epidemiologist Analysis Group, Inc. Boston, MA Marianne Cunnington, PhD, MPhil Vice President and Senior Epidemiologist Analysis Group, Inc. London, UK

Marketing Authorization Holder(s)

Marketing Authorization Holder(s)	Pfizer Europe MA EEIG Boulevard de la Plaine 17 1050 Bruxelles Belgium
MAH contact person	Ana Mali Pfizer, podruznica Ljubljana Letaliska cesta 29a 1000 Ljubljana Slovenia ana.mali@pfizer.com

1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ABRYSVO	Respiratory Syncytial Virus Vaccine
ADEM	Acute disseminated encephalomyelitis
AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
AR	Adverse reaction
ATT	Average treatment effect among treated
BMI	Body mass index
CAD	Coronary artery disease
CCI	Charlson comorbidity index
CCW	Chronic Conditions Data Warehouse
CDC	Centers for Disease Prevention and Control
CHF	Congestive heart failure
CI	Confidence interval
CMCD	Clinical and Medical Controlled Document
CMS	Centers for Medicare & Medicaid Services
CMV	Cytomegalovirus
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus Disease 19
CPT	Current Procedural Terminology
DME	Durable medical equipment
DUA	Data use agreement
EBV	Epstein-Barr virus
EC	Ethics Committee
ED	Emergency department
EMA	European Medicines Agency
ESRD	End-Stage Renal Disease
EU PAS	European Union Post-Authorization Study
FDA	Food and Drug Administration
FFS	Fee-For-Service
GBS	Guillain-Barré Syndrome

Abbreviation	Definition
GEP	Good Epidemiological Practice
GPP	Guidelines for Good Pharmacoepidemiology Practices
HBV	Hepatitis B virus
HCPCS	Healthcare Common Procedure Coding System
HCV	Hepatitis C virus
HEV	Hepatitis E virus
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HR	Hazard ratio
HSCT	Hematopoietic stem cell transplant
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
ICD-10-PCS	International Classification of Diseases, Tenth Revision, Procedure Coding System
IEA	International Epidemiological Association
IP	Inpatient
IQR	Interquartile range
IRB	Institutional Review Board
IRR	Incidence rate ratio
MBSF	Master beneficiary summary file
MenACWY	Meningococcal conjugate vaccine
MenB	Serogroup B meningococcal vaccine
mRNA-1345	Messenger Ribonucleic Acid-1345 Vaccine
MVA-BN-RSV	Modified Vaccinia Ankara-Bavarian Nordic-Respiratory Syncytial Virus Vaccine
NCT	National Clinical Trial
NDC	National Drug Codes
NI	Non-interventional
NMO	Neuromyelitis optica
ON	Optic neuritis
OP	Outpatient
PharMetrics Plus	IQVIA PharMetrics® Plus

Abbreviation	Definition
PASS	Post-authorization safety study
PCR	Polymerase chain reaction
PDE	Part D Event
PPV	Positive predictive value
preF	Prefusion F
PS	Propensity score
RENOIR	RSV vaccine Efficacy study iNOlder adults Immunized against RSV disease
ResDAC	Research Data Assistance Center
RIF	Research identifiable file
RSV	Respiratory syncytial virus
RSV F	Respiratory Syncytial Virus Fusion Nanoparticle Vaccine
SAP	Statistical analysis plan
SAS	Statistical Analysis System
SCRI	Self-controlled risk interval
SD	Standard deviation
SNF	Skilled nursing facility
Td	Tetanus and diphtheria vaccine
Tdap	Tetanus diphtheria and acellular pertussis vaccine
TM	Transverse myelitis
US	United States
VRDC	Virtual Research Data Center
VSD	Vaccine Safety Datalink
VTE	Venous thromboembolism

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

Name, Degree(s)	Job Title	Affiliation	Address
Joanne (Juan) Wu, ScD, MS	Director, Epidemiology, Safety Surveillance Research, Worldwide Medical and Safety	Pfizer, Inc.	66 Hudson Blvd E, New York, NY 10001
Mei Sheng Duh, ScD, MPH	Managing Principal and Chief Epidemiologist Department Associate, Department of Biostatistics	Analysis Group, Inc. Harvard T. H. Chan School of Public Health	111 Huntington Ave 14th Floor Boston, MA 02199 677 Huntington Ave Boston, MA 02115

4. ABSTRACT

Title: A Post-Authorization Safety Study of Guillain-Barré Syndrome (GBS) Following ABRYSVO™ Among Older Adults in the United States

Protocol Version: 6.0; Date of Protocol: 15 April 2026

Authors: Joanne Wu, ScD, Pfizer, Inc.; Mei Sheng Duh, ScD, MPH, Analysis Group, Inc.

Rationale and background:

ABRYSVO™ (Pfizer; C3671013) was approved by the FDA on 31 May 2023 for active immunization for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older. ABRYSVO is a bivalent recombinant protein subunit vaccine which consists of equal amounts of stabilized prefusion F antigens from the two major RSV subgroups: RSV A and RSV B (RSVpreF). Pfizer's pivotal Phase 3 clinical trial, RENOIR (**R**SV vaccine **E**fficacy study i**N** **O**lder adults **I**mmunized against **R**SV disease; C3671013) in adults 60 years and older reported a vaccine efficacy of 66.7% (96.66% CI: 28.8%-85.8%) in preventing RSV-associated lower respiratory tract illness with at least two signs or symptoms lasting more than one day, and 85.7% (96.66% CI: 32.0%-98.7%) in preventing RSV-associated lower respiratory tract illness with at least three signs or symptoms.[1, 2] The pivotal Phase 3 study, and additional preclinical and clinical data from the older adult development program demonstrate a highly favorable benefit-to-risk.

At the time of the original biologic license application, among all clinical studies evaluating RSVpreF among individuals ≥60 years of age, 2 cases of GBS were observed among 20,752 vaccinated participants within a 21-day risk interval.[3] The investigator determined that these two cases were possibly related to RSVpreF, with one case meeting the level 1 Brighton Definition Criteria (highest level of diagnostic certainty) and the other case deemed to be Miller Fisher syndrome (considered a variant of GBS).[3] In addition, after 8 and 14 months of follow-up, two additional cases of GBS were diagnosed, one in the RSVpreF group and one in the placebo group. The investigator assessed that these cases were not temporally related to RSVpreF, as they occurred outside of the plausible risk window. GBS is the most common type of acute polyneuropathy, a group of acquired, generally immune-mediated or infectious disorders that cause dysfunction and sometimes degeneration of nerves.[4] One case of sensory-motor axonal polyneuropathy with symptom onset 21 days after receiving RSVpreF was observed in the RENOIR study. GBS is also a type of demyelinating condition where there is damage to the protective covering surrounding the affected nerve fibers. No additional cases of immune mediated demyelinating conditions were observed in the clinical trials other than those already described.

As the pivotal Phase 3 trial in older adults was not sufficiently powered to evaluate the risk of rare adverse events, Pfizer, in collaboration with Analysis Group, herein propose to conduct a PASS to assess the risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among adults age 60 years or older in a large

heterogeneous real-world population during a study period following the availability of the ABRYSVO.

This non-interventional study is designated as a PASS and is a commitment to the EMA and post marketing requirement to the US FDA.

Research question and objectives:

Research question: What are the incidence rates of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among adults 60 years and older who are vaccinated with ABRYSVO as compared to expected rates of those events?

Primary study objective:

- To estimate the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO among adults 60 years and older

Secondary study objective:

- To assess whether adults 60 years and older experience an increased risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO

Study design:

This non-interventional PASS will assess the risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following receipt of ABRYSVO among US Medicare beneficiaries 65 years of age and older, as well as commercially insured adults aged 60-64 years, from the earliest date of vaccine availability to 31 December 2027. The following retrospective, longitudinal, observational cohort study designs will be implemented:

- The incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO will be assessed in the pre-specified post-vaccination period for each outcome (e.g., 21 days for GBS).

- In the Medicare population, an SCRI design will be used to compare the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions during the post-vaccination risk window (e.g., days 1-21 following vaccination) to the post-vaccination control window (e.g., days 43-63 following vaccination) among ABRYSVO vaccinated Medicare beneficiaries.

- In both the Medicare and commercially insured populations, an internal comparator cohort design will also be used, where the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions will be estimated among individuals who received ABRYSVO. The incidence in this cohort will be compared

to the incidence in two separate random samples of contemporaneous, index-matched older adult controls:

- Primary analysis: Individuals who were not vaccinated with any vaccine on the index date but had at least one vaccination claim in the year prior to the index date (i.e., contemporaneous unvaccinated control cohort)

- Secondary analysis: Individuals who were vaccinated with another vaccine (e.g., influenza vaccine, COVID-19 vaccine, other RSV vaccines) on the index date (e.g., +/- 30 days)

Population: The study population will be US Medicare beneficiaries 65 years of age and older, and commercially insured adults 60-64 years of age captured in the IQVIA PharMetrics® Plus (PharMetrics Plus) database, who receive ABRYSVO from the earliest date of ABRYSVO availability until 31 December 2027. Individuals will be included if they have a claim for at least one dose of ABRYSVO. For the Medicare population, individuals must have aged into Medicare and be at least 65 years of age on the date of receipt of ABRYSVO (i.e., index date). For the commercially insured older adult population, individuals must be 60-64 years of age on the index date. Contemporary unvaccinated controls will be included if they have no record of any vaccination on the index date, no record of ABRYSVO vaccination during the baseline period or on the index date, and at least one vaccination claim in the year prior to the index date. The unvaccinated controls will be assigned an index date matched to a corresponding ABRYSVO vaccinee's vaccination date and will be required to be at least 65 years of age (for Medicare) or 60-64 years of age (for commercially insured adults in PharMetrics Plus) on the matched index date. Contemporary vaccinated controls will be included if they have no record of an ABRYSVO vaccine, but have a claim for another vaccine within 30 days of a corresponding ABRYSVO vaccinee's vaccination date which will serve as the vaccinated control's index date. They will be required to be at least 65 years (for Medicare) or 60-64 years of age (for commercially insured adults in PharMetrics Plus) on the matched index date. All individuals will be required to have at least 12 months of continuous enrollment (i.e., baseline period) prior to the index date.

Variables:

- Exposure: Administration of ABRYSVO will be identified based on the following:

    - CPT code 90678, OR

    - 10 and 11-digit NDCs 0069-0207-01, 0069-0250-01, 0069-0344-01, 0069-0344-05, 0069-0344-10

Relevant codes will be reviewed and amended if new codes are added during the study.

- Outcomes: The study's primary outcome, new onset GBS, will be identified by an inpatient claim with GBS as the primary diagnosis. This will represent the date of GBS onset unless there is a claim with a GBS diagnosis in another medical setting in the 7 days prior to the inpatient claim. In that case, the earlier medical claim will represent the date of onset. To be considered a new onset case, there should be no diagnosis for GBS observed in the 12 months prior to the index date (i.e., "clean window").

  Secondary outcomes will include new onset acute polyneuropathies and other immune-mediated demyelinating conditions. Claims for outpatient (including emergency department) and/or inpatient settings will be used to identify secondary outcomes, depending on the type of event. A clean window without a claim with diagnosis of the safety event in the 12 months prior to the index date will also be required for each individual safety event risk analysis.

  Event specific risk intervals were selected based on the published literature and biological plausibility. A safety event will be counted if it can be assigned to 1) the risk interval following ABRYSVO, 2) the post-vaccination control interval (SCRI design), or 3) risk interval for the contemporary vaccinated or unvaccinated controls. The risk intervals for outcome evaluation for the contemporary vaccinated or unvaccinated control cohorts will be the same as for the individuals who received ABRYSVO.

- Key Covariates: Baseline demographic (i.e., age, sex, race/ethnicity, geographic region) and clinical characteristics (i.e., smoking, BMI, history of anaphylaxis/allergic reactions, previous anaphylaxis to vaccine component, history of hospitalizations, history of admission into nursing home/SNF, prior infections, surgery, trauma or bone marrow transplant, frailty index, CCI, selected comorbidities, and concurrent immunizations and concomitant medications) will be assessed based on available data (i.e., during 12-month baseline). The final list of baseline characteristics will be defined in the SAP based on feasibility and availability.

Data sources: The study will use the CMS CCW Medicare administrative database capturing all paid claims for FFS billable healthcare services in inpatient and outpatient settings, SNF, hospice, and home health services. The CCW Medicare database also includes claims related to DME as well as Part D claims for prescription drugs/vaccines.

The CMS's FFS Medicare database represents the largest dataset of healthcare service utilization in US adults aged 65 years and older and is well suited to study rare outcomes such as GBS. Medicare claims data contain the key data elements required for this study from routine clinical practice, including demographics, diagnoses in different healthcare service settings, vaccination information (covered under Part B and/or D), prescription drugs (for those with Part D coverage), and date of death.[5] It is also important to note that Medicare data have been used by federal health agencies to successfully monitor and evaluate the risk of GBS following other types of vaccinations.[6-8]

The study will also use the PharMetrics Plus database which offers a wide representation of employer, payer and provider health plans, and geographic zones covering all 50 states of the US. Patients in this database are generally representative of the <65-years-of-age, commercially-insured population in the US with respect to age and sex.[9, 10] The database contains information on patient demographics, plan enrollment, and adjudicated inpatient, emergency room, outpatient, and pharmacy claims. The insurance claims data can also be enhanced with mortality data.

Study size and power: All Medicare and commercially insured older adults who meet the eligibility criteria during the study period will be included. The sample size achieved will depend on the number of individuals administered ABRYSVO and identified within the Medicare and PharMetrics Plus databases during the study period. Uptake will be monitored throughout the course of the study to ensure sufficient sample size to address the study objectives.

Based on a background rate of 4.6 per 100,000 person-years for incident GBS in the Medicare population 65 years of age and older[11], and using a 21-day risk interval, a sample size of 8,846,154 individuals vaccinated with ABRYSVO is required to detect a 2-fold increase in risk with a power of 80% and an alpha level of 0.05. Given the limited age range for commercially insured adults 60-64 years, analyses for this age group will be primarily descriptive based on available sample size.

Data analysis: Analyses will be conducted separately for commercially insured adults 60-64 years and for Medicare insured adults 65 years and older. Baseline demographics and clinical characteristics for individuals administered ABRYSVO and contemporary vaccinated and unvaccinated controls will be summarized using descriptive statistics. Descriptive statistics will also be used to summarize vaccination patterns for ABRYSVO.

Incidence rates per 100,000 patient-years (and corresponding 95% CIs) will be calculated for GBS, acute polyneuropathies, and other immune-mediated acute demyelinating conditions as the total number of incident events divided by the total observation time.

Incidence rates for the primary and secondary outcomes will be compared to rates observed in the following control groups for the Medicare population 65 years and older:

- Self-controls: cases who experience safety events following vaccination using the SCRI design to compare the risk interval following vaccination to post-vaccination non-risk intervals in the same individual. Individuals must have post-index enrollment equivalent to the duration of the risk and control intervals to be included in this analysis. A conditional Poisson regression model will be used to compare the rates of safety events in the risk interval vs post-vaccination control time period. From this model we will report rate ratios and 95% CIs that will be interpreted as the relative incidence for the safety event in the risk interval compared to the control interval. PPV-adjusted estimates specific to the risk and control window will be applied as appropriate and will be reported alongside the primary results.

- Internal comparator cohorts: two random samples of contemporaneous vaccinated and unvaccinated matched controls. ATT weighting, based on propensity scores, will be used to ensure baseline comparability between the ABRYSVO vaccinated cohort and contemporary unvaccinated controls, as well as the ABRYSVO vaccinated cohort and contemporary vaccinated controls. ATT weighted Cox regression with robust standard errors to account for within-subject correlation will be conducted to compare the risk of safety events between cohorts. Hazard ratios and corresponding 95% CIs will be summarized. PPV-adjusted estimates will be reported alongside the primary results.

If an increased risk of GBS following ABRYSVO vaccination is observed from the comparative analyses described above, a risk factor analysis will be conducted via logistic regression among individuals vaccinated with ABRYSVO adjusting for baseline characteristics and coadministration of vaccines selected a priori.

Various sensitivity analyses will also be conducted, including analysis of a longer risk interval of 42 days, analysis of negative control outcomes, and quantitative bias analysis to assess possible influence of outcome misclassification. Further details and any additional sensitivity analyses that may be conducted will be described in the SAP.

For commercially insured adults 60-64 years, the incidence of outcomes of interest in the ABRYSVO vaccinated, contemporary unvaccinated and contemporary vaccinated cohorts will be reported and descriptively compared. PPV-adjusted estimates will be reported alongside the primary results. Further analytical comparisons may be considered contingent on sample size.

To obtain combined summary outcome measures across the full older adult age range (i.e., those who are 60 years and older), patient characteristics will be assessed as well as heterogeneity in the incidence rate estimates among the 60-64 year and ≥65 years age groups from the PharMetrics Plus and Medicare databases, respectively, will be assessed using a two-population test (e.g., Fisher's exact test or Z-test). If appropriate, a weighted average (e.g., by inverse variance or sample size) will be calculated across the full older adult age range. If sample size is sufficient in the 60-64 year group, a combined comparative risk estimate across datasets and age groups will also be generated using appropriate statistical methods. If significant heterogeneity is evident with respect to patient characteristics and risk estimates, these will be reported separately for each age group.

Milestones:

- Registration in the EU PAS register: EUPAS1000000753
- IRB approval: 11 October 2024
- Start of data collection: 31 August 2026
- End of data collection: 31 May 2029

- Interim report 1: 31 May 2027
- Interim report 2: 31 May 2028
- Final study report: 31 May 2030

5. AMENDMENTS AND UPDATES

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
2.0	07 February 2024	Substantial	Section 4 Abstract and Section 9.5.1 Power	The text and tables 2 and 3 were updated to reflect that the study will aim to be powered to detect relative risk of 2 for GBS.	To align with the FDA recommendation (communicated on 31 January 2024) that the study should have sufficient power to detect a relative risk of 2 for GBS.
3.0	20 February 2024	Substantial	Section 9.7.2 .4 Analysis of Risk Factors for GBS	The text has been updated to reflect that an analysis of risk factors for GBS will be conducted when an IRR or HR of greater than 2 for GBS is observed in the main comparative cohort or SCRI analyses	To align with the FDA recommendation (communicated on 15 February 2024) that the risk factor analysis should be aligned to the study power statement. The study aims to be adequately powered detect an IRR or HR of 2 for GBS. The risk factor analysis for GBS will therefore be performed if an IRR or HR >2.0 is observed.
4.0	13 August 2024	Substantial	Section 4 Abstract, Section 6 Milestones, Section 7 Rationale and Background, Section 8 Research Question and Objectives, Section 9 Research Methods	The study has been updated to reflect inclusion of adults 60-64 years (60 years and older overall) captured in IQVIA PharMetrics® Plus data. The text in the Abstract, Milestones, Rationale and Background, and Research Question and Objectives sections has been updated to reflect the inclusion of adults commercially insured adults 60-64 years from PharMetrics Plus. The text in the Research Methods section has been updated, specifically: • Section 9.1: updated text describes the inclusion of adults 60-64 years within the internal comparator cohort design	To incorporate FDA's agreement (communicated on 24 July 2024) to include IQVIA PharMetrics® Plus data to capture information on individuals 60-64 years of age who are vaccinated with ABRYSVO. To additionally align with FDA recommendation (communicated on 24 July 2024) to exclude individuals who have missing data on sex from the study population.

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
				• Section 9.2: additional text describes of the source population for 60-64 year old adults from the PharMetrics Plus database and specific inclusion/ exclusion criteria related to this age group. Missing data on sex was also added as a specific exclusion criterion across all ages. • Section 9.4: additional text describes the PharMetrics Plus database • Section 9.5: additional text describes the sample size considerations for the 60-64 year adult age group • Section 9.6: additional text describes the data management approach for PharMetrics Plus data • Section 9.7: updated text clarifies the age groups 60-64 and 65+ years will be analyzed separately. Additional text describes analyses specific to the 60-64 year old age group • Section 9.9: updated text includes strengths and limitations specific to the PharMetrics Plus data.	
5.0	11 September 2024	Substantial	Section 4 Abstract, Section 9 Research Methods	The protocol has been updated to describe the generation of combined risk estimates across the Medicare and PharMetrics Plus databases representing the full older adult population.	To incorporate FDA's request (communicated on 30 August 2024) to consider pooling data from IQVIA PharMetrics® Plus and Medicare claims to describe GBS risk

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
				The text in the Abstract describes an analysis of heterogeneity across risk estimates and statistical methods to combine risk estimates if appropriate. The text in the Research Methods section has been updated, specifically: • Section 9.1: text describing the analyses to assess heterogeneity and generate combined risk estimates across the Medicare and PharMetrics data sets if appropriate. • Section 9.7: a sub-section describing analysis of heterogeneity across risk estimates and statistical methods to combine risk estimates across datasets if appropriate. • Section 9.9: text on the potential strengths of generating combined risk estimates.	among all adults aged 60 years and above
6.0	15 April 2026	Administrative	Section 4 Abstract, Section 6 Milestones, Section 7 Rationale and Background, Section 9 Research Methods Annex 3	The protocol was updated to align with the most recent template version (CT24-WI-GL02-RF02 8.0 Non-Interventional Study Protocol Template for Secondary Data Collection Study 02-Mar-2026). Corresponding updates to formatting and language, including the title page and headers/footers, have been made to align with the updated template. In the abstract and Section 6, the EU PAS registration number, milestone dates and the	To incorporate FDA's agreement (communicated on 02 March 2026) to omit the originally planned 1st interim report, and to conduct interim analyses using monthly Medicare data refreshes for more timely readout

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
				number of interim reports to be delivered were updated. The text in the abstract background section (Section 7) was updated to describe the expanded indication of ABRYSVO beyond older adults. The text in the Data Sources, Data Management, and Data Analysis sections have been updated, specifically: • Section 9.4 Data Sources: text clarifying that monthly Medicare refreshes will be used for interim reports with shorter associated time lag for delivery of more timely data for interim analyses. Fully adjudicated Medicare data are maintained for the final analyses. • Section 9.6 Data Management: updated with a description of the data management for the monthly Medicare refreshes used in the interim analyses. Fully adjudicated Medicare data are maintained for the final analyses. • Section 9.7.2 in Data Analysis: text describing reporting of PPV-adjusted estimates alongside the primary safety results. The abstract text has been updated to reflect corresponding revisions to the analysis section related to PPV adjustment. The code list in Annex 3 was updated to include the most recently	

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
				available administrative codes for RSV vaccines.	

6. MILESTONES

Milestone	Planned Date
Registration in the EU PAS register	EUPAS1000000753
IRB approval	11 October 2024
Start of data collection	31 August 2026
End of data collection	31 May 2029
Interim report 1[1,2]	31 May 2027
Interim report 2[2, 3]	31 May 2028
Final study report[2, 4]	31 May 2030

1. Interim report 1 will include data accrued to December 2025 reflecting data from the 2023-2024 and 2024-2025 RSV season plus half of 2025-2026 RSV season.
2. Due to differences in data lags between Medicare and PharMetrics Plus databases, more current data may be available for the 60-64 year age group in interim and final reports.
3. Interim report 2 will include data accrued to December 2026 reflecting data from the 2023-2024, 2024-2025 and 2025-2026 RSV seasons plus half of 2026-2027 RSV season.
4. The final study report will include data accrued to December 2027 reflecting data from the 2023-2024, 2024-2025, 2025-2026 and 2026-2027 RSV seasons plus half of 2027-2028 RSV season.

7. RATIONALE AND BACKGROUND

RSV is a major cause of respiratory infection in both infants and older adults.[12] The CDC estimates that among adults 65 years and older in the US, RSV is responsible for approximately 60,000 – 160,000 hospitalizations, 6,000 – 13,000 deaths, and 0.9 – 1.4 million medical encounters annually.[13-19] However, the current documented disease burden of RSV is most likely underestimated due to variable RSV testing rates and surveillance, with routine testing less common in older adults than in children.[16, 20, 21] Routine testing of suspected RSV cases is essential for accurate estimation of the burden of RSV disease as RSV does not produce a distinctive clinical syndrome in adults.[20, 21] Rather, RSV manifestations can be difficult to distinguish from those associated with other respiratory viruses.[22] RSV can lead to mild cold-like symptoms in adults, but more serious presentations are possible including tracheobronchitis, other lower respiratory tract disease (e.g., pneumonia), or severe respiratory distress.[14, 22] Traditionally, detection methods such as cell culture and rapid antigen tests for RSV were cumbersome with low sensitivity.[23] The recent development and increased availability of less invasive and highly sensitive multiphasic PCR respiratory panel tests has enabled clinicians to recognize how common and serious RSV is in older adults.[23]

With increased routine PCR testing, epidemiological data have shown that the burden of RSV in older adults is similar to seasonal influenza, with comparable rates of infection and severity of illness.[20] Older adults are at higher risk of RSV illness, especially those aged 65 years and older, and have a higher risk of hospitalization and death with RSV compared with younger adults.[20, 21, 24-26] This may reflect age-related immunosenescence and a weakened immune response to pathogens, decreased strength of the respiratory muscle and diaphragm, and decreased protective mucus levels, lung compliance, and elastin.[24-26] RSV

can trigger exacerbations of underlying comorbid conditions in older adults, such as COPD and CHF.[21] RSV has also been recognized as a significant cause of severe illness across broader age groups in populations with underlying cardiopulmonary disease and among those who are immunocompromised, including HSCT recipients, patients undergoing intensive chemotherapy, and lung transplant patients.[12] RSV infection does not confer lasting immunity and re-infections occur throughout individual lifespans.[27]

RSV is therefore a disease for which a highly effective vaccine could have a large public health impact among older adults, with the potential to avert a similar number of hospitalizations as the seasonal influenza vaccine program in the same age group.[16] Up until 2023 there were no vaccines licensed for the prevention of RSV infection in older adults and treatment for this population consisted primarily of supportive care.[28, 29] However, two vaccines have recently been approved by the US FDA for the prevention of acute respiratory disease and lower respiratory tract disease caused by RSV in adults 60 years of age or older including: ABRYSVO™ (Respiratory Syncytial Virus Vaccine [Pfizer; NCT05035212]; authorized on 31 May 2023), and AREXVY™ ([GlaxoSmithKline; NCT04886596]; authorized on 03 May 2023).[30, 31] Since these initial approvals, the indicated population for ABRYSVO has expanded, with ABRYSVO™ also approved by the US FDA for use in pregnant individuals (32–36 weeks' gestation) ([Pfizer; NCT04424316]; authorized on 21 August 2023) and younger adults (aged 18–59 years) at increased risk of lower respiratory tract disease caused by RSV ([Pfizer; NCT05842967]; authorized on 22 October 2024).[32, 33] Several additional vaccines, using different technology platforms, were also investigated in Phase 3 clinical trials, including ResVax, RSV F (Novavax; NCT02608502), mRNA-1345 (Moderna; NCT05127434), and MVA-BN-RSV (Bavarian Nordic; NCT05238025), though primary endpoints were not met.[34-36]

The ABRYSVO™ vaccine is a bivalent recombinant protein subunit vaccine which consists of equal amounts of stabilized prefusion F antigens from the two major RSV subgroups: RSV A and RSV B (RSVpreF). Pfizer's pivotal Phase 3 clinical trial, RENOIR (**R**SV vaccine **E**fficacy study i**N** **O**lder adults **I**mmunized against **R**SV disease; C3671013), was initiated in September 2021 to evaluate the efficacy, immunogenicity, and safety of a single 120 µg dose of RSVpreF in adults 60 years or older.[1, 2] As of 14 July 2022, the cut-off date for the pre-planned interim analysis, 77.0% of all participants (N=34,284) had at least 6 months of follow-up post vaccination. Vaccine efficacy in preventing RSV-associated lower respiratory tract illness with at least two signs or symptoms lasting more than one day was reported to be 66.7% (96.66% CI: 28.8%-85.8%), and the vaccine efficacy in preventing RSV-associated lower respiratory tract illness with at least three signs or symptoms was reported to be 85.7% (96.66% CI: 32.0%-98.7%). Vaccine efficacy was maintained through the end of the first RSV season following administration (31 August 2021 through 14 July 2022).[2] Efficacy results from a pre-specified interim analysis met the pre-defined success criterion (lower limit of confidence interval exceeding 20%) for a decrease in the incidence of RSV-associated lower respiratory tract illness with at least two signs or symptoms, and a decrease in the incidence of RSV-associated lower respiratory tract illness with at least three signs or symptoms. Most ARs were mild to moderate in severity with resolution within the 1-2 days after vaccination. The pivotal Phase 3 study, and additional preclinical and clinical

data from the older adult development program, demonstrate a highly favorable benefit-to-risk profile.

At the time of the original biologic license application, among all clinical studies evaluating RSVpreF among individuals ≥60 years of age, 2 cases of GBS were observed among 20,752 vaccinated participants within a 21-day risk interval.[3] The investigator determined that these two cases were possibly related to RSVpreF, with one case meeting the level 1 Brighton Definition Criteria (highest level of diagnostic certainty) and the other case deemed to be Miller Fisher syndrome (considered a variant of GBS).[3] In addition, after 8 and 14 months of follow-up, two additional cases of GBS were diagnosed, one in the RSVpreF group and one in the placebo group, respectively. The investigator assessed that these cases were not temporally related to RSVpreF, as they occurred outside of the plausible risk window. GBS is an acute autoimmune polyradiculopathy with symptoms that vary from mild, transient muscle weakness to paralysis.[37] The risk of developing GBS increases with age and has been associated with viral infection.[37] Among US Medicare beneficiaries 65 years of age and older, the background rate of GBS was 4.6 per 100,000 person years.[11] GBS is the most common type of acute polyneuropathy, a group of acquired, generally immune-mediated or infectious disorders that cause dysfunction and sometimes degeneration of nerves.[4] One case of sensory-motor axonal polyneuropathy with symptom onset 21 days after receiving RSVpreF was also observed in the RENOIR study. GBS is also a type of demyelinating condition where there is damage to the protective covering surrounding the affected nerve fibers. No additional cases of immune mediated demyelinating conditions were observed in the RSVpreF clinical trials other than those already described.

As the pivotal Phase 3 trial in older adults was not sufficiently powered to evaluate the risk of rare adverse events, Pfizer in collaboration with Analysis Group herein propose a PASS to assess the risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among adults aged 60 years and older in a large heterogenous real-world population during a study period following the availability of the ABRYSVO.

This non-interventional study is designated as a PASS and is a commitment to the EMA and post marketing requirement to the US FDA .

8. RESEARCH QUESTION AND OBJECTIVES

Research question: What are the incidence rates of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among adults 60 years and older who are vaccinated with ABRYSVO as compared to expected rates of those events?

Primary study objective:

- To estimate the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO among adults 60 years and older

Secondary study objective:

- To assess whether adults 60 years and older experience an increased risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO

9. RESEARCH METHODS

9.1. Study Design

This non-interventional PASS will assess the risk of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following receipt of ABRYSVO among US Medicare beneficiaries 65 years of age and older, as well as commercially insured adults 60-64 years of age, from earliest date of vaccine availability to 31 December 2027. The following retrospective, longitudinal, observational cohort study designs will be implemented:

- The incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions following administration of ABRYSVO will be assessed in the pre-specified post-vaccination period for each outcome (e.g., 21 days for GBS).

- For the Medicare population 65 years and older, an SCRI design will be used to compare the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions during the post-vaccination risk window (e.g., days 1-21 following vaccination) to the post-vaccination control window (e.g., days 43-63 following vaccination) among ABRYSVO vaccinated Medicare beneficiaries 65 years of age and older.

- For the Medicare population 65 years and older an internal comparator cohort design will also be used, where the incidence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions will be estimated among those who received ABRYSVO. The incidence among this cohort will be compared to the incidence in two random samples of contemporaneous, index date-matched controls among Medicare beneficiaries 65 years of age and older:

    - Primary analysis: Individuals who were not vaccinated with any vaccine on the index date but had at least one vaccination claim in the year prior to the index date (i.e., contemporaneous unvaccinated control cohort).

    - Secondary analysis: Individuals who were vaccinated with another vaccine (e.g., influenza vaccine, COVID-19 vaccine, other RSV vaccines or other pre-specified vaccine) on the index date (e.g., +/- 30 days).

This will provide additional context for the interpretation of any potential observed excess risk as the controls will reflect the background rate of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions among vaccinated and unvaccinated individuals in the Medicare population.

The internal comparator cohort design will also be applied to commercially insured adults 60-64 years. However, comparisons between the ABRYSVO vaccinated and control cohorts will be primarily descriptive, contingent on sample size.

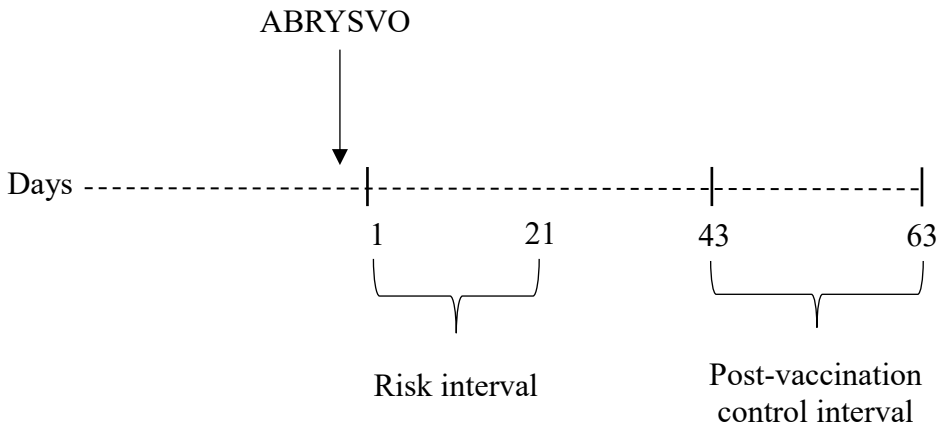
The potential to combine risk estimates from the Medicare and PharMetrics databases will be assessed based on an assessment of heterogeneity in the risk estimates across the two databases. Should combining results across the datasets be deemed appropriate, analyses may be conducted to generate combined incidence and effect estimates (see Section 9.7.2.4).

9.1.1. SCRI Design with Post-Vaccination Control Interval

The SCRI design uses data from cases (i.e., individuals who experience a safety event following vaccination) to compare the incidence in the risk interval following vaccination to the incidence in a post-vaccination non-risk interval ("post-vaccination control interval") in the same individual.[38, 39] A length of 21 days has been previously used to define the post vaccination risk interval for GBS in SCRI studies.[40, 41] Only ABRYSVO vaccinated individuals enrolled for at least the full duration of the post-vaccination risk interval and post-vaccination control interval, and who experience an outcome of interest within the risk or control interval will contribute to the SCRI analysis. For example, for the primary GBS analysis, ABRYSVO vaccinated individuals who have 63 days post index enrollment (e.g., days 1-21 for the risk interval and days 43-63 for the control interval) and who experienced GBS during the risk or control interval will be included. To address potential uncertainties around the risk interval for an outcome, a wash out period will be introduced between the end of the risk interval and start of the control interval (e.g., days 22-42). As the SCRI design is a within-person analysis, it implicitly controls for time fixed confounders. Time varying confounders still need to be controlled for, but with short, defined risk windows the risk of time varying confounding is limited.

The SCRI design with a post-vaccination control interval is presented in Figure 1 below.

Figure 1. Example of SCRI design for assessment of a safety event with a 21-day risk interval in an individual who receives ABRYSVO, with post-vaccination control interval*



* The length of the risk interval may vary across each safety event and may be subject to change based on clinical input. Day 0 is defined as the day of vaccination.

9.1.2. Internal Comparator Cohort Design (Contemporary Control Design)

Multivariable adjusted analyses (where appropriate) will also be performed comparing the incidence of safety events in individuals who received ABRYSVO to the incidence in individuals 1) who were not vaccinated with any vaccine on the index date but had at least one vaccination claim in the year prior to the index date and 2) who received another vaccine (e.g., influenza vaccine, COVID-19 vaccine, other vaccines listed in Section 9.3.3) on the index date (+/- 30 days) [i.e., contemporary vaccinated controls).

The unvaccinated controls will be assigned an index date matched to a corresponding ABRYSVO vaccinee's vaccination date. Unvaccinated controls cannot be vaccinated with any vaccine on the index date. Individuals in the unvaccinated cohort who go on to receive ABRYSVO following their index date will be censored at the time of ABRYSVO vaccination and may contribute to the ABRYSVO cohort if all eligibility criteria are met. To address possible selection bias due to health seeking behaviors, the unvaccinated controls will be randomly selected from a population of patients who have regular use of preventive medical care, defined as at least one vaccination claim in the 12 months prior to the index date.

The index date for the contemporary unvaccinated controls will be selected based on the observed index dates in the vaccinated cohort. If vaccination is associated with a regular healthcare encounter, the contemporary unvaccinated control will be required to have an encounter within 30 days of the assigned index date, and the date of encounter will be set as the index date to ensure comparability of covariate measurement.

The vaccinated controls' index date will be defined as the date on which the individual received another vaccine that is within 30 days of a corresponding ABRYSVO vaccinee's vaccination date. Individuals in this cohort who go on to receive ABRYSVO following their index date will be censored at the time of ABRYSVO vaccination and may contribute to the ABRYSVO cohort if all eligibility criteria are met.

The ABRYSVO exposed and control cohorts will be followed for up to 21 days post-index to assess the occurrence of GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions. Individuals will be followed from index until the earliest of a safety event, the end of follow up (21 days post index), receipt of an ABRYSVO vaccine (unvaccinated and vaccinated control cohorts), disenrollment from Medicare or a commercial insurance plan, or death.

9.2. Setting

The study population will be adults 60 years of age and older who receive the ABRYSVO vaccine, and index-matched vaccinated and unvaccinated controls, between the earliest date of ABRYSVO vaccine availability and 31 December 2027.

9.2.1. Medicare

The CMS is the US federal agency responsible for oversight and management of the Medicare program. Medicare is a federal health insurance program, funded by the US government, to subsidize healthcare services for individuals 65 years of age and older, or individuals with an additional qualifying condition other than age. The following individuals are eligible for Medicare[42]:

- People who are 65 years of age and older
- People who are under the age of 65 with certain disabilities
- People of all ages with ESRD (permanent kidney failure requiring dialysis or a transplant)

The vast majority (86.2%) of Medicare beneficiaries are 65 years of age and older.[43] In 2021, approximately 62% of the 63 million individuals enrolled in Medicare were enrolled in FFS coverage as opposed to a Medicare Advantage plan (i.e., Part C described below).[43, 44] Among those enrolled in Medicare FFS, 23.9 million were enrolled in Part D which covers prescriptions and some vaccinations.[45]

Individuals who are enrolled in Medicare receive benefits from up to four different 'parts' of Medicare insurance. These are referred to as Parts A, B, C, and D. Medicare Part C (also known as Medicare Advantage) is supplemental coverage, provided by non-CMS entities. As such, services provided under Part C are not available in the FFS claims database for US

Medicare beneficiaries. Beneficiaries of Medicare FFS with Part D coverage are the source population for this study. Data from Parts A, B, and D are further described below.

- **Part A** (Hospital Insurance): covers inpatient hospital stays, skilled nursing facility care (excluding custodial or long-term care), hospice care, and some home health care[46]
- **Part B** (Medical Insurance): covers two types of services: medically necessary services and preventative services. Medically necessary services include services and supplies that are needed to diagnose and treat medical conditions (e.g., certain doctors' services, outpatient care, medical supplies). Preventative services include health care to prevent illness and conduct early-stage detection (e.g., influenza vaccination, mammograms)[46]
- **Part D** (prescription drug coverage): helps to cover the cost of prescription drugs (including many recommended vaccines). Medicare Part D is a voluntary outpatient prescription benefit for individuals enrolled in Medicare[47]

Medicare Parts A, B, and D provide information on ABRYSVO exposure, while Parts A and B provide information on the outcomes of interest.

9.2.2. PharMetrics Plus

PharMetrics Plus database is a health plan claims database comprised of fully adjudicated medical and pharmacy claims for more than 215 million unique enrollees (since 2006), of which over 160 million are covered by health plans with both medical and pharmacy benefits. Data contributors are largely commercial health plans, and the database is representative of the commercially insured US national population for patients under 65 years of age. [9, 10]

The database offers a diverse representation of employer, payer and provider health plans, and geographic zones covering all 50 states in the United States. Roughly 95% of the overall sample consists of commercially insured patients, 2% have Medicare Advantage, and 3% have other types of insurance (e.g., Managed Medicaid).

Variables in the database include claims for inpatient and outpatient diagnoses and procedures, and prescriptions. In addition, information on patients' pharmacy and medical benefits (copayment, deductible), inpatient stays, and provider details are available. Additional data elements encompass dates of service, demographic variables, plan type, payer type, and start and stop dates of health plan enrollment. PharMetrics Plus can also be supplemented with mortality data.

9.2.3. Inclusion Criteria

Three cohorts will be defined for the main analyses.

A. A cohort of individuals who received ABRYSVO will form the ABRYSVO cohort and must have:

   - A claim for at least one dose of ABRYSVO in the study period from earliest date of vaccine availability to 31 December 2027
   - No record of an RSV vaccine from a manufacturer other than Pfizer

B. A cohort of individuals who did not receive ABRYSVO or another vaccine will form the contemporary unvaccinated control cohort and must have:

   - No claim for any vaccine on the index date
     - This cohort will be assigned an index date matched to a corresponding ABRYSVO vaccinee's vaccination date. If the vaccination is associated with a healthcare encounter (i.e., inpatient or outpatient visit), the unvaccinated control will be required to have a healthcare encounter within 30 days of the assigned index date, and the date of the healthcare encounter will be set as the index date for the unvaccinated control. If the ABRYSVO vaccinee's index date (i.e., vaccination) is not associated with a healthcare encounter and there is a pharmacy claim for the vaccination, then the unvaccinated individual will be assigned a random index date that matches the ABRYSVO vaccinee's vaccination date, where the unvaccinated individual does not need to have a health encounter near/on the specific index date
   - No claim for an ABRYSVO vaccine on the index date or in the baseline period (i.e., 12 months prior to the index date)
     - Individuals in the unvaccinated cohort who go on to receive an ABRYSVO vaccine following their index date will be censored at the time of ABRYSVO vaccination. These individuals will contribute to the ABRYSVO cohort starting at the date of ABRYSVO receipt if all other eligibility criteria are met.
   - Regular use of preventive medical care, defined as at least one vaccination claim in the 12-month baseline period

C: A cohort of individuals who did not receive ABRYSVO but received another vaccine will form the contemporary vaccinated control cohort and must have:

   - A claim for another vaccine (e.g., influenza vaccine, COVID-19 vaccine, other vaccines listed in Section 9.3.3) within 30 days of the corresponding

ABRYSVO vaccinee's vaccination date, which will be used as this cohort's index date

- No claim for an ABRYSVO vaccine on the index date or in the baseline period (i.e., 12 months prior to the index date)
    - Individuals in the vaccinated control cohort who go on to receive ABRYSVO following their index date will be censored at the time of vaccination and may contribute to the ABRYSVO cohort starting from the date of ABRYSVO receipt as long as all relevant eligibility criteria are met

In addition, individuals in all cohorts must meet the following inclusion criteria to be eligible for the study.

In the Medicare population:

- At least 65 years of age on the index date and
- Medicare beneficiaries who aged into Medicare; and

  Beneficiaries who qualify due to disability differ from beneficiaries who qualify due to age in several ways, including their demographic, socioeconomic, and health status profiles. To reduce potential confounding from this specific frail Medicare population that could have a different association between vaccination and GBS, they are not included in the study population.[48]

- At least 12 months of continuous enrollment in Medicare Parts A, B and D (i.e., the baseline period) prior to date of ABRYSVO administration or matched index date for unvaccinated controls.

In the PharMetrics Plus commercially insured population:

- Between 60-64 years of age on the index date and
- At least 12 months of continuous enrollment in medical and pharmacy benefits in PharMetrics Plus (i.e., the baseline period) prior to date of ABRYSVO administration or matched index date for unvaccinated controls.

9.2.4. Exclusion Criteria

Individuals meeting any of the following criteria will be excluded from the study:

- Individuals with a claim for the outcome of interest during the baseline period will be excluded from that specific outcome analysis. For example, for the GBS analysis, those with a claim for GBS during the baseline period will be excluded.

- Individuals with missing data on sex.

9.3. Variables

9.3.1. Exposure of Interest

Administration of ABRYSVO will be identified based on the following (see Annex 3 Table A-1 for additional details):

- CPT code 90678, OR
- 10 and 11-digit NDCs 0069-0207-01, 0069-0250-01, 0069-0344-01, 0069-0344-05, 0069-0344-10

Relevant codes will be reviewed and amended if new codes are added.

9.3.2. Outcomes

The study's primary outcome, new onset GBS, will be identified by an inpatient claim with GBS as the primary diagnosis. This will represent the date of GBS onset unless there is a claim with a GBS diagnosis in another medical setting (e.g., outpatient) in the prior 7 days. In that case, the earlier claim, irrespective of healthcare setting, will represent the date of onset. This claims-based algorithm in Medicare data has previously been validated against the Brighton Collaboration Definition for GBS via chart confirmation of cases in previous vaccine safety studies among Medicare beneficiaries demonstrating a sufficiently high PPV of 71.2% – 78.6%.[7, 49] PPV-based quantitative bias sensitivity analyses will be performed to assess the potential influence of outcome misclassification on effect estimates (Section 9.7.3.3).

To be considered a new onset case, there should be no diagnosis of GBS, in any setting, observed in the 12 months prior to the index date (i.e., "clean window"). This event-free baseline period is used to define incident outcomes and individuals only enter the study cohort if the safety event did not occur during that 12-month pre-index period.

Secondary outcomes will include new onset acute polyneuropathies and other immune-mediated demyelinating conditions. Operational definitions, based on ICD-10-CM diagnosis codes, for the study outcomes are outlined in Table 1. Claims for outpatient (including emergency department) and/or inpatient settings will be used to identify secondary outcomes, depending on the type of event. The specific encounter setting considered for each safety event is summarized in Table 1. A clean window without a claim with diagnosis of the safety event in the 12 months prior to the index date will also be required for each individual risk analysis. The risk intervals for each secondary outcome are described in Table 1. These risk intervals reflect the published literature and recommendations by the CDC's VSD program and the Brighton Collaboration's SPEAC Project.[40, 41, 50-52]

Acute polyneuropathies will be a composite endpoint that includes inflammatory polyneuropathies, drug-induced polyneuropathy, and other polyneuropathies that are not associated with underlying chronic diseases (e.g., diabetic polyneuropathy). GBS is a type of

inflammatory polyneuropathy and will be excluded from the outcome definition of acute polyneuropathies. A claim with a diagnosis of an acute polyneuropathy (excluding GBS) in any setting during the 21-day risk window will be considered an event, based on the VSD surveillance program risk window definition for GBS.[40, 41] Unlike GBS, as a broader category of polyneuropathies, the diagnosis can occur in either an inpatient or outpatient setting (i.e., is not restricted to the inpatient setting).

Other immune-mediated demyelinating conditions will include ADEM, TM, ON, NMO, and other acute demyelinating diseases. Most of the secondary outcomes (ON, NMO and other de-myelinating conditions) will require a claim for a diagnosis of the corresponding event in any healthcare setting[53] within the 1-21 days following ABRYSVO administration.[40, 41, 52] However, ADEM will be defined by a claim with a diagnosis from an inpatient or emergency department setting,[53] with a post-vaccination risk interval of 5-28 days following ABRYSVO administration based on prior literature and recommendations by the Brighton Collaboration.[50] TM will be defined by a claim with a relevant diagnosis code in either the inpatient or emergency department setting,[53] with a post-vaccination risk interval of 1-21 days based on the definition by the VSD surveillance program.[40, 41, 51] Alternative risk windows (1-42 days) will be considered as a sensitivity analysis.[40, 53]

Table 1. Safety events, including outcome algorithms and risk intervals

Outcome	Operational Definition Defined by the presence of any of the following **ICD-10-CM** codes (inclusive)	Setting (IP, ED, OP)	Clean Window	Risk Interval (Days)	Post-Vaccination Control Interval (Days)
GBS[41] (primary outcome)	G61.0, Guillain-Barre syndrome A diagnosis of GBS in any setting within 7 days prior to the IP primary diagnosis will define the date of GBS event	IP, primary position	12 months	1-21	43-63
Acute polyneuropathies excluding GBS (secondary outcome)	G61, Inflammatory polyneuropathy G61.1, Serum neuropathy G61.8, Other inflammatory polyneuropathies G61.81, Chronic inflammatory demyelinating polyneuritis G61.82, Multifocal motor neuropathy G61.89, Other inflammatory polyneuropathies G61.9, Inflammatory polyneuropathy, unspecified G62, Other polyneuropathies G62.0, Drug-induced polyneuropathy G62.8, Other specified polyneuropathies G62.89, Other specified polyneuropathies G62.9, Polyneuropathy, unspecified	IP, ED, or OP	12 months	1-21	43-63
ADEM[50, 54] (secondary outcome)	G04.00, Acute disseminated encephalitis and encephalomyelitis, unspecified G04.02 Post-immunization acute disseminated encephalitis, myelitis and encephalomyelitis	IP or ED	12 months	5-28	43-66
TM[40, 41, 51] (secondary outcome)	G37.3, Acute transverse myelitis in demyelinating disease of central nervous system	IP or ED	12 months	1-21	43-63
ON (secondary outcome)	H46.00, Optic papillitis, unspecified eye H46.01, Optic papillitis, right eye H46.02, Optic papillitis, left eye H46.03, Optic papillitis, bilateral H46.10, Retrobulbar neuritis, unspecified eye H46.11, Retrobulbar neuritis, right eye H46.12, Retrobulbar neuritis, left eye H46.13, Retrobulbar neuritis, bilateral H46.3, Toxic optic neuropathy H46.8, Other optic neuritis	IP, ED, or OP	12 months	1-21	43-63

Table 1. Safety events, including outcome algorithms and risk intervals

Outcome	**Operational Definition** Defined by the presence of any of the following **ICD-10-CM** codes (inclusive)	**Setting (IP, ED, OP)**	**Clean Window**	**Risk Interval (Days)**	**Post-Vaccination Control Interval (Days)**
	H46.9, Unspecified optic neuritis				
NMO[52] (secondary outcome)	G36.0, Neuromyelitis optica [Devic]	IP, ED, or OP	12 months	1-21	43-63
Other acute demyelinating diseases (secondary outcome)	G37.1, Central demyelination of corpus callosum G37.2, Central pontine myelinolysis G37.8, Other specified demyelinating diseases of central nervous system G37.9, Demyelinating disease of central nervous system, unspecified G61.81, Chronic inflammatory demyelinating polyneuritis	IP, ED, or OP	12 months	1-21	43-63

Abbreviations: ADEM, acute disseminated encephalomyelitis; ED, emergency department; GBS, Guillain-Barré Syndrome; IP, inpatient; NMO, neuromyelitis optica; ON, optic neuritis; OP, outpatient; TM, transverse myelitis.

The risk intervals were selected based on the published literature and biological plausibility. Control intervals are given the same duration as the risk interval. A safety event will be counted if it can be assigned to 1) the risk interval following ABRYSVO, 2) the post-vaccination control interval (SCRI design), or 3) risk interval for the contemporary vaccinated or unvaccinated controls. The risk intervals for outcome evaluation for contemporary vaccinated and unvaccinated controls (i.e., individuals who did not receive ABRYSVO) will be the same as for individuals who received ABRYSVO.

Events outside these intervals will not be counted. Only the individual's first instance of a claim for a safety event following the 12-month clean window will be included; this means that if a safety event is identified, but diagnosis codes corresponding to the safety event are also observed during the clean window, the event will not be counted as a new onset event.

9.3.3. Baseline Characteristics

Data elements regarding baseline demographic and clinical characteristics will be assessed on the index date or during the 12-month baseline period prior to the date of claim for ABRYSVO or assigned index date for contemporary vaccinated and unvaccinated controls. The demographic and clinical characteristics that will be assessed may include, but are not limited to, those that are listed below. The final list of baseline characteristics will be defined in the SAP based on feasibility and availability. All diagnoses, procedures, and medications/vaccines will be identified by the ICD-10-CM diagnosis codes, ICD-10-PCS (procedure coding system) codes, CPT or HCPCS procedure codes, and generic drug names, as appropriate (Annex 3 Table A-2, Annex 3 Table A-3, and Annex 3 Table A-4; codes listed in the Annexes will be reviewed and updated in the SAP as needed).

The following demographic and clinical characteristics will be assessed:

Demographics:

- Age
- Sex
- Race/ethnicity
- Geographic region in the US

ABRYSVO characteristics:

- Month and year of vaccination
- Care setting of vaccination

Clinical characteristics:

- Smoking status
- BMI
- History of anaphylaxis/allergic reactions
- Previous anaphylaxis of vaccine component
- History of hospitalizations

- History of admission into nursing home/SNF
- Prior infections
    - Campylobacter enteritis
    - CMV
    - COVID-19
    - EBV
    - HEV
    - Influenza virus
    - RSV
    - Zika virus
- Frailty index
- CCI
- Selected comorbidities
    - Cardiovascular
        - Cardiomyopathy
        - CAD
        - CHF
        - Heart failure
        - Hypertension
        - Stroke/Transient ischemic attack
    - Hematological
        - Bleeding diathesis or condition associated with prolonged bleeding
        - Hematologic malignancy
        - Sickle cell disease
        - VTE
    - Hepatic
        - HBV
        - HCV
        - Liver disease
    - Immunological
        - Autoimmune disease including systematic lupus erythematosus and sarcoidosis
        - Immunocompromising conditions
            - Solid organ transplant
            - HSCT
            - Hematologic or solid malignancy
            - HIV/AIDS
            - Other immune deficiencies
    - Neurological
        - Dementia (i.e., Alzheimer's disease and related disorders, senile dementia)
        - Neurological disease
    - Respiratory
        - Asthma

        - Chronic bronchiectasis
        - COPD/interstitial lung disease
    - Other
        - Cancer including Hodgkin Lymphoma
        - Chronic kidney disease/dialysis
        - Diabetes mellitus
        - Down syndrome
        - Gout
        - Hyperlipidemia
        - Hypothyroidism
- Prior surgery (i.e., anesthesia or conscious sedation)
- Prior trauma*
- Prior bone marrow transplant*
- Concurrent immunizations
    - Seasonal influenza vaccine
    - COVID-19
    - RSV (other than ABRYSVO)*
    - Td and Tdap
    - Chickenpox (varicella)
    - Shingles (herpes zoster recombinant and/or live)
    - HPV
    - Pneumococcal conjugate
    - Pneumococcal polysaccharide
    - Hepatitis A
    - Hepatitis B
    - MenACWY and MenB
    - Haemophilus influenzae type b
- Concomitant medications* including, but not limited to[55]:
    - TNF-alpha antagonists
    - Immune checkpoint inhibitors
    - Immunosuppressant therapies
    - Isotretinoin
    - Suramin

* ICD-10-CM diagnosis codes, ICD-10-PCS codes, CPT, or HCPCS procedure codes or NDCs will be provided in the SAP.

9.4. Data Sources

9.4.1. Medicare

The study will use the CMS CCW Medicare administrative database with monthly data refreshes capturing all paid claims for FFS billable healthcare services in inpatient and outpatient settings, SNF, hospice, and home health services. The CCW Medicare database also includes claims related to DME as well as Part D claims for prescription drugs/vaccines.

The CMS's FFS Medicare database represents the largest dataset of healthcare service utilization in US adults 65 years of age and older and is well suited to study rare outcomes such as GBS. Medicare claims data contain the key data elements required for this study from routine clinical practice, including demographics, diagnoses in different healthcare service settings, vaccination information (covered under Part B and/or D), prescription drugs (for those with Part D coverage), and date of death.[5] It is also important to note that Medicare data have been used by federal health agencies to successfully monitor and evaluate the risk of GBS following other types of vaccinations.[6-8] The monthly data consists of a mixture of pre-adjudicated and adjudicated claims; prior research shows that the diagnosis codes rarely change (<0.5%) after adjudication.[56-58] The use of adjudicated and pre-adjudicated claims data in this study enables near real-time assessment of a potential safety signal.

Medicare FFS claims data are comprised of six different types of data files, with a unique identifier for each beneficiary, allowing linkage across all data files. Below is a summary of the different datasets:

MBSF: This dataset contains information on beneficiary enrollment for each calendar month in Medicare Parts A, B, and D. Eligibility for sample selection, including original and current enrollment reason, and baseline characteristics, specifically demographic information, will be obtained from these data files.

Inpatient Claim File: FFS claims submitted by providers for cost reimbursement for services received during hospitalizations and ED visits are included in this dataset. Up to 25 diagnosis fields, including the admission diagnosis as well as a principal diagnosis, are available on each claim.

Outpatient Claim File: FFS claims that institutional, outpatient providers submit for reimbursement are available in this dataset. These include outpatient departments, rural health clinics, renal dialysis facilities, outpatient rehabilitation facilities, comprehensive outpatient rehabilitation facilities, Federally Qualified Health Centers, and community mental health centers. Up to 25 diagnosis fields as well as CPT codes are available for each outpatient claim.

Carrier File: Carrier datasets contain FFS claims submitted by professional providers, including physicians, physician assistants, clinical social workers, and nurse practitioners. Claims from freestanding facilities (e.g., independent clinical laboratories) are also present in the Carrier files. These files contain up to 12 diagnosis fields as well as CPT codes.

SNF Claim File: This dataset contains FFS claims for paid services that are submitted by SNF institutional facility providers. Up to 25 diagnosis fields, including the admission diagnosis as well as a principal diagnosis, are available on each claim.

PDE File: All medications dispensed at outpatient pharmacies that are submitted for reimbursement are available in this dataset. The NDC variable will be used in this study to

identify all medications dispensed, and will also include some vaccinations, including ABRYSVO.

Medicare claims from each of the databases are over 99% complete by 12 months post-service date. This reduces the likelihood of missing information, and therefore the data for the final study report will be based on the Medicare data with a minimum of a one-year lag period. Historically, inpatient and outpatient Medicare claims are approximately 90% complete by 2 months post-service date. Interim reports using Medicare data will be conducted with monthly data refreshes and will therefore use data with shorter lag periods, which may be less complete than the final dataset.

This study uses Medicare data curated for research; investigators cannot access medical charts for case adjudication. Outcome identification will be limited to use of algorithms that use medical billing diagnosis codes.

9.4.2. PharMetrics Plus

The study will also use the PharMetrics Plus commercial insurance database to assess the incidence of GBS. PharMetrics Plus offers a wide representation of employer, payer and provider plans across all 50 states of the US. It contains around 40 million patients with both medical and pharmacy benefits in any given recent year, with an average length of health plan enrollment of approximately 39 months. Patients in this database are generally representative of the <65-years-of-age, commercially insured population in the US with respect to age and sex.[9, 10] Roughly 95% of the overall sample consists of commercially insured patients. The database contains information on patient demographics, plan enrollment, and adjudicated inpatient, emergency room, outpatient, and pharmacy claims. Claims are sourced from a variety of providers (e.g., laboratories, hospitals, clinics, and pharmacies). Diagnoses and procedures can be identified using ICD, HCPCS, and CPT codes.

PharMetrics Plus data are comprised of two main file types: enrollment and claims files. The enrollment files contain one record per individual enrolled in the health care plan and captures patient demographics and high-level characteristics of patients' coverage (e.g., group or individual level plan). A second enrollment file contains data at the patient-month level and captures the type of enrollment (i.e., medical and/or pharmacy benefits) as well as the product and payer type information for that month. Within the claims files, each record is classified into one of six types: facility, pharmacy, surgery, management, ancillary (for procedures or services not meeting other record types) and reconciliation (when total claim cost does not equal cost of individual claim lines). There are up to 13 total diagnosis fields provided on each claims record, one being an unconfirmed admission diagnosis. Treatments, captured via NDC or HCPCS codes, represent dispensed or administered therapies and treatments administered in the inpatient setting may be bundled and presented via revenue codes. Provider specialties are mapped to one of the standard specialties for PharMetrics Plus and there can be more than one provider specialty on a claim record. Inpatient and outpatient procedures are captured via different standard coding schemes (CPT, HCPCS, ICD-10 PCS, revenue codes) in multiple fields in the database.

Data are de-identified and compliant with the Health Insurance Portability and Accountability Act to preserve patient anonymity and confidentiality.

9.5. Study Size

All Medicare beneficiaries aged 65 years and older and commercially insured adults aged 60-64 years who meet the eligibility criteria as described in Section 9.2 will be included. The sample size achieved will depend on the number of individuals administered ABRYSVO and identified within the Medicare and PharMetrics Plus databases during the study period. Uptake in the Medicare and commercially insured populations will be monitored throughout the course of the study.

9.5.1. Power

9.5.1.1. Medicare

The primary study population will consist of Medicare beneficiaries 65 years of age and older without a prior history of GBS as assessed during a 12-month baseline period. Table 2 illustrates the estimated sample size required for the conditional Poisson regression using the SCRI design, which requires a greater sample size than the contemporary vaccinated/unvaccinated control design to detect the same IRR and thus presents a more conservative estimate. Based on an expected background rate of 4.6 per 100,000 person-years for incident GBS in the Medicare population 65 years of age and older[11], and a 21-day risk window, a sample size of 8,846,154 individuals vaccinated with ABRYSVO is needed to detect a twofold increase in risk with a power of 80% and an alpha level of 0.05.[59]

Vaccine uptake will be monitored throughout the study period and reported in interim report(s). The secondary objective's comparative analyses will only be conducted when sufficient GBS events have been observed for the analyses to be adequately powered. If a sufficient number of GBS events is not observed to detect a twofold increased risk of GBS by the end of the planned study period (Section 6 Milestones), Pfizer will discuss contingency plans (e.g., extending the study period) with the FDA and the EMA.

Table 2. Sample size calculations for the conditional Poisson regression using the SCRI design

Incidence Rate Ratio	Total number of GBS events needed	Number of events expected in control interval	Number of vaccinated individuals needed for 21-day period (N)	Number of vaccinated individuals needed for 42-day period (N)
5.0	15	3	1,153,846	566,038
4.5	17	4	1,538,462	754,717
4.0	20	4	1,538,462	754,717
3.5	23	6	2,307,692	1,132,075
3.0	29	8	3,076,923	1,509,434
2.5	41	12	4,615,385	2,264,151

Table 2. Sample size calculations for the conditional Poisson regression using the SCRI design

Incidence Rate Ratio	Total number of GBS events needed	Number of events expected in control interval	Number of vaccinated individuals needed for 21-day period (N)	Number of vaccinated individuals needed for 42-day period (N)
2.0	**69**	**23**	**8,846,154**	**4,339,623**

Table 3 illustrates the estimated sample size required for the weighted Cox regression using the internal comparator cohort design. Based on the expected background rate of 4.6 per 100,000 person-years for incident GBS in the Medicare population 65 years of age and older[11], assuming controls (vaccinated or unvaccinated) will be matched to ABRYSVO vaccinated individuals on a 2:1 ratio, a sample size of 7,547,000 individuals vaccinated with ABRYSVO is needed to detect a 2-fold increase in the IRR within a 21-day risk interval with a power of 80% and an alpha level of 0.05.

Table 3. Sample size calculations for the contemporary vaccinated/unvaccinated control design

RR	Cumulative number of GBS cases	*21-day risk interval*		*42-day risk interval*	
		Number of vaccinated individuals needed, N	Number of unvaccinated controls needed[1], N	Number of vaccinated individuals needed, N	Number of unvaccinated controls needed[1], N
5.0	19	1,037,713	2,075,425	509,067	1,018,133
4.0	21	1,232,164	2,464,327	604,458	1,208,915
4.5	24	1,509,400	3,018,800	740,461	1,480,921
3.5	28	1,932,032	3,864,064	947,790	1,895,579
3.0	34	2,641,450	5,282,900	1,295,806	2,591,612
2.5	47	4,025,067	8,050,134	1,974,561	3,949,122
2.0	**78**	**7,547,000**	**15,094,000**	**3,702,302**	**7,404,604**

Notes: Assuming 1:2 matching ratio; alternative matching ratios may be considered depending on ABRYSVO uptake.
The power calculations are based on assuming two sided α=0.05, a power of 80%, and a risk interval of 21 or 42 days. A background rate of 4.6 incident GBS events per 100,000 person years (i.e., 2.6 events per million individuals per 21-day risk period and 5.3 events per million individuals per 42-day risk period) as observed among Medicare beneficiaries 65 years of age and older was used.

In 2021, 23.9 million Medicare FFS beneficiaries were enrolled in Part D.[45] Even with moderate uptake of ABRYSVO, using Medicare claims will maximize the opportunity to meet power requirements of this study.

9.5.1.2. PharMetrics Plus

For the PharMetrics Plus analysis, the primary study population will consist of adults 60-64 years of age enrolled in healthcare plans captured in the PharMetrics Plus database without a prior history of GBS as assessed during a 12-month baseline period.

Based on medical and pharmacy claims through December 31, 2023, approximately 46,000 individuals between 60 and 64 years of age received ABRYSVO in the PharMetrics Plus database; 36,000 had one year of continuous medical and pharmacy benefits enrollment prior to ABRYSVO receipt. The PharMetrics Plus analysis will be descriptive in nature and no hypothesis testing or comparisons are planned. Uptake will be monitored throughout the course of the study to assess the precision of the estimates.

9.6. Data Management

9.6.1. Medicare

Data for this study will be stored and extracted from the Medicare CCW (previously described in Section 9.4.1) that contains information about patient demographics, vaccinations, procedures, diagnoses, and death. Individual-level patient data will reside on CCW servers only and will not be transferred to third parties (see Section 10.1 for further details).

For interim analyses, monthly Medicare data will be accessed through a third-party innovator license holder with data accessed according to the relevant CMS license agreement and the third-party's procedures. Support will be provided by the third-party license holder to resolve any quality control issues identified during the initial data cleaning procedure, including if the files received appear to be incomplete or the data values are implausible.
Events will be required to have a valid start date. Record counts will be cross-checked for validation and compared to the original data counts. Applicable medical/pharmacy plan enrollment information in the study database will be processed and checked, and all fields and sample records will be checked to ensure validity.

The final study analyses will use fully adjudicated Medicare data obtained through the ResDAC and CMS approval process. Analysis Group will access data from the secure CCW VRDC. The CCW VRDC is a virtual research environment that provides access to Medicare data. Analysis Group researchers working in the CCW VRDC will have direct access to approved data files and will be able to conduct their analysis within the CCW secure environment. The CCW VRDC satisfies all CMS privacy and security requirements.

To gain access to the CCW VRDC, a research request packet will be completed and submitted to ResDAC. The research request packet includes a DUA, RIF application, information on key personnel involved in the study, collaborating organizations, and a specifications worksheet, which collects detailed requester information and includes a Part D event justification tab. ResDAC reviews the research packet, and a final packet will be compiled after a round of edits. Following ResDAC approval, the final packet will be submitted to the CMS Privacy Board. Once approved, the data will be processed and delivered to the CCW VRDC, where it can be securely accessed by Analysis Group researchers.

9.6.2. PharMetrics Plus

Data for this study will be extracted from PharMetrics Plus database (previously described in Section 9.4.2) that contains information about patient demographics, vaccinations, procedures, diagnoses, and death. Data will be stored and maintained on a secure, encrypted, cloud-based platform at Pfizer or Analysis Group. The PharMetrics Plus data will be delivered in a de-identified format in compliance with applicable laws where it can be securely accessed by Analysis Group researchers.

9.7. Data Analysis

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a SAP, which will be dated, filed, and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

Data analyses will be conducted using SAS Enterprise Guide version 7.1 (SAS Institute Inc., Cary, NC) or R Version 3.5.3 or its latest version (R Core Team, Vienna, Austria).

Analyses will be conducted separately for commercially insured adults 60-64 years and for Medicare beneficiaries 65 years and older.

9.7.1. Baseline Characteristics

Baseline demographics and clinical characteristics for individuals administered ABRYSVO and contemporary unvaccinated controls will be summarized using descriptive statistics, consisting of the mean, SD, median, and IQR values for continuous variables and frequency distributions for categorical variables. Standardized differences will be calculated between individuals who received ABRYSVO and contemporary vaccinated controls as well as between individuals who received ABRYSVO and contemporary unvaccinated controls. Standardized differences <10% will indicate that the characteristics between recipients of ABRYSVO and the comparator cohorts are balanced.

Descriptive statistics will also be used to summarize patterns of vaccination with ABRYSVO, including calendar year and month of vaccination and care setting of vaccination (e.g., outpatient clinic, pharmacy, inpatient ward).

9.7.2. Safety Analyses

Several analyses corresponding to the SCRI and contemporary vaccinated and unvaccinated control designs will be conducted to evaluate safety events associated with ABRYSVO. Analyses will be conducted among all individuals meeting the study eligibility criteria.

9.7.2.1. Incidence Rates of Safety Events

Incidence rates per 100,000 patient-years (and corresponding 95% CIs) will be calculated for GBS, acute polyneuropathies, and other immune-mediated acute demyelinating conditions as the total number of incident events observed in the risk interval divided by the total

observation time. Incidence rates will be calculated using the cohort study design for the vaccinated, comparator vaccinated and unvaccinated cohorts.

9.7.2.2. SCRI Design using Conditional Poisson Regression for Comparison with Post-Vaccination Control Intervals

For the Medicare population 65 years and older, the SCRI design will be applied and the post-vaccination control time period will include cases (i.e., individuals vaccinated with ABRYSVO who experience safety events following vaccination) who have post index enrollment equivalent to at least the duration of the relevant risk and control intervals. The incidence of safety events occurring in the risk interval following vaccination will be compared with the incidence of safety events occurring during the post-vaccination control interval.

A conditional Poisson regression model will be used to compare the rates of safety events in the risk interval (e.g., 21 days) vs post-vaccination control time period (e.g., 43-63 days). From this model we will report IRRs and 95% CIs that will be interpretated as the relative incidence for the safety event in the risk interval compared to the control interval.

Safety estimates of GBS will be further evaluated with PPV-adjusted estimates specific to the risk and control window applied as appropriate. These estimates, along with corresponding 95% intervals, will be reported alongside the primary results. Further details are provided in Section 9.7.3.3.

9.7.2.3. Comparison with Contemporary Controls

For Medicare beneficiaries 65 years and older, analytical comparisons will be performed. ATT weighting will be used to ensure baseline comparability between the ABRYSVO vaccinated cohort and contemporary vaccinated control cohort and between the ABRYSVO vaccinated cohort and the contemporary unvaccinated control cohort. ATT weighting creates a “pseudo-population” in which the distribution of covariates is, on average, the same in each cohort.[60] Specifically, ATT weights will be calculated to allow for estimation of the average treatment effect among individuals receiving ABRYSVO.[61] This approach will be taken to ensure that inference from the analysis will be applicable to this population. Individuals receiving ABRYSVO will receive an ATT weight of one. Individuals not receiving ABRYSVO will receive an ATT weight equal to the odds of receiving ABRYSVO conditional on their demographic and clinical characteristics as of the index date, which will be calculated based on the PS. The PS is defined as an individual’s probability of receiving ABRYSVO, conditional on observed baseline covariates, and will be calculated using a logistic regression model. The logistic regression model will include the cohort variable (i.e., ABRYSVO vs. vaccinated or unvaccinated control) as the dependent variable, and the independent variables will include the baseline covariates that have standardized differences ≥10% between the two cohorts. Specifically, ATT weights will be PS/(1-PS) for individuals with no record of ABRYSVO. The distribution of weights will be examined to assess extreme values, and truncation will be considered if necessary.

Weighted Cox regression with robust standard errors to account for within-subject correlation will be conducted to compare the risk of safety events between cohorts. HRs and corresponding 95% CIs will be summarized.

For commercially insured adults 60-64 years, the incidence of outcomes of interest in the ABRYSVO vaccinated and control cohorts will be reported and descriptively compared. Further analytical comparisons may be considered contingent on sample size.

Safety estimates of GBS will be further reported with PPV-adjusted estimates and corresponding 95% intervals, alongside the primary results. Further details are provided in Section 9.7.3.3.

9.7.2.4. Combined Outcome Estimates for Adults 60 Years and Older

To obtain combined outcome measures across the full older adult age range (i.e., those who are 60 years and older), the following methods will be employed. First, baseline characteristics will be descriptively compared and heterogeneity in the incidence rate estimates among the 60-64 year and ≥65 years age groups from the PharMetrics Plus and Medicare databases, respectively, will be assessed using a two-population test (e.g., Fisher's exact test or Z-test). If appropriate, a weighted average (e.g., by inverse variance or sample size) will be calculated across the full older adult age range. In addition, if sample size is sufficient to allow comparative cohort analyses to be performed in persons 60-64 years of age from PharMetrics Plus, as well as persons aged ≥65 years from Medicare, risk estimates will be weighted (also by inverse variance or sample size) to produce a pooled estimate and the p-values corresponding to the risk estimates from the two datasets will be combined by appropriate statistical methods (e.g., Fisher's method) to test the overall null hypothesis that there is no statistically increased risk after vaccination with ABRYSVO among adults 60 years and older. If significant heterogeneity is observed with respect to patient characteristics (other than age) and risk estimates, the latter will be reported separately for each age group**.** Further details will be provided in the SAP.

9.7.2.5. Analysis of Risk Factors for GBS

If there is an IRR or HR of greater than 2 reported in either comparative analysis described above, a risk factor analysis will be conducted via logistic regression among individuals vaccinated with ABRYSVO. Specifically, up to ten baseline characteristics will be selected a priori (e.g., age, sex, race/ethnicity, co-administration of influenza vaccine, COVID-19 vaccine, or other pre-specified vaccines listed in Section 9.3.3, recent infections and surgery) and included in a multivariable logistic regression model with GBS as the outcome to determine if any of the select baseline characteristics may be risk factors associated with GBS.

Claims histories, including co-administration with other vaccines, as defined below, and patient characteristics during the 12-month baseline period will also be described to enhance understanding of the healthcare profiles of GBS cases. Co-administration will be defined as a claim for ABRYSVO and another vaccine (i.e., influenza vaccine, COVID-19 vaccine, or other pre-specified vaccines listed in Section 9.3.3) on the same day.[62, 63]

9.7.3. Sensitivity Analysis

The following sensitivity analyses will be conducted to better understand the role of potential bias primarily in the context of the comparative analyses performed within the Medicare population 65 years and older. Further details and any additional sensitivity or subgroup analyses that may be conducted will be described in the SAP.

9.7.3.1. SCRI with Alternative Risk and Control Intervals

It is possible that the safety events do not have a precise time interval from which to evaluate risk, for example if biological plausibility is unknown or the diagnostic time window is narrower or more delayed than anticipated. In these cases, misspecification of the risk (and control) intervals could result in misclassification and introduce bias, often toward the null. For instance, the assumption of a longer risk interval than is true may result in "washing out" the signal, and an erroneously short risk interval may similarly result in underestimation of effect when using post-vaccination time intervals for self-control. To address this, sensitivity analyses with a 42-day risk interval[40, 51, 53, 64] will be conducted to increase the likelihood that the safety risk for GBS, acute polyneuropathies, and other immune-mediated demyelinating conditions is accurately evaluated. Safety analyses as described in Section 9.7.2 will be conducted with this longer risk interval.

Alternative risk intervals within the context of the internal comparator cohort may also be considered (e.g., incidence with 21-day and 42-day windows) for both the Medicare population 65 years and older and the commercially insured adult population 60-64 years.

9.7.3.2. Safety Analyses of Negative Control Outcomes

A negative control outcome is defined as an outcome that shares the same potential sources of bias with the primary outcome (i.e., GBS) but cannot plausibly be related to the exposure of interest (i.e., vaccination with ABRYSVO).[65] As such, assessment of negative control outcomes is a helpful tool to detect unmeasured confounding, selection bias, and misclassification bias in epidemiological studies.[65, 66]

Risk of select negative control outcomes following vaccination with ABRYSVO will be assessed following the same methodology described in Section 9.7.2. A null association between ABRYSVO and a negative control outcome suggests any observed association between ABRYSVO and the study specific outcomes of interest (e.g., GBS) is unlikely to be due to confounding or other bias, thus providing additional support for the validity of the analysis.

The specific negative control outcome for this study will be specified in the SAP and will be based on FDA-suggested negative health seeking behavior outcomes, such as hospitalized cataracts, hemorrhoids, and appendicitis, evaluated in past vaccine studies conducted by the CDC and FDA.[67-69]

9.7.3.3. Quantitative Bias Analysis for Outcome Misclassification

Quantitative bias analysis will be conducted to account for the possible influence of outcome misclassification on estimated measures of association between ABRYSVO and GBS. The range of plausible effect estimates will be quantified based on bias parameters (e.g., PPV) from literature[7] using the methods of Lash, Fox, and Fink.[70] Probability distributions will be specified for bias parameters as applicable. Bias parameters will be repeatedly drawn from the distribution and applied to bias formulas (i.e., to calculate the "expected truth" given observed data) to estimate a distribution of bias-adjusted hazard ratios. The bias adjusted hazard ratio and a 95% simulation interval will be derived and compared to the estimate from the study to understand the impact of outcome misclassification on findings.

9.8. Quality Control

Analysis Group will access Medicare data from the secure CCW VRDC. Analysis Group researchers working in the CCW VRDC will have direct access to approved data files and be able to conduct their analysis within the CCW secure environment. In addition, Analysis Group will have direct access to approved, de-identified data files from PharMetrics Plus data. Each data content area will be subject to high level variable name/type checks and to detailed trending comparisons. As an example, the diagnostic data is subject to the following checks:

- Referenced table exists
- Diagnosis type is correctly assigned by codes defining the diagnosis
- Percentages, rates, are as expected (check ranges and for missing)
- Both inpatient and outpatient diagnosis codes are captured. Referenced variables exist and are of appropriate length and type

Data retrieval will be coordinated by an experienced programmer/analyst. The analyst will write programming for retrieval of each data element from the electronic databases. Double programming will be performed for the first iteration of the analyses; results/datasets will be compared, and if any discrepancies are identified, both programmers will determine a resolution, bringing in a third programmer if needed. Subsequent iterations of analyses (i.e., re-runs of the analyses) will be audited by a senior programmer. All tables will be reviewed by the project manager and the principal investigator to evaluate internal consistency of counts and totals. All calculated variables will be checked against the component variables (cross tabs) to ensure accuracy. For example, categorical age will be compared with continuous age to confirm that each category of age contains only individuals of the expected age ranges within that category.

9.9. Strengths and Limitations of the Research Methods

The proposed SCRI method offers some key strengths including inherent accounting for both measured and unmeasured time invariant confounders due to the within-individual design.

While time-varying confounding is not inherently accounted for in the SCRI design, the shorter analysis period within the SCRI design is an additional strength, making it less sensitive to time-varying confounding. The control intervals for the SCRI study can be defined both pre- and post-vaccination. However, the current study will only use a post-vaccination control period. This is because there is a potential for differential reporting of adverse safety events pre- and post-vaccination, with individuals more likely to report possible safety events after they receive a vaccine, which may bias the comparison between a post-vaccine risk interval with a pre-vaccine control interval.[71] A limitation to the SCRI design is that it may be less interpretable than other study designs.

There are several strengths to the internal comparator cohort design. The comparison of individuals vaccinated with ABRYSVO to contemporary vaccinated or unvaccinated controls yields a complementary and more interpretable result than planned analyses using SCRI (i.e., the increased risk of experiencing a specific safety event due to ABRYSVO versus no ABRYSVO or versus other vaccines). The potential for selection bias (i.e., confounding by indication, healthy user bias) will be mitigated by comparing baseline demographic and clinical characteristics between those administered ABRYSVO and the vaccinated or unvaccinated controls. Potential confounders will be accounted for in the statistical analysis to achieve balance between cohorts, using methods such as ATT weighting.[60] One limitation is that unmeasured confounding may remain, but this will be assessed through sensitivity analyses using negative control outcome. To further reduce the potential for healthy user bias, unvaccinated controls will be required to have similar healthcare-seeking behaviors as ABRYSVO vaccinees, including at least one vaccination claim during the 12 months prior to their matched index date. Finally, another strength of the comparative cohort design is that it is not limited to the assumptions required by the SCRI design (e.g., the occurrence of risk of adverse event in one risk interval is independent of the occurrence in the subsequent or previous interval).

Although the power for analytical comparisons may be more limited within the commercially insured 60-64 year old age group, the internal comparator cohort design does provide control cohorts for contextualization of the observed incidence rates for events of interest in the ABRYSVO vaccinated 60-64 year old cohort. Inclusion of this commercially insured older adult cohort also provides more complete representation of the full ABRYSVO indicated population. Heterogeneity will be assessed between the PharMetrics Plus and Medicare databases, and if appropriate, pooled incidence rate and effect estimates for all adults 60 years and older between the ABRYSVO vaccinated and comparator control cohorts will be generated.

Vaccination can be received in different healthcare settings and through different channels. As vaccination status is based solely on the claims data, one limitation is that exposure misclassification is possible. Here, the SCRI design is a strength, as it only considers individuals with a claim for vaccination. Failing to capture vaccinations outside of the system may impact sample size and power but will not impact the validity of the SCRI analyses.

New onset or incident events are of primary interest in the proposed study as those most likely to be associated with vaccination. To capture these incident events, a clean window of 12 months will be used in the analysis. A time period of 12 months was chosen to maximize

sample size while still having a sufficient washout period prior to ABRYSVO vaccination. A limitation of using 12 months as the clean window is that a longer clean window (e.g., 2 years) would be ideal to ensure that events that occur within the risk interval are true incident events. However, requiring 2 years of continuous enrollment would limit the sample size considerably. Maintaining a large sample size is prioritized to ensure sufficient power to capture rare events such as GBS. The study also relies on a specific GBS case definition (e.g., primary diagnosis on inpatient claims), which could exclude some GBS cases. However, considering that GBS is a well-defined acute disease that usually leads to hospitalization, this specific and validated definition provides higher confidence in identifying true cases.

The study population has been kept as broad as possible to capture safety events that occur among all individuals vaccinated with ABRYSVO. However, individuals who ever had a claim for an RSV vaccine from a different manufacturer are excluded from the ABRYSVO cohort to ensure that safety signals are not attributable to different RSV vaccines. Thus, the safety of RSV vaccines from other manufacturers will not be evaluated in this study.

Another strength of this study is that both the Medicare CCW and PharMetrics Plus data provide a range of benefits, including comprehensive structure, large number of variables, and electronic accessibility. It is estimated that over 98% of adults 65 years of age and older and over are enrolled in Medicare, making Medicare data one of the richest sources of health information for older adults in the US.[5] FFS Medicare remains the largest Medicare provider representing approximately 62% of Medicare beneficiaries.[43] Similarly, PharMetrics Plus represents a large and geographically diverse sample of commercially insured adults 60-64 years broadly representative of the general commercially-insured US population within that age group.[9, 10] However, there are several limitations that should be noted. Within the Medicare data, ABRYSVO will be captured under Medicare Part D and not all FFS beneficiaries will have Part D coverage reducing the source population. In addition, there could be gaps in the data since individuals may receive healthcare services outside of Medicare Parts A, B, or D. Covered services for which claims are not submitted are not included in the data (e.g., immunizations provided through grocery-store immunization clinics). Other medical information on baseline characteristics, such as comorbidity history, may be similarly under-captured in the Medicare database if individuals seek care in outside of coverage, resulting in potential residual confounding. These limitations similarly apply to the PharMetrics data when individuals receive healthcare services outside of their commercial insurance plan. Lastly, to the extent that the older adults in the FFS Medicare database are different from individuals outside of FFS Medicare, as well as PharMetrics only representing a commercially insured population, the results may not be generalizable to the broader US population.

A final limitation is that data on clinical metrics, such as laboratory values and illness severity, that could have been used to enhance case identification are not available in the claims data. In addition, chart validation cannot be conducted. These limitations may result in outcome misclassification. However, a strength of this study is that outcome misclassification will be further investigated for the primary outcome (GBS) through

quantitative bias analysis using information from previous validation studies of GBS. A potential for bias may also be introduced as different types of care may be subject to different payment rules. This implies that, for example, comorbidity and severity of illness information may be inconsistently recorded if they are subject to varying payment rules. Such missing information may result in residual confounding. However, the latter will be investigated through sensitivity analyses using a negative control outcome.

9.10. Other Aspects

Not applicable.

10. PROTECTION OF HUMAN PARTICIPANTS

10.1. Patient Information

This study involves data that exist in deidentified/anonymized structured format and contain no patient personal information.

10.2. Patient Consent

As this study involves deidentified/anonymized structured data, which according to applicable legal requirements do not contain data subject to privacy laws, obtaining informed consent from patients by Pfizer is not required.

10.3. Institutional Review Board (IRB)/Ethics Committee (EC)

There must be prospective approval of the study protocol, protocol amendments, and other relevant documents (e.g., informed consent forms if applicable) from the relevant IRBs/ECs. All correspondence with the IRB/EC must be retained. Copies of IRB/EC approvals must be forwarded to Pfizer.

10.4. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in Guidelines for GPP issued by the International Society for Pharmacoepidemiology[72], the FDA Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting, Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data[73] and GEP guidelines issued by the IEA.[74]

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

Structured Data Analysis

This study involves data that exist as structured data by the time of study start. In these data sources, individual patient data are not retrieved or validated, and it is not possible to link (i.e., identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an AE (i.e., identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

This protocol will be posted on publicly available registers (i.e., EU PAS) prior to the start of data collection. The final study results will be made publicly available and may be submitted for publication in a peer reviewed medical journal.

In the event of any prohibition or restriction imposed (e.g., clinical hold) by an applicable competent authority in any area of the world, or if the party responsible for collecting data from the participant is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

13. REFERENCES

1. ClinicalTrials.gov. (2023). Study to Evaluate the Efficacy, Immunogenicity, and Safety of RSVpreF in Adults. (RENOIR). Available from: https://www.clinicaltrials.gov/ct2/show/NCT05035212. Accessed on: May 1, 2023.
2. Walsh EE, Pérez Marc G, Zareba AM, Falsey AR, Jiang Q, Patton M, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med. 2023;388(16):1465-77.
3. Pfizer Inc. Respiratory Syncytial Virus Stabilized Bivalent Prefusion F Subunit Vaccine (RSVpreF / Abrysvo)
Briefing Document For Vaccines And Related Biological Products Advisory Committee Meeting 28 February 2023 – 01 March 2023. 2023. Contract No.: May 15, 2023.
4. Jones HR, Grattan-Smith PJ, Ryan MM. Chapter 20 - Acute Polyneuropathies. In: Darras BT, Jones HR, Ryan MM, De Vivo DC, editors. Neuromuscular Disorders of Infancy, Childhood, and Adolescence (Second Edition). San Diego: Academic Press; 2015. p. 379-97.
5. Research and Data Assistance Center (ResDAC). (2018). Strengths and Limitations of CMS Administrative Data in Research. Available from: https://resdac.org/articles/strengths-and-limitations-cms-administrative-data-research. Accessed on: May 15, 2023.
6. Perez-Vilar S, Wernecke M, Arya D, Lo AC, Lufkin B, Hu M, et al. Surveillance for Guillain-Barré syndrome after influenza vaccination among U.S. Medicare beneficiaries during the 2017-2018 season. Vaccine. 2019;37(29):3856-65.
7. Goud R, Lufkin B, Duffy J, Whitaker B, Wong HL, Liao J, et al. Risk of Guillain-Barré Syndrome Following Recombinant Zoster Vaccine in Medicare Beneficiaries. JAMA Intern Med. 2021;181(12):1623-30.
8. Polakowski LL, Sandhu SK, Martin DB, Ball R, Macurdy TE, Franks RL, et al. Chart-confirmed guillain-barre syndrome after 2009 H1N1 influenza vaccination among the Medicare population, 2009-2010. Am J Epidemiol. 2013;178(6):962-73.
9. Mannino D, Bogart M, Germain G, Huang SP, Ismaila AS, Laliberte F, et al. Benefit of Prompt versus Delayed Use of Single-Inhaler Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) Following a COPD Exacerbation. Int J Chron Obstruct Pulmon Dis. 2022;17:491-504.
10. Ciarametaro M, Kleinrock M, Campbell A, Buelt L, Dubois RW. Health spending expenditures for commercial plans are predominantly concentrated among a small population of high-intensity consumers across settings of care. J Manag Care Spec Pharm. 2022;28(2):180-7.
11. Moll K, Lufkin B, Fingar KR, Ke Zhou C, Tworkoski E, Shi C, et al. Background Rates Of Adverse Events Of Special Interest For Covid-19 Vaccine Safety Monitoring In The United States, 2019-2020. Vaccine. 2023;41(2):333-53.
12. Walsh EE. Respiratory Syncytial Virus Infection: An Illness for All Ages. Clin Chest Med. 2017;38(1):29-36.
13. Branche AR, Saiman L, Walsh EE, Falsey AR, Sieling WD, Greendyke W, et al. Incidence of Respiratory Syncytial Virus Infection Among Hospitalized Adults, 2017–2020. Clinical Infectious Diseases. 2021;74(6):1004-11.

14. Centers for Disease Control and Prevention. (2022). ACIP Adult RSV Work Group Considerations. Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/04-RSV-Adults-Melgar-508.pdf. Accessed on:
15. Hansen CL, Chaves SS, Demont C, Viboud C. Mortality Associated With Influenza and Respiratory Syncytial Virus in the US, 1999-2018. JAMA Netw Open. 2022;5(2):e220527.
16. McLaughlin JM, Khan F, Begier E, Swerdlow DL, Jodar L, Falsey AR. Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis. Open Forum Infect Dis. 2022;9(7):ofac300.
17. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, et al. Mortality Associated With Influenza And Respiratory Syncytial Virus In The United States. JAMA. 2003;289(2):179-86.
18. Widmer K, Zhu Y, Williams JV, Griffin MR, Edwards KM, Talbot HK. Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus, and influenza virus in older adults. J Infect Dis. 2012;206(1):56-62.
19. Zheng Z, Warren JL, Shapiro ED, Pitzer VE, Weinberger DM. Estimated incidence of respiratory hospitalizations attributable to RSV infections across age and socioeconomic groups. Pneumonia. 2022;14(1):6.
20. Branche AR, Falsey AR. Respiratory Syncytial Virus Infection In Older Adults: An Under-Recognized Problem. Drugs Aging. 2015;32(4):261-9.
21. Murata Y, Falsey AR. Respiratory Syncytial Virus Infection in Adults. Antivir Ther. 2007;12(4_part_2):659-70.
22. Falsey AR, Walsh EE. Respiratory syncytial virus infection in adults. Clin Microbiol Rev. 2000;13(3):371-84.
23. Busack B, Shorr AF. Going Viral-RSV as the Neglected Adult Respiratory Virus. Pathogens. 2022;11(11).
24. Pera A, Campos C, López N, Hassouneh F, Alonso C, Tarazona R, et al. Immunosenescence: Implications for response to infection and vaccination in older people. Maturitas. 2015;82(1):50-5.
25. Anderson LJ, Dormitzer PR, Nokes DJ, Rappuoli R, Roca A, Graham BS. Strategic priorities for respiratory syncytial virus (RSV) vaccine development. Vaccine. 2013;31 Suppl 2(Suppl 2):B209-15.
26. Anderson CA, Belongia EA, AS M, PA P, LM P, PG R, et al. Respiratory syncytial virus in older adults: a hidden annual epidemic. A report from the National Foundation for Infectious Diseases. In: Bethesda, MD: National Foundation for Infectious Diseases.; 2016 2016.
27. Falsey AR, Singh HK, Walsh EE. Serum Antibody Decay In Adults Following Natural Respiratory Syncytial Virus Infection. J Med Virol. 2006;78(11):1493-7.
28. Colosia AD, Yang J, Hillson E, Mauskopf J, Copley-Merriman C, Shinde V, et al. The Epidemiology Of Medically Attended Respiratory Syncytial Virus In Older Adults In The United States: A Systematic Review. PLoS One. 2017;12(8):e0182321.
29. Florin TA, Plint AC, Zorc JJ. Viral Bronchiolitis. Lancet. 2017;389(10065):211-24.
30. Pfizer Inc. (2023). U.S. FDA Approves ABRYSVO™, Pfizer's Vaccine for the Prevention of Respiratory Syncytial Virus (RSV) in Older Adults. Available from:

https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-abrysvotm-pfizers-vaccine-prevention. Accessed on: 06-05-2023.
31. GlaxoSmithKline. (2023). US FDA approves GSK's Arexvy, the world's first respiratory syncytial virus (RSV) vaccine for older adults. Available from: https://www.gsk.com/en-gb/media/press-releases/us-fda-approves-gsk-s-arexvy-the-world-s-first-respiratory-syncytial-virus-rsv-vaccine-for-older-adults/. Accessed on: May 9.
32. Pfizer Inc . (2023). U.S. FDA Approves ABRYSVO™, Pfizer's Vaccine for the Prevention of Respiratory Syncytial Virus (RSV) in Infants Through Active Immunization of Pregnant Individuals 32-36 Weeks of Gestational Age. Available from: https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-abrysvotm-pfizers-vaccine-prevention-0. Accessed on: 03-20-2026.
33. Pfizer Inc. (2024). U.S. FDA Approves Pfizer's RSV Vaccine ABRYSVO® for Adults Aged 18 to 59 at Increased Risk for Disease. Available from: https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-pfizers-rsv-vaccine-abrysvor-adults-aged-18. Accessed on: 03-20-2026.
34. ClinicalTrials.gov. (2023). A Study to Evaluate the Efficacy of an RSV F Vaccine in Older Adults. Available from: https://clinicaltrials.gov/ct2/show/NCT02608502. Accessed on: May 8, 2023.
35. ClinicalTrials.gov. (2023). A Study to Evaluate the Safety and Efficacy of mRNA-1345 Vaccine Targeting Respiratory Syncytial Virus (RSV) in Adults ≥60 Years of Age. Available from: https://clinicaltrials.gov/ct2/show/NCT05127434. Accessed on: May 1, 2023.
36. ClinicalTrials.gov. (2023). MVA-BN-RSV Vaccine Trial. Available from: https://clinicaltrials.gov/ct2/show/NCT05238025. Accessed on: May 1, 2023.
37. Centers for Disease Control and Prevention. (2023). Guillain-Barré Syndrome and Vaccines. Available from: https://www.cdc.gov/vaccinesafety/concerns/guillain-barre-syndrome.html#print. Accessed on: May 15, 2023.
38. Fireman B, Lee J, Lewis N, Bembom O, van der Laan M, Baxter R. Influenza vaccination and mortality: differentiating vaccine effects from bias. Am J Epidemiol. 2009;170(5):650-6.
39. Korves C, Izurieta HS, Smith J, Zwain GM, Powell EI, Balajee A, et al. Relative effectiveness of booster vs. 2-dose mRNA Covid-19 vaccination in the Veterans Health Administration: Self-controlled risk interval analysis. Vaccine. 2022;40(33):4742-7.
40. Klein NP, editor Rapid cycle analysis to monitor the safety of COVID-19 vaccines in near real-time within the Vaccine Safety Datalink : Myocarditis and anaphylaxis. Advisory Committee on Immunization Practices COVID-19 Vaccines; 2021 August 30, 2021; United States.
41. Klein NP, Lewis N, Goddard K, Fireman B, Zerbo O, Hanson KE, et al. Surveillance for Adverse Events After COVID-19 mRNA Vaccination. JAMA. 2021;326(14):1390-9.
42. U.S. Centers for Medicare and Medicaid Services. What's Medicare? Available from: https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare. Accessed on: June 12, 2023.

43. Tarazi WW, WP.; Nguyen, N.; Bosworth, A.; Sheingold, S.; De Lew, N.; Sommers, BD. . Medicare Beneficiary Enrollment Trends and Demographic Characteristics. In: Office of the Assistant Secretary for Planning and Evaluation USDoHaHS, editor. 2022.
44. Centers for Medicare & Medicaid Services. (2023). CMS Fast Facts. Available from: https://data.cms.gov/fact-sheet/cms-fast-facts. Accessed on: May 15, 2023.
45. Cubanski J, Damico A. (2021). Key Facts About Medicare Part D Enrollment, Premiums, and Cost Sharing in 2021. Available from: https://www.kff.org/medicare/issue-brief/key-facts-about-medicare-part-d-enrollment-premiums-and-cost-sharing-in-2021/. Accessed on: May 15, 2023.
46. U.S. Department of Health and Human Services. What is Medicare Part A? Accessed on: June 12, 2023.
47. The Henry J. Kaiser Family Foundation. (2022). An Overview of the Medicare Part D Prescription Drug Benefit. Available from: https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/. Accessed on:
48. Cubanski JN, Tricia; Damico, Anthony. (2016). Medicare's Role for People Under Age 65 with Disabilities. Available from: https://files.kff.org/attachment/issue-brief-Medicares-Role-for-People-Under-Age-65-with-Disabilities. Accessed on: June 12, 2023.
49. Perez-Vilar S, Hu M, Weintraub E, Arya D, Lufkin B, Myers T, et al. Guillain-Barré Syndrome After High-Dose Influenza Vaccine Administration in the United States, 2018-2019 Season. J Infect Dis. 2021;223(3):416-25.
50. Law B. (2021). Guillain Barré and Miller Fisher Syndromes. Available from: https://brightoncollaboration.us/wp-content/uploads/2021/03/SPEAC_D2.5.2.1-GBS-Case-Definition-Companion-Guide_V1.0_format12062-1.pdf. Accessed on: June 12, 2023.
51. Lee GM, Greene SK, Weintraub ES, Baggs J, Kulldorff M, Fireman BH, et al. H1N1 and seasonal influenza vaccine safety in the vaccine safety datalink project. Am J Prev Med. 2011;41(2):121-8.
52. Anamnart C, Tisavipat N, Owattanapanich W, Apiwattanakul M, Savangned P, Prayoonwiwat N, et al. Newly diagnosed neuromyelitis optica spectrum disorders following vaccination: Case report and systematic review. Multiple Sclerosis and Related Disorders. 2022;58:103414.
53. U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) Office of Biostatistics and Epidemiology. (2021). Master Protocol: Assessment of Risk of Safety Outcomes Following COVID-19 Vaccination. Available from: https://www.bestinitiative.org/wp-content/uploads/2021/04/COVID-19-Vaccine-Safety-Inferential-Draft-Master-Protocol.pdf. Accessed on: May 15, 2023.
54. Rowhani-Rahbar A, Klein NP, Dekker CL, Edwards KM, Marchant CD, Vellozzi C, et al. Biologically plausible and evidence-based risk intervals in immunization safety research. Vaccine. 2012;31(1):271-7.
55. Chandrashekhar S, Dimachkie MM. Guillain-Barré syndrome in adults: Pathogenesis, clinical features, and diagnosis. In: Shefner JM, Rabinstein AA, editors. UpToDate. Waltham, MA: UpToDate; 2023.
56. US-FDA Biologics Effectiveness and Safety (BEST) Protocol: Evaluation of Multiple Safety Outcomes following Respiratory Syncytial Virus (RSV) Vaccination in Adults 60 Years and Older. 2023.

57. US Department of Health and Human Services (US-HHS) CfMaMS. Medicare Claims Maturity - Chronic Conditions Data Warehouse White Paper: 2.0 edition. 2017.
58. US-HHS Centers for Medicare and Medicaid Services Preliminary Medicare COVID-19 data snapshot. 2021.
59. Signorini DF. Sample size for Poisson regression. Biometrika. 1991;78(2):446-50.
60. Hernán MA, Robins JM. Estimating causal effects from epidemiological data. J Epidemiol Community Health. 2006;60(7):578-86.
61. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med. 2015;34(28):3661-79.
62. Wyman MJ, Stabi KL. Concomitant administration of pneumococcal-23 and zoster vaccines provides adequate herpes zoster coverage. Ann Pharmacother. 2013;47(7-8):1064-8.
63. Lazarus R, Baos S, Cappel-Porter H, Carson-Stevens A, Clout M, Culliford L, et al. Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): a multicentre, randomised, controlled, phase 4 trial. Lancet. 2021;398(10318):2277-87.
64. Yih WK, Lee GM, Lieu TA, Ball R, Kulldorff M, Rett M, et al. Surveillance for adverse events following receipt of pandemic 2009 H1N1 vaccine in the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) System, 2009-2010. Am J Epidemiol. 2012;175(11):1120-8.
65. Arnold BF, Ercumen A. Negative Control Outcomes: A Tool to Detect Bias in Randomized Trials. Jama. 2016;316(24):2597-8.
66. Lipsitch M, Tchetgen Tchetgen E, Cohen T. Negative controls: a tool for detecting confounding and bias in observational studies. Epidemiology. 2010;21(3):383-8.
67. U.S. Food and Drug Administration (FDA), editor Understanding the Use of Negative Controls to Assess the Validity of Non-Interventional Studies of Treatment Using Real-World Evidence: Virtual Public Workshop2023.
68. Yang Q, Chang A, Tong X, Merritt R. Herpes Zoster Vaccine Live and Risk of Stroke Among Medicare Beneficiaries: A Population-Based Cohort Study. Stroke. 2021;52(5):1712-21.
69. Izurieta HS, Lu M, Kelman J, Lu Y, Lindaas A, Loc J, et al. Comparative Effectiveness of Influenza Vaccines Among US Medicare Beneficiaries Ages 65 Years and Older During the 2019-2020 Season. Clin Infect Dis. 2021;73(11):e4251-e9.
70. Lash TLF, Matthew P.; Fink, Aliza K. Applying Quantitative Bias Analysis to Epidemiologic Data. 1 ed. New York, NY: Springer; 2009.
71. Hoffman KB, Demakas AR, Dimbil M, Tatonetti NP, Erdman CB. Stimulated reporting: the impact of US food and drug administration-issued alerts on the adverse event reporting system (FAERS). Drug Saf. 2014;37(11):971-80.
72. Guidelines for good pharmacoepidemiology practices (GPP). Pharmacoepidemiol Drug Saf. 2008;17(2):200-8.
73. U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER). (2013). Best practices for conducting and reporting pharmacoepidemiologic safety studies using electronic healthcare data. Available from: https://www.fda.gov/regulatory-

information/search-fda-guidance-documents/best-practices-conducting-and-reporting-pharmacoepidemiologic-safety-studies-using-electronic. Accessed on: May 15, 2023.
74. International Epidemiological Association (IEA). (2007). Good Epidemiological Practice (GEP), IEA Guidelines for Proper Conduct of Epidemiological Research. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/best-practices-conducting-and-reporting-pharmacoepidemiologic-safety-studies-using-electronic. Accessed on: May 15, 2023.
75. Segal JB, Chang HY, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a Claims-based Frailty Indicator Anchored to a Well-established Frailty Phenotype. Med Care. 2017;55(7):716-22.
76. Menendez ME, Neuhaus V, van Dijk CN, Ring D. The Elixhauser comorbidity method outperforms the Charlson index in predicting inpatient death after orthopaedic surgery. Clin Orthop Relat Res. 2014;472(9):2878-86.

14. LIST OF TABLES

15. LIST OF FIGURES

ANNEX 1. LIST OF STANDALONE DOCUMENTS

None.

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Study title: A Post-Authorization Safety Study of Guillain-Barré Syndrome (GBS) Following ABRYSVO™ Among Older Adults in the United States

EU PAS Register® number: To be registered before the start of data collection
Study reference number (if applicable): Not applicable

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☒	☐	☐	6
1.1.2 End of data collection[2]	☒	☐	☐	6
1.1.3 Progress report(s)	☐	☐	☒	
1.1.4 Interim report(s)	☒	☐	☐	6
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	6
1.1.6 Final report of study results.	☒	☐	☐	6

Comments:

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	8
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	7
2.1.2 The objective(s) of the study?	☒	☐	☐	8
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	8
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

[1] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.

[2] Date from which the analytical dataset is completely available.

Section 3: Study design		**Yes**	**No**	**N/A**	**Section Number**
3.1	Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	9.1
3.2	Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	9.1, 9.4
3.3	Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☒	☐	☐	9.1, 9.7
3.4	Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☒	☐	☐	9.1, 9.7
3.5	Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	11

Comments:

Section 4: Source and study populations		**Yes**	**No**	**N/A**	**Section Number**
4.1	Is the source population described?	☒	☐	☐	9.2
4.2	Is the planned study population defined in terms of:				
	4.2.1 Study time period	☒	☐	☐	9.2.1
	4.2.2 Age and sex	☒	☐	☐	9.2.3
	4.2.3 Country of origin	☒	☐	☐	9.2
	4.2.4 Disease/indication	☐	☐	☒	
	4.2.5 Duration of follow-up	☒	☐	☐	9.2
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	9.2.1, 9.2.2

Comments:

Section 5: Exposure definition and measurement		**Yes**	**No**	**N/A**	**Section Number**
5.1	Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☒	☐	☐	9.3.1
5.2	Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☒	☐	☐	9.9
5.3	Is exposure categorised according to time windows?	☒	☐	☐	9.2.1
5.4	Is intensity of exposure addressed? (e.g. dose, duration)	☐	☐	☒	
5.5	Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.6	Is (are) (an) appropriate comparator(s) identified?	☒	☐	☐	9.1

Comments:

Section 6: Outcome definition and measurement		**Yes**	**No**	**N/A**	**Section Number**
6.1	Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	9.3.2
6.2	Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	9.3.2
6.3	Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☒	☐	☐	9.3.2, 9.7.3.3
6.4	Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☐	☒	

Comments:

Section 7: Bias		**Yes**	**No**	**N/A**	**Section Number**
7.1	Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☒	☐	☐	9.7.2.2, 9.7.2.3, 9.9
7.2	Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☒	☐	☐	9.7.3.2, 9.9
7.3	Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☒	☐	☐	9.7.3.2, 9.7.3.3, 9.9

Comments:

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	9.4
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☒	☐	☐	9.4
9.1.3 Covariates and other characteristics?	☒	☐	☐	9.4
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	9.4
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☒	☐	☐	9.4
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☒	☐	☐	9.4
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☒	☐	☐	9.3.1
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☒	☐	☐	9.3.2
9.3.3 Covariates and other characteristics?	☒	☐	☐	9.3.3
9.4 Is a linkage method between data sources described? (e.g., based on a unique identifier or other)	☐	☐	☒	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	9.7
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	9.5
10.3 Are descriptive analyses included?	☒	☐	☐	9.7
10.4 Are stratified analyses included?	☐	☐	☒	
10.5 Does the plan describe methods for analytic control of confounding?	☒	☐	☐	9.7
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☒	☐	☐	9.7.3.3
10.7 Does the plan describe methods for handling missing data?	☐	☐	☒	
10.8 Are relevant sensitivity analyses described?	☒	☐	☐	9.7.3

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	9.6
11.2 Are methods of quality assurance described?	☒	☐	☐	9.8
11.3 Is there a system in place for independent review of study results?	☒	☐	☐	9.8

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	9.9
12.1.2 Information bias?	☒	☐	☐	9.9
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	☒	☐	☐	9.9
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	9.2, 9.5

Comments:

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☒	☐	☐	10.3
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3 Have data protection requirements been described?	☒	☐	☐	10

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	5

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g., to regulatory authorities)?	☒	☐	☐	12
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	12

Comments:

Name of the main author of the protocol:	Joanne Wu	
Date: dd/Month/year	29 November 2023	
Signature:		

ANNEX 3. ADDITIONAL INFORMATION

Annex 3 Table A-1. RSV Vaccine Exposure CPT and NDC Codes

Code Type	Code	Manufacturer/Descriptions
NDC	0069-0207-01	Pfizer, Inc.
	0069-0250-01	Pfizer, Inc.
	0069-0344-01	Pfizer, Inc.
	0069-0344-05	Pfizer, Inc.
	0069-0344-10	Pfizer, Inc.
	0069-0651-01	Pfizer, Inc.
	0069-1265-10	Pfizer, Inc.
	0069-1265-20	Pfizer, Inc.
	0069-2465-19	Pfizer, Inc.
	0069-2465-01	Pfizer, Inc.
	0069-2465-10	Pfizer, Inc.
CPT	90678	A bivalent preF vaccine product administered into the muscle to protect against respiratory syncytial virus

Note: Additional codes will be added for RSV vaccines as they become available.

Annex 3 Table A-2. Demographic and Clinical Characteristics Definitions

Variable	Description	Operational definition
Demographic Characteristics		
Age	Continuous variable; Categorical variable: • 65–69 • 70-74 • 75-79 • 80-84 • 85-89 • ≥90	Age on the date of ABRYSVO vaccination (or assigned index date for contemporary unvaccinated controls)
Sex	Categorical variable: • Male • Female • Unknown	
Race/ethnicity	Categorical variable: • White	

Variable	Description	Operational definition
	• Black • Hispanic ethnicity • Asian • North American Native • Two or more races • Unknown	
Care setting of vaccination	Geographic regions in the US; Categorical variable: • South • Midwest • West • Northeast • Other • Unknown	Region associated with the index date
Clinical Characteristics		
Smoking Status	Dichotomous variable	ICD-10-CM codes: • F17.200, Nicotine dependence, unspecified, uncomplicated • Z7.20, Tobacco use • Z87.891, Personal history of nicotine dependence
Body mass index (BMI)	Categorical variable: • ≤ 19.9 • 20-29 • 30-39 • ≥ 40 • Unknown	ICD-10-CM codes: • Z68.1, Body Mass Index 19.9 or less, adult • Z68.2, Body mass index 20-29, adult • Z68.3, Body mass index between 30-39, adult • Z68.4, Body mass index 40 and over, adult
History of anaphylaxis/ allergic reactions	Dichotomous variable	ICD-10-CM code: • Z87.892 Personal history of anaphylaxis

Variable	Description	Operational definition
		• Z88.0–Z88.6, Z88.8, Z88.9, Allergy status to drugs, medications and biological substances, excluding serum and vaccine • T78.00xx–T78.09xx, Anaphylactic reaction due to food, initial encounter, subsequent encounter and sequela • T78.2xxx, Anaphylactic shock, initial encounter, subsequent encounter and sequela • T78.3xxx, Angioneurotic edema, initial encounter, subsequent encounter and sequela • T78.41xx, Arthus phenomenon • T80.51xx, Anaphylactic reaction due to administration of blood and blood products, initial encounter, subsequent encounter and sequela • T80.59xx, Anaphylactic reaction due to other serum, initial encounter, subsequent encounter and sequela • T88.6xxx, Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered, initial encounter, subsequent encounter and sequela
Previous anaphylaxis of vaccine component	Dichotomous variable	ICD-10-CM codes: • T80.52xx, Anaphylactic reaction due to vaccination, initial encounter, subsequent encounter and sequela • Z28.04, Immunization not carried out because of patient

Variable	Description	Operational definition
		allergy to vaccine or component • Z88.7, Allergy status to serum and vaccine
History of hospitalizations	Dichotomous variable; Continuous variable	Defined by having any hospitalizations (dichotomous) and number of hospitalizations (continuous)
History of admission into nursing home/SNF	Dichotomous variable; Continuous variable	Defined by having any admissions (dichotomous) and number of admissions (continuous)
Prior infections	Categorical variable for specified prior infections	ICD-10-CM codes: • A04.5, Campylobacter enteritis • B25.x, B27.1x, P35.1, CMV • U07.1, COVID-19 • B27.0x, D82.3, EBV • B17.2, HEV • J09.xx – J11.xx, Influenza virus • B96.0, J15.7, J20.0, Mycoplasma pneumonia • B97.4, J12.1, J20.5, J21.0 Respiratory syncytial virus • A92.5, P35.4, Zika virus
Frailty index[75]	Continuous variable	ICD-9-CM codes available in Appendix Table 1 of Segal et al, 2017. ICD-9-CM codes mapped to ICD-10-CM codes.
Charlson Comorbidity Index (CCI)_ENREF_76[76]	Continuous variable	ICD-10-CM codes: • I21.x, I21.xx, I22.x, I25.2, Myocardial infarction • I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43, I43.x, I50.x, I50.xx, Congestive heart failure

Variable	Description	Operational definition
		• I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9, Peripheral vascular disease • G45, G45.x, G46.x, H34.0, I60.x–I63.x, I60.xx–I63.xx, I60.xxx–I63.xxx, I65.x–I69.x, I65.xx–I69.xx, I65.xxx–I69.xxx, Cerebrovascular disease • F00.x–F03.x, F00.xx–F03.xx, F05, F05.1, G30.x, G31.1, Dementia • I27.8, I27.9, J40.x–J47.x, J40.xx–J47.xx, J40.xxx–J47.xxx, J60.x–J67.x, J68.4, J70.1, J70.3, Chronic pulmonary disease • M05, M05.x, M05.xx, M05.xxx, M06, M06.x, M06.xx, M06.xxx, M31.5, M32.x–M34.x, M32.xx–M34.xx, M35.1, M35.3, M36.0, Rheumatic disease • K25.x–K28.x, Peptic ulcer disease • B18.x, K70.0–K70.3, K70.9, K71.3–K71.5, K71.7, K73.x, K74.x, K74.xx, K76.0, K76.2–K76.4, K76.8, K76.9, Z94.4, Mild liver disease • E10.0, E10.1x, E10.6x, E10.6xx, E10.8, E10.9, E11.0x, E11.1x, E11.6x, E11.6xx, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0x, E13.1x, E13.6x, E13.6xx, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9, Diabetes without chronic complication • E10.2x–E10.5x, E10.2xx–E10.5xx, E10.7, E11.2x–

Variable	Description	Operational definition
		E11.5x, E11.2xx–E11.5xx, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5x, E13.7, E14.2–E14.5, E14.7, Diabetes with chronic complication • G04.1, G11.4, G80.1, G80.2, G81.x, G81.xx, G82.x, G82.xx, G83.0, G83.1–G83.3, G83.1x–G83.3x, G83.4, G83.9, Hemiplegia or paraplegia • I12.0, I13.1x, N03.2–N03.7, N05.2–N05.7, N18.x, N19, N25.0, Z49.0x–Z49.3x, Z94.0, Z99.2, Renal disease • C00–C75, C00.x–C75.x, C00.xx–C75.xx (excluding C44, C44.x and C44.xx), C7A., C7A.x, C7A.xx, C7B., C7B.x, C7B.xx, C76–C80, C76.x–C80.x, C76.xx–C80.xx, C81–C96, C81.x–C96.x, C81.xx–C96.xx, Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin • I85.0, I85.9, I86.4, I98.2, K70.4x, K71.1x, K72.1x, K72.9x, K76.5, K76.6, K76.7, Moderate or severe liver disease • C77.x–C80.x, C77.xx–C80.xx, Metastatic solid tumor • B20, B97.35, AIDS/HIV
Comorbidities	Categorical variable *Cardiovascular* • Cardiomyopathy • CAD • CHF • Heart failure • Hypertension	*Cardiovascular* Cardiomyopathy: • ICD-10-CM codes: ○ I42.x, Cardiomyopathy CAD: • ICD-10-CM codes: ○ I24.0, I24.8, I24.9, I25.10, I25.110, I25.111, I25.118,

Variable	Description	Operational definition
	• Stroke/Transient ischemic attack *Hematological* • Bleeding diathesis or condition associated with prolonged bleeding • Hematologic malignancy • Sickle cell disease • VTE *Hepatic* • HBV • HCV • Liver disease *Immunological* • Autoimmune disease • Immunocompromising conditions o Solid organ transplant o HSCT o Hematologic or solid malignancy o HIV/AIDS o Other immune deficiencies *Neurological* • Dementia (i.e., Alzheimer's disease and related disorders, senile dementia) • Neurological disease *Respiratory* • Asthma • Chronic bronchiectasis • COPD/interstitial lung disease *Other* • Cancer	I25.119, I25.41, I25.42, I25.700, I25.701, I25.708, I25.709, I25.710, I25.711, I25.718, I25.719, I25.720, I25.721, I25.728, I25.729, I25.730, I25.731, I25.738, I25.739, I25.750, I25.751, I25.758, I25.759, I25.760, I25.761, I25.768, I25.769, I25.790, I25.791, I25.798, I25.799, I25.810, I25.811, I25.812, CAD CHF: • ICD-10-CM codes: o I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43, I43.x, I50.x, I50.xx, CHF Heart failure: • ICD-10-CM codes: o 150.x, 150.xx, Heart failure Hypertension: • ICD-10-CM codes: o H35.03x, Hypertensive retinopathy o I10, I11.x–I16.x, I13.xx, Hypertensive diseases o I67.4, Hypertensive encephalopathy diseases Stroke/transient ischemic attack: • ICD-10-CM codes: o G43.601, G43.609, G43.611, G43.619, I60.9, I62.00, I61.9, I62.1, I62.9, I63.019, I63.119, I63.139, I63.20, I63.219, I63.22, I63.239, I63.30, I63.40, I63.50, I63.59, I66.09, I66.19, I66.29, I66.9, I67.89, I69.898, I69.90, I69.910, I69.911, I69.912, I69.913, I69.914, I69.915,

Variable	Description	Operational definition
	• Chronic kidney disease/dialysis • Diabetes mellitus • Down syndrome • Gout • Hyperlipidemia • Hypothyroidism	I69.918, I69.919, I69.920, I69.921, I69.922, I69.923, I69.928, I69.941, I69.942, I69.943, I69.944, I69.949, I69.951, I69.952, I69.953, I69.954, I69.959, I69.961, I69.962, I69.963, I69.964, I69.965, I69.969, I69.990, I69.991, I69.992, I69.993, I69.998, Stroke ○ G45, Transient ischemic attack *Hematological* Bleeding diathesis or condition associated with prolonged bleeding: • ICD-10-CM codes: ○ D65, Disseminated intravascular coagulation ○ D66, Hereditary factor VIII deficiency ○ D67, Hereditary factor IX deficiency ○ D68, D68.x, D68.xx, Other coagulation defects ○ D69, D69.x, D69.xx, Purpura and other hemorrhagic conditions Hematologic malignancy: • ICD-10-CM codes: ○ C81, C82, C83, C88, C89, C90, C91, C92, C93, C94, C95, C96, Hematologic malignancy Sickle cell disease: • ICD-10-CM codes: ○ D57, D57.x, D57.xx, D57.xxx, Sickle-cell disorders VTE: • ICD-10-CM codes: ○ I26, I26.x, I26.xx, Pulmonary embolism

Variable	Description	Operational definition
		○ I80, I80.x, I80.xx, I80.xxx, Phlebitis and thrombophlebitis ○ I81, Portal vein thrombosis ○ I82, I82.x, I82.xx, I82.xxx Other venous embolism and thrombosis *Hepatic* HBV: • ICD-10-CM codes: ○ B18.0, B18.1, Chronic viral hepatitis B ○ B19.1, B19.1x, Unspecified viral hepatitis B HCV: • ICD-10-CM codes: ○ B18.2, Chronic viral hepatitis C ○ B19.2x, Unspecified viral hepatitis C Liver disease: • ICD-10-CM codes: ○ K70.x, K70.xx, Alcoholic fatty liver ○ K71.x, K71.xx, Toxic liver disease ○ K72.xx, Hepatic failure, not elsewhere classified ○ K73.x, Chronic hepatitis, not elsewhere specified ○ K74.x, K74.xx, Fibrosis and cirrhosis of liver ○ K75.x, K75.xx, Other inflammatory liver diseases ○ K76.x, K76.xx, Other diseases of liver ○ K77, Liver disorders in diseases classified elsewhere *Immunological* Autoimmune disease: • ICD-10-CM codes:

Variable	Description	Operational definition
		○ D69.3, Immune thrombocytopenic purpura ○ D86.x, Sarcoidosis ○ E06.3, Autoimmune thyroiditis ○ G35, Multiple sclerosis ○ G61.0 and G65.0, GBS and sequelae of GBS ○ L40.x, L40.5x, Psoriasis ○ L93.x, Lupus erythematosus ○ M05.x, M05.xx, M05.xxx, Rheumatoid arthritis with rheumatoid factor ○ M06.x, M06.xx, M06.xxx, Other rheumatoid arthritis ○ M31.5, M31.6, Giant cell arteritis ○ M35.0x, Sicca (Sjogren's) syndrome ○ M32.x, Systemic Lupus Erythematosus ○ N05.9, Glomerulonephritis ○ D84.9, Immunodeficiency, unspecified Immunocompromising conditions: • Solid organ transplant ○ CPT codes: ▪ 32850–32856, Transplantation of lung ▪ 33930–33945, Transplantation of heart ▪ 44132, 44133, 47133, 47135, 47140–47147, Transplantation of liver ▪ 44135–44137, 44715, 44720, 44721, Transplantation of intestine ▪ 48160, 48550–48552, 48554, 48556,

Variable	Description	Operational definition
		Transplantation of pancreas ▪ 50300, 50320, 50323, 50325, 50327, 50328, 50329, 50340, 50360, 50365, 50370, 50380, Renal transplantation o ICD-10-PCS codes: ▪ 02YA0Z0, 02YA0Z1, Transplantation of heart ▪ 0BYC0Z0, 0BYC0Z1, 0BYD0Z0, 0BYD0Z1, 0BYF0Z0, 0BYF0Z1, 0BYG0Z0, 0BYG0Z1, 0BYH0Z0, 0BYH0Z1, 0BYJ0Z0, 0BYJ0Z1, 0BYK0Z0, 0BYK0Z1, 0BYL0Z0, 0BYL0Z1, 0BYM0Z0, 0BYM0Z1, Transplantation of lung ▪ 0DY60Z0, 0DY60Z1, Transplantation of stomach ▪ 0DY80Z0, 0DY80Z1, Transplantation of small intestine ▪ 0DYE0Z0, 0DYE0Z1, Transplantation of large intestine ▪ 0FY00Z0, 0FY00Z1, Transplantation of liver ▪ 0FYG0Z0, 0FYG0Z1, Transplantation of pancreas ▪ 0TY00Z0, 0TY00Z1, 0TY10Z0, 0TY10Z1, Transplantation of kidney • HSCT: o CPT codes: ▪ 38240, 38241, 38242, 38243

Variable	Description	Operational definition
		○ HCPCS: ▪ S2150, S2142 ○ ICD-10-PCS: ▪ 30230Y0, 30230Y1, 30230Y2, 30230Y3, 30230Y4, 30233Y0, 30233Y1, 30233Y2, 30233Y3, 30233Y4, 30240Y0, 30240Y1, 30240Y2, 30240Y3, 30240Y4, 30243Y0, 30243Y1, 30243Y2, 30243Y3, 30243Y4, 30250X0, 30250X1, 30250Y0, 30250Y1, 30253X0, 30253X1, 30253Y0, 30253Y1, 30260X0, 30260X1, 30260Y0, 30260Y1, 30263X0, 30263X1, 30263Y0, 30263Y1, 30230AZ, 30230G1, 30230G2, 30230G3, 30230G4, 30230X1, 30230X2, 30230X3, 30230X4, 30233AZ, 30233G1, 30233G2, 30233G3, 30233G4, 30233X1, 30233X2, 30233X3, 30233X4, 30240AZ, 30240G1, 30240G2, 30240G3, 30240G4, 30240X1, 30240X2, 30240X3, 30240X4, 30243AZ, 30243G1, 30243G2, 30243G3, 30243G4, 30243X1, 30243X2, 30243X3, 30243X4, 30250G1, 30253G1, 30260G1, 30263G1, 38240, 38241, 38242,

Variable	Description	Operational definition
		38243, 30230G0, 30230U2, 30230U3, 30230U4, 30230X0, 30233G0, 30233U2, 30233U3, 30233U4, 30233X0, 30240G0, 30240U2, 30240U3, 30240U4, 30240X0, 30243G0, 30243U2, 30243U3, 30243U4, 30243X0 • Hematologic or solid malignancy: o ICD-10-CM codes: ▪ C81, C82, C83, C88, C89, C90, C91, C92, C93, C94, C95, C96, Hematologic malignancy ▪ C00, C01, C02, C03, C04, C05, C06, C07, C11, C12, C13, C14, C15, C16, C17, C18, C19, C22, C23, C24, C25, C26, C27, C28, C29, C30, C31, C32, C33, C34, C35, C36, C37, C38, C39, C40, C41, C42, C43, C44, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C59, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C77, C78, C79, C80, Z85, C7A, C7B, D3A, D00, D01, D02, D03, D04, D05, D06, D07, D08, D09, D10, D11,

Variable	Description	Operational definition
		D12, D13, D14, D15, D16, D17, D18, D19, D20, D21, D22, D23, D24, D25, D26, D27, D28, D29, D30, D31, D32, D33, D34, D35, D36, D37, D38, D39, D40, D41, D42, D43, D44, D45, D46, D47, D48, D49, Solid malignancy • HIV/AIDs: o ICD-10-CM codes: ▪ B20, HIV disease ▪ B97.35, HIV type 2 as the cause of diseases classified elsewhere ▪ B21, B22, B23, B24, HIV/AIDs disease • Other immune deficiencies: o ICD-10-CM codes: ▪ D80, D80.x, Immunodeficiency with predominantly antibody defects ▪ D81, D81.x, D81.xx, Combined immunodeficiencies ▪ D82, D82.x, Immunodeficiency associated with other major defects ▪ D83, D83.x, Common variable immunodeficiency ▪ D84, D84.x, D84.xx, Other immunodeficiencies ▪ D86, D86.x, D86.xx, Sarcoidosis ▪ D89, D89.x, D89.xx, Other disorders

Variable	Description	Operational definition
		involving the immune mechanism, not elsewhere classified *Neurological* Dementia (i.e., Alzheimer's disease and related disorders, senile dementia): • ICD-10-CM codes: o F00.x–F03.x, F00.xx–F03.xx, F05, F05.1, G30.x, G31.1, Dementia Neurological disease: • ICD-10-CM codes: o R41, R41.x, R41.xx, Other symptoms and signs involving cognitive functions and awareness o R42, Dizziness and giddiness o R43, R43.x, Disturbances of smell and taste o R44, R44.x, Other symptoms and signs involving general sensations and perceptions o R45, R45.x, R45.xx, Symptoms and signs involving emotional state o R46, R46.x, R46.xx, Symptoms and signs involving appearance and behavior *Respiratory* Asthma: • ICD-10-CM codes: o J45.2x–J45.3x, Mild intermittent asthma o J45.4x, Moderate persistent asthma o J45.5x, Severe persistent asthma o J45.9x, Other and unspecified asthma

Variable	Description	Operational definition
		Chronic bronchiectasis: • ICD-10-CM codes: o J47.0, J47.1, J47.9, Bronchiectasis COPD/interstitial lung disease: • ICD-10-CM codes: o J41.x Simple and mucopurulent chronic bronchitis o J42, Unspecified chronic bronchitis o J43.x, Emphysema o J44.x, Other COPD o J80, J81.x, J82.xx, J84.xx, J84.xxx, Other respiratory diseases principally affecting the interstitium o M05.10, Rheumatoid lung disease with rheumatoid arthritis of unspecified site *Other* Cancer: • ICD-10-CM codes: o C00–C75, C00.x–C75.x, C00.xx–C75.xx, C7A., C7A.x, C7A.xx, C7B., C7B.x, C7B.xx, Malignant neoplasms, stated or presumed to be primary (of specified sites), and certain specified histologies, except neuroendocrine, and of lymphoid, hematopoietic and related tissue o C76–C80, C76.x–C80.x, C76.xx–C80.xx, Malignant neoplasms of ill-defined, other secondary and unspecified sites o C81–-C96, C81.x–C96.x, C81.xx–C96.xx, Malignant neoplasms of lymphoid,

Variable	Description	Operational definition
		hematopoietic and related tissue Chronic kidney disease/dialysis: • ICD-10-CM codes: o D59.3, Hemolytic-uremic syndrome o I12.x, Hypertensive chronic kidney disease o I13.x, I13.xx, Hypertensive heart and chronic kidney disease o I70.1, Atherosclerosis of renal artery o I72.2 Aneurysm of renal artery o K76.7, Hepatorenal syndrome o M10.30–M10.39, M10.30x–M10.37x, Gout due to renal impairment o M32.14, Glomerular disease in systemic lupus erythematosus o M32.15, Tubulo-interstitial nephropathy in systemic lupus erythematosus o M35.04, Sicca syndrome with tubulo-interstitial nephropathy o N00.x–N07.x, N08, Glomerular diseases o N13.1, N13.2, N13.3x, Obstructive and reflux uropathy o N14.x, Nephropathy o N15.x, Other renal tubulo-interstitial diseases o N16, Renal tubulo-interstitial disorders in diseases classified elsewhere

Variable	Description	Operational definition
		○ N17.x, N18.x, N19, Acute kidney failure and chronic kidney disease ○ N25.x, N26.x, N25.xx, Other disorders of kidney and ureter ○ Q61.02, Q61.11x, Q61.2–Q61.9, Cystic kidney disease ○ Q62.x, Q62.xx, Congenital obstructive defects of renal pelvis and congenital malformation of ureter Diabetes mellitus: • ICD-10-CM codes: ○ E10.x, E10.xx, E10.xxx, Type 1 diabetes mellitus ○ E11.x, E11.xx, E11.xxx, Type 2 diabetes mellitus Down syndrome: • ICD-10-CM codes: ○ Q90.x, Down syndrome Gout: • ICD-10-CM codes: ○ M10.00, M1A.9XX0, M1A.00X1, M1A.20X1, M1A.30X1, M1A.40X1, M1A.9XX1, M10.30, N20.0, M10.9, M10.40, M11.80, M11.819, M11.829, M11.839, M11.849, M11.859, M11.869, M11.879, M11.88, M11.89, M11.20, M11.219, M11.229, M11.239, M11.249, M11.259, M11.269, M11.279, M11.28, M11.29, M11.9, Gout or other crystal induced arthropathy Hyperlipidemia • ICD-10-CM codes:

Variable	Description	Operational definition
		○ E78.0–E78.5, E78.0x, E78.4x, Hyperlipidemia Hypothyroidism: • ICD-10-CM codes: ○ E01.8, Other iodine-deficiency related thyroid disorders and allied conditions ○ E02.x, Subclinical iodine-deficiency hypothyroidism ○ E03.x, Other hypothyroidism ○ E89.0, Postprocedural hypothyroidism
Prior surgery (i.e., anesthesia or conscious sedation)	Categorical variable for prior surgery (i.e., anesthesia or conscious sedation)	See Annex 3 Table A-4.
Prior trauma	Categorical variable for prior trauma	Codes will be provided in the SAP
Prior bone marrow transplant	Categorical variable for prior bone marrow transplant	Codes will be provided in the SAP
Immunization history	Categorical variable (not mutually exclusive): • Seasonal influenza • COVID-19 • RSV (not ABRYSVO) • Tetanus diphtheria and pertussis (Tdap or Td) • Chickenpox (Varicella) • Shingles (Herpes Zoster recombinant and/or live) • Human papillomavirus (HPV) • Pneumococcal conjugate	See Annex 3 Table A-3.

Variable	Description	Operational definition
	• Pneumococcal polysaccharide • Hepatitis A • Hepatitis B • Meningococcal conjugate (MenACWY) and serogroup B meningococcal (MenB) • Haemophilus influenza type b	

Annex 3 Table A-3. Immunization history and Vaccine Co-administration CPT, HCPCS, and NDC Codes

Vaccine	Code Type	Code	Manufacturer/Descriptions
COVID-19	CPT	91300	Pfizer
		91305	Pfizer
		91307	Pfizer
		91308	Pfizer
		91315	Pfizer (bivalent)
		91317	Pfizer (bivalent)
		91312	Pfizer (bivalent)
		91301	Moderna
		91306	Moderna
		91309	Moderna
		91311	Moderna
		91314	Moderna (bivalent)
		91316	Moderna (bivalent)
		91313	Moderna (bivalent)
		91302	AstraZeneca
		91303	Janssen
		91304	Novavax
	HCPCS	0001A	Pfizer
		0002A	Pfizer
		0003A	Pfizer
		0004A	Pfizer
		0051A	Pfizer
		0052A	Pfizer
		0053A	Pfizer
		0054A	Pfizer
		0071A	Pfizer
		0072A	Pfizer
		0073A	Pfizer
		0074A	Pfizer
		0081A	Pfizer
		0082A	Pfizer
		0083A	Pfizer
		0121A	Pfizer (bivalent)
		0124A	Pfizer (bivalent)
		0151A	Pfizer (bivalent)
		0154A	Pfizer (bivalent)
		0171A	Pfizer (bivalent)
		0172A	Pfizer (bivalent)
		0173A	Pfizer (bivalent)

Vaccine	Code Type	Code	Manufacturer/Descriptions
		0174A	Pfizer (bivalent)
		0011A	Moderna
		0012A	Moderna
		0013A	Moderna
		0064A	Moderna
		0091A	Moderna
		0092A	Moderna
		0093A	Moderna
		0094A	Moderna
		0111A	Moderna
		0112A	Moderna
		0113A	Moderna
		0134A	Moderna (bivalent)
		0141A	Moderna (bivalent)
		0142A	Moderna (bivalent)
		0144A	Moderna (bivalent)
		0164A	Moderna (bivalent)
		0021A	AstraZeneca
		0022A	AstraZeneca
		0031A	Janssen
		0034A	Janssen
		0041A	Novavax
		0042A	Novavax
		0044A	Novavax
		M0201[b]	Covid-19 vaccine administration inside a patient's home; reported only once per individual home per date of service when only covid-19 vaccine administration is performed at the patient's home
	NDC	5926710001	Pfizer
		59267100001	Pfizer
		5926710002	Pfizer
		59267100002	Pfizer
		5926710003	Pfizer
		59267100003	Pfizer
		5926710251	Pfizer
		59267102501	Pfizer
		5926710253	Pfizer
		5926710254	Pfizer
		0069100001[a]	Pfizer
		0069100002[a]	Pfizer

Vaccine	Code Type	Code	Manufacturer/Descriptions
		0069100003[a]	Pfizer
		0069202510	Pfizer
		0069202525	Pfizer
		0069202501	Pfizer
		5926710551	Pfizer
		59267105501	Pfizer
		59267102503	Pfizer
		5926710252	Pfizer
		59267102502	Pfizer
		59267102504	Pfizer
		00069202501	Pfizer
		00069202510	Pfizer
		00069202525	Pfizer
		5926700781	Pfizer
		59267007801	Pfizer
		5926700784	Pfizer
		59267007804	Pfizer
		5926710552	Pfizer
		59267105502	Pfizer
		5926710554	Pfizer
		59267105504	Pfizer
		5926705651	Pfizer (bivalent)
		59267056501	Pfizer (bivalent)
		5926705652	Pfizer (bivalent)
		59267056502	Pfizer (bivalent)
		5926706091	Pfizer (bivalent)
		59267060901	Pfizer (bivalent)
		5926706092	Pfizer (bivalent)
		59267060902	Pfizer (bivalent)
		5926703042	Pfizer (bivalent)
		59267030402	Pfizer (bivalent)
		5926703041	Pfizer (bivalent)
		59267030401	Pfizer (bivalent)
		5926714042	Pfizer (bivalent)
		59267140402	Pfizer (bivalent)
		5926714041	Pfizer (bivalent)
		59267140401	Pfizer (bivalent)
		0310122210	AstraZeneca
		0310122215	AstraZeneca
		00310122210	AstraZeneca
		00310122215	AstraZeneca

Vaccine	Code Type	Code	Manufacturer/Descriptions
		59676058005	Janssen
		59676058015	Janssen
		5967658005	Janssen
		5967658015	Janssen
		80631010210	Novavax
		8063110210	Novavax
		80631010201	Novavax
		8063110201	Novavax
		80631100001	Novavax
		8063110010	Novavax
		80631010010	Novavax
		8063110001	Novavax
		80631010001	Novavax
		8077710099	Moderna
		80777010099	Moderna
		8077710098[a]	Moderna
		80777010098[a]	Moderna
		80777027705[a]	Moderna
		8077727705[a]	Moderna
		80777027799[a]	Moderna
		8077727799[a]	Moderna
		80777027905	Moderna
		8077727905	Moderna
		80777027999	Moderna
		8077727999	Moderna
		8077710015[a]	Moderna
		80777027310	Moderna
		80777027399	Moderna
		8077727398	Moderna
		80777027398	Moderna
		8077727315	Moderna
		80777027315	Moderna
		8077710011	Moderna
		80777010011	Moderna
		8077727599	Moderna
		80777027599	Moderna
		8077727505	Moderna
		80777027505	Moderna
		8077727310	Moderna
		8077727399	Moderna
		80777028302	Moderna (bivalent)

Vaccine	Code Type	Code	Manufacturer/Descriptions
		8077728302	Moderna (bivalent)
		80777028399	Moderna (bivalent)
		8077728399	Moderna (bivalent)
		8077728299	Moderna (bivalent)
		80777028299	Moderna (bivalent)
		8077728205	Moderna (bivalent)
		80777028205	Moderna (bivalent)
Seasonal Influenza[c]	CPT	90470	H1N1 Immunization administration (intramuscular, intranasal), including counseling when performed
	CPT	90630	Vaccine for influenza for injection into skin, quadrivalent, preservative free
	CPT	90653	Vaccine for influenza for injection into muscle, inactivated, subunit, adjuvanted
	CPT	90654	Vaccine for influenza injection into skin, trivalent, preservative free
	CPT	90655	Vaccine for influenza for administration into muscle, 0.25 ml dosage, trivalent, split virus, preservative free
	CPT	90656	Vaccine for influenza for administration into muscle, 0.5 ml dosage, trivalent, preservative free
	CPT	90657	Vaccine for influenza for administration into muscle, 0.25 ml dosage, trivalent (pediatric use)
	CPT	90658	Vaccine for influenza for administration into muscle, 0.5 ml dosage, trivalent
	CPT	90659	Influenza virus vaccine, whole virus, for intramuscular or jet injection use
	CPT	90660	Vaccine for influenza for nasal administration, trivalent
	CPT	90661	Vaccine for influenza for administration into muscle, 0.5 ml dosage, trivalent, cell culture-based, preservative and antibiotic free
	CPT	90662	Vaccine for influenza for injection into muscle, split virus, enhanced immunogenicity via increased antigen content
	CPT	90663	Influenza virus vaccine, pandemic formulation, H1N1

Vaccine	Code Type	Code	Manufacturer/Descriptions
	CPT	90664	Vaccine for influenza for nasal administration, pandemic formulation
	CPT	90666	Vaccine for influenza for injection into muscle, pandemic formulation
	CPT	90667	Vaccine for influenza for injection into muscle, pandemic formulation
	CPT	90668	Vaccine for influenza for injection into muscle, pandemic formulation
	CPT	90672	Vaccine for influenza for nasal administration, tetravalent
	CPT	90673	Vaccine for influenza administered into muscle, preservative and antibiotic free, trivalent, recombinant DNA, hemagglutinin (HA) protein only
	CPT	90674	Vaccine for influenza for administration into muscle, 0.5 ml dosage, tetravalent, cell-culture based, preservative and antibiotic free
	CPT	90682	Influenza virus vaccine, quadrivalent (RIV4), derived from recombinant DNA, hemagglutinin (HA) protein only, preservative and antibiotic free
	CPT	90685	Vaccine for influenza for administration into muscle, 0.25 ml dosage, quadrivalent, preservative free
	CPT	90686	Vaccine for influenza for administration into muscle, 0.5 ml dosage, quadrivalent, preservative free
	CPT	90687	Vaccine for influenza for administration into muscle, 0.25 ml dosage, quadrivalent (pediatric use)
	CPT	90688	Vaccine for influenza for administration into muscle, 0.5 ml dosage, quadrivalent
	CPT	90694	Vaccine for influenza for administration into muscle, 0.5 ml dosage, quadrivalent, inactivated, adjuvanted, preservative free
	CPT	90724	Immunization, active; influenza virus vaccine
	CPT	90756	Influenza virus vaccine, quadrivalent (ccIIV4), derived from cell cultures, subunit, antibiotic free
	HCPCS	G0008	Administration of influenza virus vaccine

Vaccine	Code Type	Code	Manufacturer/Descriptions
	HCPCS	G9141	Influenza a (H1N1) immunization administration (includes the physician counseling the patient/family)
	HCPCS	G9142	Influenza a (H1N1) vaccine, any route of administration
	HCPCS	Q2033	Influenza vaccine, recombinant hemagglutinin antigens, for intramuscular use (flublok)
	HCPCS	Q2034	Influenza virus vaccine, split virus, for intramuscular use (agriflu)
	HCPCS	Q2035	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use (afluria)
	HCPCS	Q2036	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use (flulaval)
	HCPCS	Q2037	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use (fluvirin)
	HCPCS	Q2038	Influenza virus vaccine, split virus, when administered to individuals 3 years of age and older, for intramuscular use (fluzone)
	HCPCS	Q2039	Influenza virus vaccine, not otherwise specified
	NDC	70461031803	FLUCELVAX
	NDC	70461031804	FLUCELVAX
	NDC	70461041810	FLUCELVAX
	NDC	70461041811	FLUCELVAX
	NDC	33332051925	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	33332062910	Influenza virus vaccine (IIV), pandemic formulation, split virus, for intramuscular use
	NDC	66521020010	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	49281065090	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	49281065070	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	49281065050	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	49281065025	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	49281065010	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	66521020002	Influenza virus vaccine (IIV), pandemic formulation, split virus, for intramuscular use
	NDC	49281064015	Influenza virus vaccine (IIV), pandemic formulation, split virus, for intramuscular use
	NDC	66019020010	Influenza virus vaccine, live (LAIV), pandemic formulation, for intranasal use
	NDC	66019020001	Influenza virus vaccine, live (LAIV), pandemic formulation, for intranasal use
	NDC	76420048301	Influenza virus vaccine, quadrivalent (IIV4), split virus, preservative free, 0.5 mL dosage, for int
	NDC	76420048201	Influenza virus vaccine, quadrivalent (IIV4), split virus, preservative free, 0.5 mL dosage, for int
	NDC	58160080815	Influenza A (H5N1) Monovalent Vaccine, Adjuvanted
	NDC	58160080401	Influenza A (H5N1) Monovalent Vaccine, Adjuvanted
	NDC	58160080202	Influenza A (H5N1) Monovalent Vaccine, Adjuvanted
	NDC	33332051901	Influenza virus vaccine (IIV), pandemic formulation, split virus, preservative free, for intramuscul
	NDC	19515081652	Flulaval Quadrivalent
	NDC	19515084511	FLULAVAL
	NDC	19515085052	FLULAVAL
	NDC	19515089711	Flulaval Quadrivalent
	NDC	19515090011	Flulaval Quadrivalent

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	19515090152	Flulaval Quadrivalent
	NDC	19515090652	Flulaval Quadrivalent
	NDC	19515090952	Flulaval Quadrivalent
	NDC	33332001801	AFLURIA
	NDC	33332011810	AFLURIA
	NDC	33332021920	Afluria Quadrivalent
	NDC	33332022020	Afluria Quadrivalent
	NDC	33332031801	AFLURIA QUADRIVALENT
	NDC	33332031901	Afluria Quadrivalent
	NDC	33332032001	Afluria Quadrivalent
	NDC	33332041610	AFLURIA QUADRIVALENT
	NDC	33332041810	AFLURIA QUADRIVALENT
	NDC	33332041910	Afluria Quadrivalent
	NDC	33332042010	Afluria Quadrivalent
	NDC	49281012065	FLUZONE High-Dose Quadrivalent Northern Hemisphere
	NDC	49281018125	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281032050	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281033615	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281040565	FLUZONE High-Dose
	NDC	49281041810	FLUZONE QUADRIVALENT
	NDC	49281041850	FLUZONE QUADRIVALENT
	NDC	49281041910	FLUZONE QUADRIVALENT
	NDC	49281041950	FLUZONE QUADRIVALENT
	NDC	49281042010	FLUZONE QUADRIVALENT
	NDC	49281042050	FLUZONE QUADRIVALENT
	NDC	49281051825	FLUZONE QUADRIVALENT
	NDC	49281051925	FLUZONE QUADRIVALENT
	NDC	49281052025	FLUZONE QUADRIVALENT
	NDC	49281062915	FLUZONE QUADRIVALENT
	NDC	49281063115	FLUZONE QUADRIVALENT
	NDC	49281063315	FLUZONE QUADRIVALENT
	NDC	49281071810	Flublok Quadrivalent
	NDC	49281071910	Flublok Quadrivalent
	NDC	49281072010	Flublok Quadrivalent Northern Hemisphere
	NDC	58160088352	FLUARIX
	NDC	58160088552	FLUARIX QUADRIVALENT

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	58160089652	FLUARIX QUADRIVALENT
	NDC	58160089852	FLUARIX QUADRIVALENT
	NDC	63851061301	FLUCELVAX
	NDC	66019030510	FluMist Quadrivalent
	NDC	66019030610	FluMist Quadrivalent
	NDC	66019030710	FluMist Quadrivalent
	NDC	70461001803	FLUAD
	NDC	70461001903	FLUAD
	NDC	70461002003	FLUAD
	NDC	70461012003	FLUAD QUADRIVALENT
	NDC	70461031903	FLUCELVAX QUADRIVALENT
	NDC	70461032003	FLUCELVAX QUADRIVALENT
	NDC	70461041910	FLUCELVAX QUADRIVALENT
	NDC	70461042010	FLUCELVAX QUADRIVALENT
	NDC	19515080852	Flulaval Quadrivalent - 2022-23 Outer Carton
	NDC	49281037950	FLUZONE High-Dose Quadrivalent Southern Hemisphere
	NDC	49281035515	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281042210	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23
	NDC	49281032350	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281042250	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23 Syringe
	NDC	33332042210	Afluria Quadrivalent - 2022-23
	NDC	49281063715	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23
	NDC	49281032250	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE - 2022-23
	NDC	58160089052	FLUARIX QUADRIVALENT - 2022-23
	NDC	70461012203	FLUAD QUADRIVALENT - 2022-23
	NDC	70461042210	Flucelvax Quadrivalent - 2022-23
	NDC	33332032203	Afluria Quadrivalent - 2022-23
	NDC	49281012265	FLUZONE High-Dose Quadrivalent Northern Hemisphere - 2022-23
	NDC	70461032203	Flucelvax Quadrivalent - 2022-23
	NDC	49281072210	Flublok Quadrivalent Northern Hemisphere - 2022-23

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	49281033915	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE - 2022-2023
	NDC	19515080841	Flulaval Quadrivalent - 2022-23 Outer Carton
	NDC	49281037988	FLUZONE High-Dose Quadrivalent Southern Hemisphere
	NDC	49281035578	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281042258	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23
	NDC	49281032388	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE
	NDC	49281042288	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23 Syringe
	NDC	33332042211	Afluria Quadrivalent - 2022-23
	NDC	49281063778	FLUZONE QUADRIVALENT NORTHERN HEMISPHERE - 2022-23
	NDC	49281032288	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE - 2022-23
	NDC	58160089041	FLUARIX QUADRIVALENT - 2022-23
	NDC	70461012204	FLUAD QUADRIVALENT - 2022-23
	NDC	70461042211	Flucelvax Quadrivalent - 2022-23
	NDC	33332032204	Afluria Quadrivalent - 2022-23
	NDC	49281012288	FLUZONE High-Dose Quadrivalent Northern Hemisphere - 2022-23
	NDC	70461032204	Flucelvax Quadrivalent - 2022-23
	NDC	49281072288	Flublok Quadrivalent Northern Hemisphere - 2022-23
	NDC	49281033978	FLUZONE QUADRIVALENT SOUTHERN HEMISPHERE - 2022-2023
Tetanus diphtheria and pertussis (Tdap or Td)	CPT	90714	Tetanus and diphtheria toxoids adsorbed (Td), preservative free, when administered to individuals 7 years or older, for intramuscular use
	CPT	90715	Tdap administered to individuals 7 years or older, for intramuscular use
	CPT	90718	Tetanus and diphtheria toxoids (Td) adsorbed when administered to individuals 7 years or older, for intramuscular use
	NDC	49281040015	Adacel
	NDC	49281040088	Adacel

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	14362011104	TDVAX
	NDC	14362011103	TDVAX
	NDC	49281021515	TENIVAC
	NDC	49281021588	TENIVAC
	NDC	49281040005	Adacel
	NDC	58160084252	BOOSTRIX
	NDC	49281029183	DECAVAC
	NDC	17478013101	Tetanus and Diphtheria Toxoids Adsorbed
	NDC	49281029110	DECAVAC
	NDC	21695041301	Tetanus and Diphtheria Toxoids Adsorbed
	NDC	58160084234	BOOSTRIX
	NDC	49281040010	Adacel
	NDC	49281040020	Adacel
	NDC	49281021510	TENIVAC
	NDC	58160084251	BOOSTRIX
	NDC	13533013101	TDVAX
	NDC	58160084211	BOOSTRIX
	NDC	00006413341	Tetanus and Diphtheria Toxoids Adsorbed
	NDC	49281040058	Adacel
	NDC	58160084243	BOOSTRIX
	NDC	17478013100	Tetanus and Diphtheria Toxoids Adsorbed
	NDC	58160084205	BOOSTRIX
	NDC	49281040089	Adacel
	NDC	49281021558	TENIVAC
	NDC	58160084241	BOOSTRIX
	NDC	13533013100	TDVAX
	NDC	58160084201	BOOSTRIX
	NDC	00006413301	Tetanus and Diphtheria Toxoids Adsorbed
Chickenpox (Varicella)	CPT	90396	Varicella-zoster immune globulin, human, for intramuscular use
	CPT	90716	Varicella virus vaccine, live, for subcutaneous use
	NDC	00006482700	VARIVAX
	NDC	00006482600	VARIVAX
	NDC	00006482701	VARIVAX
	NDC	00006482601	VARIVAX
Shingles (Herpes Zoster recombinant and/or live)	CPT	90396	Varicella-zoster immune globulin, human, for intramuscular use
	CPT	90736	Zoster (shingles) vaccine (HZV), live, for subcutaneous injection

Vaccine	Code Type	Code	Manufacturer/Descriptions
	CPT	90750	Zoster (shingles) vaccine (HZV), recombinant, subunit, adjuvanted, for intramuscular use
	NDC	00006496300	ZOSTAVAX
	NDC	00006496341	ZOSTAVAX
	NDC	58160081912	Shingrix
	NDC	58160082311	Shingrix
	NDC	50090514700	Shingrix
	NDC	00006496301	ZOSTAVAX
	NDC	58160082801	Shingrix
	NDC	58160082803	Shingrix
Pneumococcal conjugate	CPT	90669	Pneumococcal conjugate vaccine, 7 valent, for intramuscular use
	CPT	90670	Pneumococcal conjugate vaccine, 13 valent (PCV13), for intramuscular use
	HCPCS	G0009	Administration of pneumococcal vaccine
	HCPCS	G8864	Code for Pneumococcal vaccine administered or previously received
	NDC	00005197105	PREVNAR 13
	NDC	00005197104	PREVNAR 13
	NDC	00005197102	PREVNAR 13
	NDC	00006432902	VAXNEUVANCE
	NDC	00006432903	VAXNEUVANCE
	NDC	00005200010	Prevnar 20
	NDC	00005197050	Prevnar
	NDC	00005200002	Prevnar 20
	NDC	50090602600	PREVNAR 20
	NDC	00005197101	PREVNAR 13
	NDC	00006432901	VAXNEUVANCE
	NDC	00005200001	Prevnar 20
	NDC	00005197049	Prevnar
	NDC	50090602601	PREVNAR 20
Pneumococcal polysaccharide	CPT	90732	Pneumococcal polysaccharide vaccine, 23-valent (PPSV23), adult or immunosuppressed patient dosage, when administered to individuals 2 years or older, for subcutaneous or intramuscular use
	NDC	00006473900	PNEUMOVAX 23
	NDC	00006483703	PNEUMOVAX 23
	NDC	00006494300	PNEUMOVAX 23
	NDC	54868432000	PNEUMOVAX 23

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	54868333901	PNEUMOVAX 23
	NDC	00006483702	PNEUMOVAX 23
	NDC	00006473901	PNEUMOVAX 23
	NDC	00006483701	PNEUMOVAX 23
	NDC	00006494301	PNEUMOVAX 23
	NDC	54868432009	PNEUMOVAX 23
	NDC	54868333909	PNEUMOVAX 23
Hepatitis A	CPT	90632	Hepatitis A vaccine, adult dosage, for intramuscular use
	CPT	90730	Hepatitis A vaccine
	CPT	90636	Hepatitis A and hepatitis B vaccine (HepA-HepB), adult dosage, for intramuscular use
	NDC	58160081552	TWINRIX
	NDC	00006484100	VAQTA
	NDC	58160081534	TWINRIX
	NDC	58160082652	HAVRIX
	NDC	58160081511	TWINRIX
	NDC	58160082611	HAVRIX
	NDC	58160082634	HAVRIX
	NDC	55045384101	HAVRIX
	NDC	00006409609	VAQTA
	NDC	00006409602	VAQTA
	NDC	00006484141	VAQTA
	NDC	50090150200	HAVRIX
	NDC	58160081548	TWINRIX
	NDC	58160081546	TWINRIX
	NDC	58160081543	TWINRIX
	NDC	00006484101	VAQTA
	NDC	58160081505	TWINRIX
	NDC	58160082643	HAVRIX
	NDC	58160081501	TWINRIX
	NDC	58160082601	HAVRIX
	NDC	58160082605	HAVRIX
	NDC	00006409601	VAQTA
	NDC	50090150209	HAVRIX
	NDC	58160081541	TWINRIX
Hepatitis B	CPT	90371	Hepatitis B immune globulin (HBIg), human, for intramuscular use
	CPT	90739	Hepatitis B vaccine (HepB), adult dosage, 2 dose schedule, for intramuscular use

Vaccine	Code Type	Code	Manufacturer/Descriptions
	CPT	90740	Hepatitis B vaccine (HepB), dialysis or immunosuppressed patient dosage, 3 dose schedule, for intramuscular use
	CPT	90746	Hepatitis B vaccine (HepB), adult dosage, 3 dose schedule, for intramuscular use
	CPT	90747	Hepatitis B vaccine (HepB), dialysis or immunosuppressed patient dosage, 4 dose schedule, for intramuscular use
	HCPCS	G0010	Administration of Hepatitis B vaccine
	NDC	00006499200	RECOMBIVAX HB
	NDC	00006409402	RECOMBIVAX HB
	NDC	00006499541	RECOMBIVAX HB
	NDC	58160082134	ENGERIX-B
	NDC	00006499500	RECOMBIVAX HB
	NDC	00006409409	RECOMBIVAX HB
	NDC	58160082152	ENGERIX-B
	NDC	54868073400	ENGERIX-B
	NDC	58160082111	ENGERIX-B
	NDC	54868221900	RECOMBIVAX HB
	NDC	54868221901	RECOMBIVAX HB
	NDC	00006499201	RECOMBIVAX HB
	NDC	00006409401	RECOMBIVAX HB
	NDC	00006499501	RECOMBIVAX HB
	NDC	58160082105	ENGERIX-B
	NDC	58160082143	ENGERIX-B
	NDC	58160082101	ENGERIX-B
	NDC	50090346900	HEPLISAV-B
	NDC	43528000305	HEPLISAV-B
	NDC	75052000110	PREHEVBRIO
	NDC	43528000205	HEPLISAV-B
	NDC	50090346909	HEPLISAV-B
	NDC	43528000301	HEPLISAV-B
	NDC	75052000101	PREHEVBRIO
	NDC	43528000201	HEPLISAV-B
Meningococcal conjugate (MenACWY) and serogroup B meningococcal (MenB)	CPT	90619	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, tetanus toxoid carrier (MenACWY-TT), for intramuscular use
	CPT	90620	Meningococcal recombinant protein and outer membrane vesicle vaccine, serogroup B (MenB-4C), 2 dose schedule, for intramuscular use

Vaccine	Code Type	Code	Manufacturer/Descriptions
	CPT	90621	Meningococcal recombinant lipoprotein vaccine, serogroup B (MenB-FHbp), 2 or 3 dose schedule, for intramuscular use
	CPT	90733	Meningococcal polysaccharide vaccine, serogroups A, C, Y, W-135, quadrivalent (MPSV4), for subcutaneous use 90734, Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, diphtheria toxoid carrier (MenACWY-D) or CRM197 carrier (MenACWY-CRM), for intramuscular use
	CPT	90734	Meningococcal conjugate vaccine, serogroups A, C, Y and W-135 (tetravalent), for intramuscular use
	NDC	49281048991	MENOMUNE - A/C/Y/W-135 COMBINED
	NDC	49281048901	MENOMUNE - A/C/Y/W-135 COMBINED
	NDC	49281048878	MENOMUNE - A/C/Y/W-135 COMBINED
	NDC	49281048758	MENOMUNE - A/C/Y/W-135 COMBINED
	NDC	49281059005	MenQuadfi
	NDC	50090618000	MENQUADFI
	NDC	49281059058	MenQuadfi
	NDC	50090618001	MENQUADFI
Haemophilus influenza type b	CPT	90645	Hemophilus influenza b vaccine (Hib), HbOC conjugate (4 dose schedule), for intramuscular use
	CPT	90646	Hemophilus influenza b vaccine (Hib), PRP-D conjugate, for booster use only, intramuscular use
	CPT	90647	Haemophilus influenzae type b vaccine (Hib), PRP-OMP conjugate, 3 dose schedule, for intramuscular use
	CPT	90648	Haemophilus influenzae type b vaccine (Hib), PRP-T conjugate, 4 dose schedule, for intramuscular use
	CPT	90737	Hemophilus influenza B
	CPT	90748	Hepatitis B and Haemophilus influenzae type b vaccine (Hib-HepB), for intramuscular use

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	49281051005	PENTACEL
	NDC	58160080111	Menhibrix
	NDC	58160080605	HIBERIX
	NDC	58160081811	Hiberix
	NDC	49281054503	ActHIB
	NDC	63361024315	VAXELIS
	NDC	58160080905	MENHIBRIX
	NDC	49281051105	PENTACEL
	NDC	00006489700	PedvaxHIB
	NDC	49281054505	ActHIB
	NDC	63361024510	VAXELIS
	NDC	63361024310	VAXELIS
	NDC	00006489800	COMVAX
	NDC	58160081605	Hiberix
	NDC	49281056005	PENTACEL
	NDC	49281054515	PENTACEL
	NDC	49281054858	PENTACEL
	NDC	58160080901	Menhibrix
	NDC	58160080601	HIBERIX
	NDC	49281054758	ActHIB
	NDC	63361024388	VAXELIS
	NDC	49281056101	PENTACEL
	NDC	49281054458	PENTACEL
	NDC	00006489701	PedvaxHIB
	NDC	63361024558	VAXELIS
	NDC	63361024358	VAXELIS
	NDC	00006489801	COMVAX
	NDC	58160081601	Hiberix
Other RSV vaccines	CPT	90679	Respiratory syncytial virus vaccine, preF, recombinant, subunit, adjuvanted, for intramuscular use (AREXVY)
	CPT	90683	Respiratory syncytial virus vaccine, mRNA lipid nanoparticles, for intramuscular use
	NDC	58160084811	AREXVY
	NDC	58160072303	AREXVY
	NDC	58160074403	AREXVY
	NDC	80777034561	mRESVIA
	NDC	80777034563	mRESVIA
	NDC	80777034596	mRESVIA
	NDC	80777034590	mRESVIA

Vaccine	Code Type	Code	Manufacturer/Descriptions
	NDC	80777034501	mRESVIA

Notes:
a Codes that will not be manufactured or not available in the near term according to CDC Immunization Information Systems (IIS) - COVID-19 Vaccine Related Codes (https://www.cdc.gov/vaccines/programs/iis/COVID-19-related-codes.html)
b COVID-19 vaccine home administration. This code must be accompanied by the appropriate CPT code for the product.
c Additional codes will be added for influenza vaccines as they become available.

Codes for concomitant medications will be provided in the SAP.

Annex 3 Table A-4. Conscious Sedation and General Anesthesia CPT and ICD-10-PCS codes

Type of drug induced prior to surgery	Code Type	Code	Description
Conscious Sedation	CPT	99151-99157	Under Moderate (Conscious) Sedation
General Anesthesia	CPT	00100-01999	Anesthesia
	ICD-10-PCS	3E00XBZ	Introduction of Anesthetic Agent into Skin and Mucous Membranes, External Approach
		3E013BZ	Introduction of Anesthetic Agent into Subcutaneous Tissue, Percutaneous Approach
		3E023BZ	Introduction of Anesthetic Agent into Muscle, Percutaneous Approach
		3E030FZ	Introduction of Intracirculatory Anesthetic into Peripheral Vein, Open Approach
		3E033FZ	Introduction of Intracirculatory Anesthetic into Peripheral Vein, Percutaneous Approach
		3E040FZ	Introduction of Intracirculatory Anesthetic into Central Vein, Open Approach
		3E043FZ	Introduction of Intracirculatory Anesthetic into Central Vein, Percutaneous Approach
		3E050FZ	Introduction of Intracirculatory Anesthetic into Peripheral Artery, Open Approach
		3E053FZ	Introduction of Intracirculatory Anesthetic into Peripheral Artery, Percutaneous Approach
		3E060FZ	Introduction of Intracirculatory Anesthetic into Central Artery, Open Approach
		3E063FZ	Introduction of Intracirculatory Anesthetic into Central Artery, Percutaneous Approach
		3E093BZ	Introduction of Anesthetic Agent into Nose, Percutaneous Approach

Type of drug induced prior to surgery	Code Type	Code	Description
		3E097BZ	Introduction of Anesthetic Agent into Nose, Via Natural or Artificial Opening
		3E09XBZ	Introduction of Anesthetic Agent into Nose, External Approach
		3E0B3BZ	Introduction of Anesthetic Agent into Ear, Percutaneous Approach
		3E0B7BZ	Introduction of Anesthetic Agent into Ear, Via Natural or Artificial Opening
		3E0BXBZ	Introduction of Anesthetic Agent into Ear, External Approach
		3E0C3BZ	Introduction of Anesthetic Agent into Eye, Percutaneous Approach
		3E0C7BZ	Introduction of Anesthetic Agent into Eye, Via Natural or Artificial Opening
		3E0CXBZ	Introduction of Anesthetic Agent into Eye, External Approach
		3E0D3BZ	Introduction of Anesthetic Agent into Mouth and Pharynx, Percutaneous Approach
		3E0D7BZ	Introduction of Anesthetic Agent into Mouth and Pharynx, Via Natural or Artificial Opening
		3E0DXBZ	Introduction of Anesthetic Agent into Mouth and Pharynx, External Approach
		3E0E3BZ	Introduction of Anesthetic Agent into Products of Conception, Percutaneous Approach
		3E0E7BZ	Introduction of Anesthetic Agent into Products of Conception, Via Natural or Artificial Opening
		3E0E8BZ	Introduction of Anesthetic Agent into Products of Conception, Via Natural or Artificial Opening Endoscopic
		3E0F3BZ	Introduction of Anesthetic Agent into Respiratory Tract, Percutaneous Approach

Type of drug induced prior to surgery	Code Type	Code	Description
		3E0F7BZ	Introduction of Anesthetic Agent into Respiratory Tract, Via Natural or Artificial Opening
		3E0F7DZ	Introduction of Inhalation Anesthetic into Respiratory Tract, Via Natural or Artificial Opening
		3E0F8BZ	Introduction of Anesthetic Agent into Respiratory Tract, Via Natural or Artificial Opening Endoscopic
		3E0F8DZ	Introduction of Inhalation Anesthetic into Respiratory Tract, Via Natural or Artificial Opening Endoscopic
		3E0G3BZ	Introduction of Anesthetic Agent into Upper GI, Percutaneous Approach
		3E0G7BZ	Introduction of Anesthetic Agent into Upper GI, Via Natural or Artificial Opening
		3E0G8BZ	Introduction of Anesthetic Agent into Upper GI, Via Natural or Artificial Opening Endoscopic
		3E0H3BZ	Introduction of Anesthetic Agent into Lower GI, Percutaneous Approach
		3E0H7BZ	Introduction of Anesthetic Agent into Lower GI, Via Natural or Artificial Opening
		3E0H8BZ	Introduction of Anesthetic Agent into Lower GI, Via Natural or Artificial Opening Endoscopic
		3E0J3BZ	Introduction of Anesthetic Agent into Biliary and Pancreatic Tract, Percutaneous Approach
		3E0J7BZ	Introduction of Anesthetic Agent into Biliary and Pancreatic Tract, Via Natural or Artificial Opening
		3E0J8BZ	Introduction of Anesthetic Agent into Biliary and Pancreatic Tract, Via Natural or Artificial Opening Endoscopic

Type of drug induced prior to surgery	Code Type	Code	Description
		3E0K3BZ	Introduction of Anesthetic Agent into Genitourinary Tract, Percutaneous Approach
		3E0K7BZ	Introduction of Anesthetic Agent into Genitourinary Tract, Via Natural or Artificial Opening
		3E0K8BZ	Introduction of Anesthetic Agent into Genitourinary Tract, Via Natural or Artificial Opening Endoscopic
		3E0L3BZ	Introduction of Anesthetic Agent into Pleural Cavity, Percutaneous Approach
		3E0M3BZ	Introduction of Anesthetic Agent into Peritoneal Cavity, Percutaneous Approach
		3E0N3BZ	Introduction of Anesthetic Agent into Male Reproductive, Percutaneous Approach
		3E0N7BZ	Introduction of Anesthetic Agent into Male Reproductive, Via Natural or Artificial Opening
		3E0N8BZ	Introduction of Anesthetic Agent into Male Reproductive, Via Natural or Artificial Opening Endoscopic
		3E0P3BZ	Introduction of Anesthetic Agent into Female Reproductive, Percutaneous Approach
		3E0P7BZ	Introduction of Anesthetic Agent into Female Reproductive, Via Natural or Artificial Opening
		3E0P8BZ	Introduction of Anesthetic Agent into Female Reproductive, Via Natural or Artificial Opening Endoscopic
		3E0Q0BZ	Introduction of Anesthetic Agent into Cranial Cavity and Brain, Open Approach

Type of drug induced prior to surgery	Code Type	Code	Description
		3E0Q3BZ	Introduction of Anesthetic Agent into Cranial Cavity and Brain, Percutaneous Approach
		3E0R3BZ	Introduction of Anesthetic Agent into Spinal Canal, Percutaneous Approach
		3E0S3BZ	Introduction of Anesthetic Agent into Epidural Space, Percutaneous Approach
		3E0T3BZ	Introduction of Anesthetic Agent into Peripheral Nerves and Plexi, Percutaneous Approach
		3E0U3BZ	Introduction of Anesthetic Agent into Joints, Percutaneous Approach
		3E0V3BZ	Introduction of Anesthetic Agent into Bones, Percutaneous Approach
		3E0W3BZ	Introduction of Anesthetic Agent into Lymphatics, Percutaneous Approach
		3E0X3BZ	Introduction of Anesthetic Agent into Cranial Nerves, Percutaneous Approach
		3E0Y3BZ	Introduction of Anesthetic Agent into Pericardial Cavity, Percutaneous Approach
		8E0H300	Acupuncture using Anesthesia

Document Approval Record

Document Name:	C3671031_RSV VACCINE PROTOCOL AMENDMENT 5 V6.0_15APR 2026
Document Title:	C3671031_RSV VACCINE PROTOCOL AMENDMENT 5 V6.0_15APR 2026

Signed By:	Date(GMT)	Signing Capacity
Younus, Muhammad	17-Apr-2026 12:28:29	Final Approval
De Bernardi, Barbara	20-Apr-2026 07:24:53	EUQPPV Approval