Statistical Analysis Plan (SAP) for BNT162b2 Vaccine Effectiveness (VE)

Version: 1

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1. AMENDMENTS FROM PREVIOUS VERSION(S)

None.

2. INTRODUCTION

BNT162b2 is a nucleoside-modified mRNA vaccine administered as 2 doses 21 days apart that encodes the full-length, membrane-anchored S glycoprotein of SARS-CoV-2 with two introduced proline mutations to lock it in the prefusion conformation. It was co-developed by BioNTech SE and Pfizer, Inc. The vaccine showed an acceptable safety profile in a Phase 1/2 study. In a Phase 3 trial, the vaccine was tolerable and demonstrated 95% efficacy ≥7 days after second dose against COVID-19 in persons without current or prior SARS-CoV-2 infection[2].

Pfizer-BioNTech COVID-19 Vaccine is granted approval by FDA for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older (on 23 Aug 2021) and has been authorized for use under an Emergency Use Authorization (EUA) for individuals 5-15 and as a booster dose for individuals 18 and over. However, data confirming the effectiveness of the vaccine outside of the controlled trial setting are still needed. To evaluate this in a real world setting, Pfizer has undertaken a research collaboration to study the vaccine effectiveness (VE) of BNT162b2 vaccine against acute respiratory illness requiring hospitalization due to SARS-CoV-2 infection with the following three external partners:

1. Kaiser Permanente Southern California (KPSC) [Study C4591014]

2. Emory University (Emory) [Study WI1235284]

3. Bristol University (Bristol) [Study WI255886]

While C4591014 was conducted as a Pfizer sponsored non-interventional study, studies from Emory and Bristol Universities were conducted as non Pfizer sponsored research collaborations with the respective institutions where the PI is the sponsor. As part of the post approval commitment under the EUA, Pfizer has a regulatory commitment to evaluate BNT162b2 vaccine effectiveness using real world data from these 3 protocols. Each of these three studies have other additional objectives and endpoints outside the scope of the regulatory commitment; however, a common objective in these three studies is to evaluate the VE of BNT162b2 vaccine using a Test Negative Design (TND). Full details of the primary, secondary, and exploratory objectives and their associated endpoints are described in greater detail within the respective protocols. For completeness and context, a brief description of the three protocols along with the COVID-19 related objectives and endpoints are described below within the respective sections of this Statistical Analysis Plan (SAP).

During the review and approval process of the regulatory commitment and the evolving authorizations and approvals, FDA has provided comments on the above three protocols necessitating amendments. FDA suggested to submit the amended protocols by the end of 2021 along with the SAPs. Since the primary objective is the same in all three protocols,

evaluating BNT162b2 VE using a TND, Pfizer is preparing and will be submitting a single SAP that covers the VE analyses for the above three protocols in response to the regulatory commitment. Further, the KPSC (C4591014) study will also use a full cohort design to evaluate BNT162b2 VE. Where necessary and appropriate, additional details of the study design, objectives, endpoints and analyses undertaken by KPSC using the full cohort design are also included in this SAP within each section for completeness. Additional analysis plans covering objectives that are not related to the BNT162b2 commitment may also be developed and maintained by the respective study teams.

Note that this SAP covers only the primary and secondary objectives/endpoints related to the regulatory commitment on BNT162b2. Other objectives and endpoints not related to the regulatory commitment will be described in the project specific SAPs.

Further, ad hoc or additional analyses related to BNT162b2 as insights emerge from the rapidly evolving environment will be documented according to the three respective institutional policies. Non-COVID endpoints and analyses beyond the ones documented within this SAP, if conducted, may be reported either in a separate addendum or within the final SAP at the end of each study separately for transparency.

3. STUDY DESIGN(S)

The study designs for each of the three protocols are described below in brief. For full details on these three study protocols, please refer to the individual protocols C4591014 (for KPSC), WI235284 (for Emory), and WI255886 (for Bristol), respectively.

3.1. KPSC Study C4591014 (CT-24 study) titled, "Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California"

This is a database analysis study of existing healthcare data; no patients will be actively enrolled.

This study will be conducted in the Kaiser Permanente Southern California system, a large integrated healthcare organization with over 4.7 million members who comprise a socioeconomically diverse and broadly representative population that reflects the racial/ethnic groups living in Southern California. As of May 14, 2021, KPSC has had over (b) (4) COVID-19 cases, approximately (b) (4) confirmed patients admitted to the hospital, and has vaccinated more than (b) (4) individuals. KPSC has two Regional Laboratories that process COVID-19 and other specimens. The central reference laboratories receive more than 50,000 specimens per day from the local laboratories and perform over 29 million tests annually. All laboratories undergo routine quality checks to meet or surpass accrediting body specifications.

Vaccine exposure for both study designs (TND and Cohort) considered in KPSC include initial vaccine series of 2 doses of BNT162b2 received with ≥7 days between receipt of the 2nd dose and the index date (e.g., admission); partially vaccinated, defined as 1 dose (only) of BNT162b2 received with ≥14 days between the receipt of the 1st dose and the event date; ever vaccinated, defined as ≥1 dose of BNT162b2 received with ≥14 days between the receipt of the 1st dose and the event date; and >2 doses of BNT162b2 received with ≥14 days

between the receipt of the last dose and the event date. The unexposed group will include individuals with no record of any COVID-19 vaccination at the time of the event and will serve as the reference group in the VE analyses. Additional VE analyses will compare those individuals receiving 2 doses to those receiving >2 doses. All data will be collected from KPSC electronic health records (EHRs).

Test Negative Design (TND)

A TND study will be used to evaluate the primary objective of this study, i.e., to assess effectiveness of 2 doses of Pfizer COVID vaccine >7 days after the second dose against hospitalization for ARI due to SARS-CoV-2 infection. It will include all KPSC patients meeting inclusion criteria admitted to the hospital with ARI after 14 December 2020 (date of first vaccinations at KPSC), and who had the results of a polymerase chain reaction (PCR) test for SARS-CoV-2. For the secondary objectives estimating VE against emergency department (ED) admission, the TND will include KPSC patients meeting inclusion criteria who present to the ED with (ARI after 14 December 2020 and who receive a PCR test for SARS-CoV-2. These populations will be used to evaluate additional secondary and exploratory objectives outlined in the TND proposed objectives, including VE of 1 dose, ≥1 dose, >2 doses and VE for important virus variants.

The index date will be defined as the date of hospitalization or ED admission. Patients can contribute more than one ARI event to the study if a subsequent ARI event for the same patient occurred >30 days after the previous ARI event.

Per KPSC clinical protocol, we expect that ED patients with ARI will be tested for COVID-19, and in the inpatient setting, all patients with or without ARI will get tested for COVID-19 (to be confirmed with preliminary data). VE will be estimated separately for prevention of hospitalization (primary outcome) and for prevention of ED presentation without hospitalization (a secondary outcome).

Full Cohort Design

A full cohort design will be used to further explore BNT162b2 VE in the KPSC population. The cohort study will include all KPSC members as of 14 December 2020 (date of first Pfizer vaccination at KPSC) meeting inclusion criteria for the analysis in accordance with regulatory authorizations. The exposure will be receipt of Pfizer's COVID-19 vaccine, with separate relative VEs estimated by number of doses received as stated in the TND above. In this full cohort design, a patient's vaccination status, and thus exposure, will change over time, with all patients entering the cohort as unvaccinated. The outcomes of interest may be COVID-19 associated hospitalization, ED admission, ICU admission, death, and outpatient COVID-19 diagnoses (without subsequent hospitalization within 14 days). As with the TND, the main outcome of interest will be hospitalization, and the VE of focus will be 2 doses of BNT162b2. The full cohort analysis will serve as a secondary analysis and will allow for comparability with the TND study. Cohort members will be censored at the time they disenroll from KPSC, die for reasons not related to COVID-19 (death not within the 30 days following a positive COVID-19 laboratory test), or receive any other newly licensed or

investigational COVID-19 vaccine or prophylactic agent other than Pfizer's COVID-19 vaccine.

To control for potential bias and confounding that may exist, individual-level and neighborhood-level factors will be collected for adjusted analyses. These are factors that have either been found to be important covariates in previous work, have been identified in other risk factor literature, or are variables that may be associated with the exposure as well as outcome (i.e. prior positive SARS-CoV-2 PCR test, etc.). Calendar time (days/ weeks/ months depending on data availability) as a covariate will be included in the models to adjust for phase in vaccine rollout, testing practice changes, social distancing impacts, surges, and potential changes in clinical treatments.

3.2. Emory Study WI235284 (CT-44 study) titled, "Respiratory Syncytial Virus (RSV) in Older Adults and Pregnant Women Study (ROAPS)"

Emory University, in collaboration with Pfizer, initiated a study in 2018: RSV in Older Adults and Pregnant Women Study (ROAPS) originally to evaluate the population-based incidence of RSV-related hospitalizations in pregnant women and adults ≥50 years of age. When SARS-CoV-2, the cause of COVID-19, emerged as a pathogen in humans in December 2019 and spread worldwide to become a pandemic over the next several months, ROAPS study team ended study enrollment for Season 2 in mid-March 2020. Early data from the Southern Hemisphere indicated that COVID-19 and the non-pharmaceutical interventions that had been implemented (e.g., face masks, social distancing) as well as potential changes in the willingness to seek healthcare, have had substantial impact upon the burden of influenza and the respiratory virus season. It was unknown whether such interventions might impact the influenza and RSV seasons in the US. In an effort to continue to gather data on RSV occurrence in the midst of the pandemic, Emory continued to perform prospective RSV and viral surveillance (e.g., SARS-CoV-2) among pregnant women, adults with CHF or COPD, and older adults requiring hospitalization during the pre-planned Season 3 (2020 – 2021); however, modified the approach to rely on data available via medical records and testing of standard of care specimens, rather than active enrollment, patient interviews and study-specific specimen collection, as had been done in Seasons 1 and 2. This change was made to mitigate the challenges that COVID-19 pandemic-related hospital precautions posed, including but not limited to, risk of transmission to research staff, potential shortages of personal protective equipment (PPE), and shortages of respiratory swabs.

Beginning in the summer of 2020, all admitted patients to EUH and EUHM are receiving standard of care (SOC) testing for SARS-CoV-2 using a molecular test upon hospital admission to EUH and EUHM. This provided a unique opportunity to evaluate the VE of COVID-19 vaccination with BNT162b2 against hospital admission due to ARI in adults and the protocol was further amended to include VE-related objectives and endpoints (included in main protocol as Sub-Study #6). The optimal methodology for VE studies uses the "test-negative design" (TND) in which vaccination rates among test-positive individuals ("cases") are compared with vaccination rates among test-negative individuals ("controls"). A test-negative case-control study design using a molecular assay is important in estimating VE accurately and rapidly, and can control for differences that might exist due to access to care.

Test-negative controls have been demonstrated to accurately estimate VE theoretically and through retrospective reanalysis of prospectively collected data of vaccine efficacy from randomized controlled trials. Vaccination status for all cases and controls enrolled in this study was collected through review of government-issued COVID-19 vaccination cards, medical records from relevant healthcare providers (e.g., primary care, public health department), health-insurance providers, pharmacies, and any local, state, or national adult immunization registries. For each potential source of vaccination, a record of whether BNT162b2 (or other COVID-19 vaccine) was received, including the date(s) of administration and the number of doses received, was obtained.

To control for potential bias and confounding that may exist in the absence of randomized assignment of vaccine and blinded follow-up and to construct crude OR and VE estimates, information on time of enrollment, recruitment site, and other potentially confounding sociodemographic, clinical (e.g., comorbidities, history of SARS-CoV-2 infection), behavioral, and lifestyle factors was also collected for use in logistic regression modeling to assess BNT162b2 VE after adjustment.

3.3. Bristol Study WI255886 (CT-44 study) titled, "A Pan-pandemic Acute Lower Respiratory Tract Disease (LRTD) Surveillance Study (AVONCap)"

Avon CAP originated as a multi-hospital, prospective surveillance study, designed to determine population-based incidence rates of hospitalized adults ≥18 years of age with community-acquired LRTI (including CAP) in Bristol, England. The involved Bristol hospitals' (North Bristol NHS Trust and University Hospitals Bristol) provide near complete capture of hospital admissions among residents of a well delineated geographic region, allowing for calculation of population-based incidence rates of LRTI.

As COVID-19 became a pandemic, this study was modified to include objectives to evaluate the vaccine effectiveness (VE) of BNT162b2. Real world VE estimates for COVID-19 vaccines are needed to demonstrate their effect in general populations as well as in risk groups. These can be achieved using a test negative design (TND) case control analysis. For the purpose of these TND analyses, cases are defined as individuals testing positive for COVID-19 up to 14 days prior to admission or within 3 days of admission to hospital and controls are defined as those who had a negative test result in the same timeframe. Almost all data needed to conduct these analyses are already being collected in this study, including COVID-19 disease and vaccination status from standard of care records, alongside other medical history and current illness details. To allow for more complete adjustment for potential confounders between the cases and controls, additional information on COVID-19-related behavioural risk factors are being collected from participants using a standardised questionnaire, such as occupation, frequency of mask use and social interactions particularly during periods of lockdown. For the purposes of this SAP, VE evaluation is only for Pfizer's BNT162b2 vaccine.

3.4. Test Negative Design Outcomes and Exposures

The following definitions are employed across all three study protocols for the purpose of VE assessment using this analytical plan.

Cases: Cases will be defined as those with any positive laboratory-confirmed PCR test from a sample collected within 14 days prior to hospital admission through 3 days after a hospital admission with any ARI symptoms or diagnostic code (Appendix 1).

Controls: Controls will be defined as those with laboratory confirmed negative COVID-19 (negative COVID-19 test during first 3 days of hospitalization for primary objective or ED encounter for secondary objective with an ARI symptoms or diagnostic code (Appendix 1) and no positive COVID-19 tests within 14 days prior to encounter).

Primary Exposure Definition: The exposure of interest is history of vaccination with BNT162b2. For the primary objective, patients will be considered vaccinated if they have documented evidence of receiving the second dose of BNT162b2 ≥7 days before index date (i.e., defined as the date of hospitalization or ED admission).

Six levels of exposure variable may be assessed:

1. Initial 2-dose vaccination series defined as 2 doses of BNT162b2 received with ≥7 days between receipt of the 2nd dose and the index date. This group will serve as the 'exposed' group evaluated in the primary objective. Patients who received only 1 dose or 2 doses of BNT162b2 with <7 days between receipt of the 2nd dose and the index date will be excluded from analysis. In sensitivity analyses, VE will also be calculated for 2 doses of BNT162b2 received with ≥14 days between receipt of the 2nd dose and the index date.

2. Partially vaccinated defined as 1 dose (only) of BNT162b2 received with ≥14 days between receipt of the 1st dose and the index date. This group will serve as the 'exposed' group for the secondary endpoint. Patients who received 2 doses or 1 dose of BNT162b2 with <14 days between receipt of the 1st dose and the index date will be excluded from analysis.

3. Ever vaccinated defined as ≥1 dose of BNT162b2 received with ≥14 days between index date and receipt of the 1st dose. Patients who received 1 dose of BNT162b2 received with <14 days between receipt of the 1st dose and the index date will be excluded from analysis.

4. Greater than 2 doses defined as receiving >2 doses of BNT162b2 with ≥14 days between receipt of the most recent dose and the index date.

5. Unvaccinated defined as individuals with no record of any COVID-19 vaccination at index date. This group will serve as the reference exposure group (i.e., 'unexposed' group) in the VE analyses.

6. Mixed vaccinated defined as receiving 1 or more doses of BNT162b2 and any other COVID-19 vaccination or prophylactic.

The 2 dose exposure group will be considered for the primary objective, while the partially (1 dose), ever vaccinated (≥1 dose) and additional (>2 doses) groups will be considered in

secondary objectives. Additional comparisons may be made between receiving 2 doses versus >2 doses or mixed dosing schedules as deemed necessary and will be documented in the respective protocol specific SAPs.

3.5. Full Cohort Study Design

A full cohort design will be used for secondary objectives to further explore BNT162b2 VE in the KPSC population.

The cohort study will include all KPSC members as of 14 December 2020 (date of first Pfizer vaccination at KPSC) meeting inclusion criteria for the analysis in accordance with regulatory authorizations. The exposure will be receipt of Pfizer's COVID-19 vaccine, with separate relative VEs estimated by number of doses received. In this full cohort design, a patient's vaccination status, and thus exposure, will change over time, with all patients entering the cohort as unvaccinated. The outcomes of interest may be COVID-19 infection, COVID-19 associated hospitalization, ED admission, ICU admission, death, and outpatient COVID-19 diagnoses (without subsequent hospitalization within 14 days). As with the TND, the main outcome of interest will be hospitalization, and the VE of focus will be 2 doses of BNT162b2. The full cohort analysis will serve as a secondary analysis and will allow for comparability with the TND study. Cohort members will be censored if they disenroll from KPSC, die for reasons not related to COVID-19 (death not within the 30 days following a positive COVID-19 laboratory test), receive only another newly licensed or investigational COVID-19 vaccine or prophylactic agent other than Pfizer's COVID-19 vaccine. For additional details on the cohort design, please refer to the protocol.

3.5.1. Full Cohort Design Outcomes and Exposures (KPSC only)

Main outcome

The main outcome of interest will be COVID-19 hospitalization, which will be defined as a hospitalization with a positive PCR SARS-CoV-2 test within 14 days prior and 3 days after admission date.

Other outcomes of interest

- COVID-19 ICU will be defined as time spent in an intensive care/critical care unit during a hospital stay with COVID-19 admit as defined above.
- COVID-19 ED encounter, which will be defined as an ED encounter with a positive PCR SARS-CoV-2 test within 14 days prior and 3 days after encounter.
- COVID-19 death will be defined as death within the 30 days following a positive COVID-19 laboratory test. Due to lags in compiling cause of death data in our databases, we will not have cause of death data in time for the study.
- Death during hospitalization will also be assessed.

- Laboratory-confirmed SARS-CoV-2 infection identified in the outpatient setting, without a hospitalization in the subsequent 14 days.

Exposures of interest:

The exposure will be receipt of Pfizer's COVID-19 vaccine, with separate relative VEs estimated by number of doses received as in the TND design above. In this full cohort design, a patient's vaccination status, and thus exposure, will change over time, so VE will be estimated using time-varying exposures as explained in further detail below.

Partial, Initial 2 dose series, and >2 dose vaccinated: Partial (1 dose) and initial series (2 dose) and greater than 2 dose (>2 doses) vaccination VE will be estimated using time-varying exposures, with patients initially entering the cohort as unvaccinated, then contributing person time to the partial and initial 2 dose series and additional dose(s) vaccinated exposure groups as they are receiving the vaccine over time in the real-world setting. Specifically, a patient will move to the 1-dose exposure group once 14-days have passed following the first dose, and then to the 2-dose exposure group once 7-days have passed following the second dose and then to the >2 dose exposure group once 14-days have passed following the third dose. No requirements on the timing between doses will be applied.

To explore VE durability after 2 and >2 doses, secondary models will further refine the exposure categories to include time since receipt of dose 2 and >2 doses. As in the main analysis, patients will still enter the cohort as unvaccinated on 14 December 2020 (date of first vaccinations at KPSC) and will move from unexposed to the partial and full vaccinated (2 or 3 or more doses) exposure groups as they are vaccinated over time. Once the second dose and >2 doses, is received, we will then code exposure categories as, for example, 30-day months since reaching vaccination. Each patient will contribute person time to these groups as the allotted amount of time passes since their second dose. This will allow us to analyze the relative VE during those different time periods and explore VE durability. If sample size allows, we will conduct a similar analysis looking at only 1 dose, where patients will be censored from the analyses when they receive their second dose. To inform our decisions in choice of cut points for both dose models, we will also estimate changes in relative VE continuously over time by modeling time since vaccination using restricted cubic splines.

Ever Vaccinated: Relative VE for the Ever Vaccinated (≥1 dose) group may be estimated in a separate analysis also using time varying exposures. Patients will again enter the cohort as unvaccinated, then contributing person time to the ever-vaccinated group after receiving dose 1. They will remain in this exposure group regardless of receipt of the 2nd dose or additional doses of the Pfizer COVID-19 vaccine.

Unexposed: Individuals with no record of any COVID-19 vaccination or person-time prior to vaccination among those eventually vaccinated.

4. STUDY OBJECTIVES

For all three protocols, the primary objective of the study is to estimate vaccine effectiveness (VE) of 2 doses of Pfizer's BNT162b2 vaccine against ARI requiring hospitalization due to SARS-CoV-2 infection among participants meeting the inclusion criteria of the study. VE will be evaluated using a TND, including all participants meeting the inclusion criteria of the study who are admitted to the hospital with ARI after 14 December 2020 (or using date of first BNT162b2 vaccination at the respective institution), and who receive a test for SARS-CoV-2. Secondary and exploratory objectives may examine VE for 1 dose vaccination, at least 1 dose, >2 doses as well as against ED admission, specific variants, mixed dosing schedules, durability, sequelae, other respiratory pathogens and other populations of interest. Additionally in KPSC, we will estimate VE using a full cohort design, including all participants meeting age inclusion criteria of analyses in accordance with the regulatory authorizations.

4.1. Statistical Hypotheses

4.1.1. Test Negative Design

The full list of endpoints (i.e., primary, and secondary) evaluated using TND are summarized in the table below.

Table 1. Test-Negative Design

Objective	Endpoint/Endpoint Analysis
Primary: (Common to all 3 protocols)	*Primary:*
To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization for ARI due to SARS-CoV-2 infection. *(In Kaiser only, stratified by age group 16+, 12-15 and 5-11 years of age)*	VE calculated as 1 minus the odds ratio (OR) comparing the odds of being vaccinated with 2 doses with BNT162b2 for hospitalized cases and controls, multiplied by 100%.
Secondary: (Common to all 3 protocols)	*Secondary:*
To describe the effectiveness of only 1 dose of BNT162b2 (i.e., partially vaccinated) against hospitalization for ARI due to SARS-CoV-2 infection.	VE calculated as 1 minus the OR comparing the odds of being partially vaccinated with BNT162b2 (only 1 dose) for hospitalized cases and controls, multiplied by 100%.
To describe the effectiveness of ≥1 dose of BNT162b2 (i.e., ever vaccinated) against hospitalization for ARI due to SARS-CoV-2 infection.	VE calculated as 1 minus the OR comparing the odds of ever being vaccinated (≥1 dose) with BNT162b2 for hospitalized cases and controls, multiplied by 100%.
To describe the effectiveness of >2 doses of BNT162b2 against hospitalization for ARI due to SARS-CoV-2 infection.	VE calculated as 1 minus the OR comparing the odds of >2 doses with BNT162b2 for hospitalized cases and controls, multiplied by 100%.
To further describe the effectiveness of BNT162b2 against hospitalization stratified by prevalent or important viral strains	BNT162b2 VE estimates stratified by virus variant (as determined by genotyping or genome sequencing) and select descriptive analyses described above by number of doses received

Table 1. Test-Negative Design

Objective	Endpoint/Endpoint Analysis
To evaluate the effectiveness of BNT162b2 against severe hospitalization-related outcomes (e.g., ICU admission, mechanical ventilation, and death)	BNT162b2 VE estimates against severe outcomes including ICU admission, mechanical ventilation, and death by number of doses received.
Secondary: (Specific to C4591014)	*Secondary:*
To evaluate overall and variant-specific effectiveness of BNT162b2 against SARS-CoV-2 infections and COVID-19 related hospital admissions by time since vaccination (by month)	Monthly VE estimates between variants of interest using independent Z tests of log hazard ratios.

In particular, for the primary endpoint under H_0, the VE for patients receiving 2 doses of BNT162b2 are not more than 20% for hospitalized ARI patients (VE$\leq$20%). A similar definition for H_0 is employed for each of the endpoints above where hypothesis testing is involved.

4.1.2. Full Cohort Study Design (*Kaiser only)*

The full list of endpoints (i.e. primary, and secondary) evaluated using full cohort design in C4591014 are summarized in the table below.

Table 2. Cohort Design

Objectives	Endpoints
Primary:	Primary:
1. To estimate the effectiveness of 2 doses of BNT162b2 against hospitalization due to SARS-CoV-2 infection.	VE calculated as 1 minus the hazard ratio (HR) comparing the incidence of 2 doses with BNT162b2 for hospitalization due to SARS-CoV-2 infection and not, multiplied by 100%.
Secondary:	Secondary:
1. To estimate the effectiveness of 2 doses of BNT162b2 against ED admission (without subsequent hospitalization) ED admission due to SARS-CoV-2 infection.	VE calculated as 1 minus the HR comparing the incidence of 2 doses with BNT162b2 for ED admission due to SARS-CoV-2 infection and not, multiplied by 100%.
2. To estimate the effectiveness of 2 doses of BNT162b2 against ICU admission due to SARS-CoV-2 infection	VE calculated as 1 minus the HR comparing the incidence of 2 doses with BNT162b2 for ICU admission due to SARS-CoV-2 infection and not, multiplied by 100%.
3. To estimate the effectiveness of 2 doses of BNT162b2 against death due to SARS-CoV-2 infection	VE calculated as 1 minus the HR comparing the incidence of (2 doses with BNT162b2 for death due to SARS-CoV-2 infection and not, multiplied by 100%.
4. To estimate the effectiveness of 2 doses of BNT162b2 against COVID-19 outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection	VE calculated as 1 minus the HR comparing the incidence of 2 doses with BNT162b2 for COVID-19 outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection and not, multiplied by 100%.

Table 2. Cohort Design

Objectives	Endpoints
5. To describe the effectiveness of only 1 dose of BNT162b2 (i.e., partially vaccinated) against hospitalization, ED admission, ICU admission, death, and outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection.	VE calculated as 1 minus the HR comparing the incidence of only 1 dose of BNT162b2 (i.e., partially vaccinated) for hospitalization, ED visit, death, and COVID-19 outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection and not, multiplied by 100%.
6. To describe the effectiveness of ≥1 dose of BNT162b2 (i.e., ever vaccinated) against hospitalization, ICU admission, ED admission, death, and outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection.	VE calculated as 1 minus the HR comparing the incidence ≥1 dose of BNT162b2 (i.e., ever vaccinated) for hospitalization, ED visit, death, and COVID-19 outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection and not, multiplied by 100%.
7. To describe the effectiveness of >2 doses of BNT162b2 against hospitalization, ED admission, ICU admission, death, and outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection.	VE calculated as 1 minus the HR comparing the incidence of >2 doses of BNT162b2 for hospitalization, ED visit, death, and COVID-19 outpatient visits (without subsequent hospitalization within 14 days) due to SARS-CoV-2 infection, multiplied by 100%.

In particular, for the primary endpoint under H_0, the VE for patients receiving 2 doses of BNT162b2 are not more than 20% for hospitalized ARI patients (VE<20%). A similar definition for H0 is employed for each of the endpoints above where hypothesis testing is involved.

4.2. Statistical decision rules

No adjustments for multiple comparisons will be made.

5. ANALYSIS SETS/DATA SOURCES

5.1. Full Analysis Set

The full analysis sets (FAS) for each of the protocols is described below.

5.1.1. Full analysis set for KPSC under Test Negative Design

Inclusion criteria

1. KPSC patients who are admitted to the hospital (primary and some secondary objectives) with ARI (ARI; ICD codes listed in Appendix 1) after 14 December 2020 (date of first vaccinations at KPSC), and who receive a PCR test for SARS-CoV-2.

2. For the secondary objectives estimating VE against ED admission, the TND will include KPSC patients who present to the ED with ARI after 14 December 2020, and who receive a PCR test for SARS-CoV-2.

3. We will include membership requirement of 1 year prior to index date, which is defined as the date of hospitalization or ED admission (allowing a 31-day administrative gap), to facilitate accurate capture of comorbid conditions.

Exclusion criteria

Patients who receive only another newly licensed or investigational SARS-CoV-2 vaccine or COVID-19 prophylactic agent other than Pfizer's COVID-19 vaccine prior to hospitalization (or ED) will be excluded from the analysis. When estimating VE for BNT162b2 vaccination, patients receiving another newly licensed or investigational SARS-CoV-2 vaccine or COVID-19 prophylactic agent other than Pfizer's COVID-19 vaccine prior to hospitalization or ED will be excluded from the analysis. Patients will also be excluded if the index date is within certain time windows from vaccination date, outlined further in the exposure section 3.4 above.

Age restrictions for analyses will be made based on the objective and aligned with regulatory authorization/approvals; i.e., separate VE analyses will be conducted for persons aged 12-15 and 5-11 years.

5.1.2. Full analysis set for KPSC under Full Cohort Study Design

Inclusion criteria

1. All KPSC members as of 14 December 2020 (date of first Pfizer vaccination at KPSC).

2. For the cohort study, patients must have at least 1 year of membership (allowing a 31-day administrative gap) prior to 14 December 2020 (index date, date vaccinations first began at KPSC) to facilitate accurate capture of comorbid conditions.

Exclusion criteria

There will be no exclusion criteria for the cohort design, however patients will be censored for receiving any other newly licensed or investigational SARS-CoV-2 vaccine or COVID-19 prophylactic agent other than Pfizer's COVID-19 vaccine.

5.1.3. Full analysis set for Emory Study under Test Negative Design

Inclusion Criteria

1. Age 18 years or older.

2. Admitted to hospital for ARI* at a participating site.

3. Previously provided a standard of care specimen (NP or nasal swab) on this hospital admission or willing and able to provide specimen (NP or nasal swab) and comply with all data collection requested.

4. Capable of providing informed consent (or LAR capable and willing to give informed consent), which includes compliance with the requirements and restrictions listed in the protocols. In the case a LAR is not available, a waiver of consent is requested.

*ARI for study enrollment will be defined as:

a. ARI symptoms (nasal congestion, rhinorrhea, sore throat, hoarseness, new or increased-from-baseline cough, sputum production, dyspnea, wheezing) OR

b. Admitting diagnosis suggestive of ARI (Pneumonia, Upper respiratory infection, Bronchitis, Influenza, Cough, Asthma, Viral respiratory illness, Respiratory distress, AND/OR Respiratory failure.

The ARI definition for analysis will include the WHO definition (e.g., acute symptoms of fever and cough) and variations since about 15% of patients admitted with COVID-19 do not have fever or cough.

Exclusion criteria

1. Previous enrollment in this study within the past 30 days.**

2. Any contraindication to have a NP or nasal swab (if specimen was not collected as SOC).

** Thus, patients can contribute >1 ARI event to the study if a subsequent ARI event for the same patient occurred >30 days after the previous event.

5.1.4. Full analysis set for Bristol Study under Test Negative Design

Screening Inclusion criteria

Patients must meet all the following inclusion criteria to be eligible for enrolment:

1. Aged ≥18 years of age
2. Patients with illness with following 2 characteristics:
   a. Acute illness (i.e., present for 28 days or less); AND
   b. Evidence of acute LRTD:
      i. Patients with current or suspected COVID-19 or previous proven COVID-19 within last 28 days OR
      ii. Clinical or radiologic diagnosis of pneumonia or an acute LRTI OR
      iii. New onset or worsening of ≥2 of following 8 LRTD symptoms or clinical findings:

         1. fever (>38.0°C) or hypothermia (<35.5°C) before or within 24 hours of enrolment;
         2. pleuritic chest pain;
         3. cough (including nocturnal only);

4. sputum production or purulence;
5. dyspnea (shortness of breath) including orthopnea or on exertion only;
6. tachypnea (respiratory rate ≥20/min) documented by healthcare professional;
7. abnormal auscultatory findings suggestive of LRTD (e.g., crepitations/rales or evidence of pulmonary consolidation including dullness on percussion, bronchial breath sounds, wheezing, or egophony);
8. radiologic finding that is consistent with LRTD, including pneumonia, and/or acute congestive heart failure (e.g., pleural effusion, increased pulmonary density due to infection, the presence of alveolar infiltrates (multilobar, lobar or segmental) containing air bronchograms, or interstitial oedema).

Screening Exclusion criteria

Patients meeting any of the following criteria will not be included in the study:

1. Any patient who develops signs and symptoms of LRTD after being hospitalized for ≥48 hours (either at current hospital, another transferring hospital, or a combination of these), unless admitted with current, previous proven, or suspected COVID-19 infection.
2. Previously enrolled participants readmitted ≤7 days after discharge for their study qualifying admission, unless admitted with current, previous proven, or suspected COVID-19 infection
3. At the time of enrolment, an LRTD-related diagnosis has been excluded or another diagnosis confirmed (for example, patient was found to have fever and tachypnoea due to an intraabdominal process such as cholecystitis)

5.2. Data Sources

5.2.1. KPSC Study

All data will be collected from KPSC electronic health records. This is a database analysis study of existing healthcare data; no patients will be actively enrolled. We will collect data including vaccination status and dates of vaccination, COVID-19 testing and outcomes, comorbidities, prior healthcare utilization, other vaccinations, demographic data, and other data from the EHR.

5.2.2. Emory Study

Data from the ROAPS study are collected from a variety of sources including patient interview (behavioral/social characteristics, patient-reported vaccine history), electronic medical records (standard of care testing results, clinical data, medical history data, etc.), Emory laboratory data (including whole genome sequencing results for COVID-positive NP swabs if/when available), and the Georgia Registry of Immunization Transactions and Services (GRITS) (documented vaccine registry history).

5.2.3. Bristol Study

Adults with LRTD will be screened using population-level surveillance at study hospitals, and collection of SOC data will be performed on all LRTD events, including from SOC laboratory tests. Documented or suspected COVID-19 will fulfil the study eligibility criterion for LRTD, thus if patients meet the other study entry criteria (such as age etc), LRTD patients will be offered participation in the enhanced diagnostic testing portion of this study with informed consent, which will involve collection of urine and respiratory samples. These samples will be used for study-specific testing and, if necessary, for COVID-19, pneumococcus, and RSV tests if not available from SOC records for any reason. A short patient questionnaire on COVID-related risk behaviours will also be administered. Information about the additional pneumococcal, SARS-CoV-2 and RSV infection testing will be integrated with the population-level surveillance data to allow for more accurate population-based estimates of vaccine-preventable pneumococcal and COVID-19 and RSV-related LRTD incidence. The epidemiologic data generated from the study will serve as the baseline for future vaccine effectiveness studies, including for current and possibly future SARS-CoV-2 vaccines.

6. ENDPOINTS AND COVARIATES

6.1. Endpoints

Test Negative Design

All endpoints considered in this SAP are related to VE of the BNT162b2 vaccine only and are detailed in section 4.1.1 for the TND. The definitions for cases and controls used to assess VE for BNT162b2 vaccine are also described in section 3.4 along with the definitions for exposure. The 2 dose exposure group will be considered for the primary objective, while the partially (1 dose), ever vaccinated (≥1 dose) and greater than 2 doses (>2 doses) groups will be considered in the secondary and exploratory objectives.

Full Cohort Study Design

All endpoints considered in this SAP are related to VE of the BNT162b2 vaccine only and are detailed in section 4.1.2 for the Full Cohort study design. The main outcome of interest will be COVID-19 hospitalization, and is defined as a hospitalization with a positive PCR SARS-CoV-2 test within 14 days prior and 3 days after admission date. The exposure will be receipt of Pfizer's COVID-19 vaccine, with separate relative VEs estimated for those receiving initial 2 dose series, partially (1 dose), ever vaccinated (≥1 dose), or additional doses (>2 doses) as in the TND design. However, in this full cohort study design, a patient's vaccination status, and thus exposure, will change over time, so VE will be estimated using time-varying exposures for all endpoints (primary, secondary, and tertiary/exploratory).

To explore VE durability after 2 doses, secondary models will further refine the exposure categories to include time since receipt of dose 2. As in the main analysis, patients will still enter the cohort as unvaccinated on December 14, 2020 and will move based on number of doses received over time through exposure groups as they are vaccinated . Once the second dose and >2 dose, respectively is received, we will then code exposure categories as, for example, 30-day months since reaching vaccination . Each patient will contribute person time to these groups as the allotted amount of time passes since their second dose. This will allow us to analyze the relative VE during those different time periods and explore VE durability. If sample size allows, we will conduct a similar analysis looking at only one dose, where patients will be censored from the analyses when they receive their second dose. To inform our decisions in choice of cut points for both dose models, we will also estimate changes in relative VE continuously over time by modeling time since vaccination using restricted cubic splines. For additional details, refer to section 3.5.1.

6.2. Covariates for Test Negative Design and Full Cohort Study Designs

We will consider individual-level and neighborhood-level factors listed in the table below. These are factors that we have either found to be important covariates in previous work, have been identified in other risk factor literature, or are variables that may be associated with the exposure as well as outcome (e.g., prior positive SARS-CoV-2 PCR test). We will also include calendar time as a covariate in our models to adjust for phase in vaccine rollout, testing practice changes, social distancing impacts, surges, and potential changes in clinical treatments.

Table 3. Covariates* for Test Negative Design and Full Cohort Study Designs

Demographics	Comorbidities	Care utilization prior to test	Neighborhood characteristics *(Kaiser only)*	COVID-history	Individual risk indicators
Age	Cardiac disease	Outpatient encounters	Population density	Prior negative PCR tests	Health care worker (HCW) / occupation
Sex	Organ transplant	Inpatient encounters	Median income	Prior positive PCR tests	Long-term care resident

Table 3. Covariates* for Test Negative Design and Full Cohort Study Designs

Demographics	Comorbidities	Care utilization prior to test	Neighborhood characteristics *(Kaiser only)*	COVID-history	Individual risk indicators
Race/ethnicity	Diabetes with A1c	ED encounters	Neighborhood deprivation index	Prior negative serology tests	Alcoholism (Emory)
	Chronic Obstructive Pulmonary Disease (COPD)	Influenza vaccination	Education (categorical)	Prior positive serology tests	Cigarette Smoking (Emory)
	Renal disease	Pneumococcal vaccination	Medical Center (discrete)		
	Body mass index (BMI) (Kaiser)	Virtual encounters (Kaiser)			
	Malignancy				
	Hypertension				
	Charlson Index				
	Sedentary vs. Active				
	Immunocompromised				

*Covariates included in all studies unless otherwise noted

7. HANDLING OF MISSING VALUES

Based on extensive prior experience, we expect negligible missing data. Regardless of missingness, we will present counts and percentages of missing data for all variables. If we find that data for variables included in the final models are highly complete, we will proceed with complete case analyses. If there is a substantial amount of missing data (>10%) for any variables deemed necessary to include in our final analyses, sensitivity analysis will be performed using multiple imputation for missing covariates (under the assumption of missing at random) to understand the impact of excluding patients with missing information in adjusted models.

8. STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

Statistical Analyses and methods adopted are described below.

8.1. TEST NEGATIVE DESIGN

The analyses below will be done separately based on the objective, number of doses and endpoints.

8.1.1. Descriptive Analyses

Proportion of hospitalized patients with ARI where SARS-CoV-2 was identified, as well as the proportion of patients who received 0, 1, 2, and >2 doses of BNT162b2 will be descriptively summarized by case and control status. Average and median time between the receipt of the first and second dose of BNT162b2 among patients who received 2 doses, between the receipt of the second and third doses of BNT162b2 among patients who received 3 doses, and between December 14, 2020 (beginning of vaccination) and receipt of the first and last dose of BNT162b2 will be descriptively summarized. Additionally, age, gender, race/ethnicity, clinical characteristics, and severity (ICU admission, mechanical ventilation, death), and other characteristics as collected and described in the respective protocols of any patients who received BNT162b2 and tested positive for SARS-CoV-2 will be summarized.

8.1.2. Estimated Crude (Unadjusted) VE

Odds ratios and corresponding 95% confidence intervals (CIs) of BNT162b2 vaccination (>2 doses, 2 doses, 1 dose, ≥1 dose) for cases and test-negative controls will be estimated using the Generalized Estimating Equation (GEE) with logit link function or a logistic regression model as appropriate. VE will be calculated as 1−OR multiplied by 100%.

8.1.3. Estimating Adjusted VE

In addition to constructing crude OR and VE estimates, logistic regression model or GEE with logit link function will be performed to assess BNT162b2 VE after adjustment for the potentially confounding factors will be performed. Potential confounders to include in models will be selected based on prior knowledge and empirical findings through the model building process. Findings from the phase-3 studies, expert opinion, and published studies of clinical/biologic factors will be used to generate a list of candidate variables. These will be assessed for their availability and ability for adjusting crude results, including an examination of their distributions and missingness. Bivariate associations of potential confounders with the outcome, exposure, and each other will be examined. For variables with suggestions of imbalance with respect to exposure or outcome, the association between exposure and outcome will be stratified by categories of the potential confounder to look for differences across strata (potential effect modification) and influence on summary estimates of association (confounding). The variables will ultimately be selected for inclusion in final adjusted models based on a combination of a priori decisions and a qualitative assessment of the empirical relationships. Sensitivity analyses will assess the robustness of cut-point selections and groupings and consider tightly confounded variables and their collinearity. The results of the multivariable model should be consistent with the stratified analyses. Corresponding 95% CIs will be calculated using the Wald method. A GEE estimator will be

used with a robust sandwich variance estimator to account for clustering introduced by variables measured at the neighborhood level. In addition to the fully adjusted model that includes relevant covariates, univariate VE results will be presented for each independent variable that is assessed for potential confounding. A 2-sided alpha of 0.05 will be used in all analyses.

8.1.4. Sensitivity Analyses (Kaiser only)

1. It is possible that patients that present with a COVID-19-like illness or a COVID-19 diagnosis are not tested for SARS-CoV-2 within 3 days of hospital admission but are rather tested later in their hospital stay. If this were the case, we would want to expand the requirement of a COVID-19 diagnostic test beyond 3 days following admission. To investigate the possibility of late testing, we will present data on the distribution of COVID-19 tests at time since admission for those admitted for respiratory infections. If a meaningful number of patients are tested >3 days after hospital admission, a sensitivity analysis to examine VE without time restrictions on testing following admission may also be included.

2. KPSC will use and develop Natural Language Processing (NLP) algorithms to estimate actual date of symptom onset of COVID-19 symptoms. Symptom onset will then be considered to define exposure status at the time of a qualifying event (or to censor a patient if they experience an event before 14-days after the first dose of 7-days after the second).

8.1.5. Additional analyses estimating VE for health care workers and other high risk populations in KPSC study

We know that the vaccine roll-out is following a tiered strategy, for example, with healthcare workers with direct patient contact being vaccinated first. The logic supporting tiered vaccine eligibility is based on COVID-19 risk, with highest risk populations prioritized first. To account for differing risk profiles of vaccinated individuals over time, we will account for calendar time in our model. To explore whether controlling for calendar time (length of time to be determined by sample size) is sufficient to address possible biases in VE , we will assess three options:

1. Flag healthcare worker, or other sub-population status (gold standard).

    a. This will require complete and reliable identification of healthcare worker or other sub-population status, for example, LTCF-resident, in the EHR. This is the preferred approach.

    b. Analyses will then be stratified so that both cases and controls will come from the same sub-population.

2. Assess and compare VE of models stratified by time periods.

    a. KPSC documentation of the dates of transitions between tiers will be used to create categories of vaccine distribution by time (Healthcare workers/LTCF residents only, 65+, etc.),

    b. Using these categories, we will perform stratified analyses for each phase in the vaccine rollout and examine any differences in relative VE between time strata.

3. If, through our analyses in part 2 or as the result of additional clinical input, we determine our inability to identify patients eligible for vaccination during certain vaccination tiers will result in unobserved confounding that will materially affect the reliability of our VE estimates, we will limit VE analyses to certain time periods of interest for which we know vaccinations were restricted to a particular tier – in particular we may drop analyses focused on the time period only healthcare workers were vaccinated and focus on time periods were vaccination is more widespread.

The Bristol and Emory studies have a questionnaire included in the study whereby patient risk factors are collected and assessed as covariates.

8.2. COHORT DESIGN

As in the TND, we will include those with and without prior COVID-19 diagnoses.

8.2.1. Descriptive Analyses

Proportion of patients who received 0, 1, 2, and >2 doses of BNT162b2 will be descriptively summarized. Average and median time between the receipt of the first and second dose of BNT162b2 among patients who received 2 doses, between the receipt of the second and third doses of BNT162b2 among patients who received 3 doses, and between December 14, 2020 (beginning of vaccination) and receipt of the first and last dose of BNT162b2 will be descriptively summarized. Overall incidence of the outcomes of interest will be calculated by dividing the number of outcome cases by the total number of person-years. We will also provide incidence estimates by age, gender, race/ethnicity, clinical characteristics, and other covariates described in the covariate table in section 6.2. Additionally, changes in the clinical and demographic composition of the vaccinated and non-vaccinated population over time may be explored, as this will also change with vaccine phase integration. Characteristics of those who test positive for COVID-19 and those without COVID-19 will be presented.

8.2.2. Estimated Crude (Unadjusted) VE

Vaccine effectiveness (VE) will be estimated as (1 – Hazard Ratio)*100%, and the hazard ratio (HR) will be estimated using a Cox proportional hazard model with corresponding 95% CIs calculated. Vaccination status will be time-varying as described previously in section 3.5.1.

8.2.3. Estimating Adjusted VE

Adjusted hazard ratios (HRs) and 95% CIs will be estimated by including age, sex, race, and other covariates listed in section 6.2 in Cox proportional hazard regression models. Potential confounders to include in models will be selected based on prior knowledge and empirical findings through the model building process. Findings from the phase-3 studies, expert opinion, and published studies of clinical/biologic factors will be used to generate a list of candidate variables. These will be assessed for their availability and ability for adjusting crude results, including an examination of their distributions and missingness. Bivariate associations of potential confounders with the outcome, exposure, and each other will be examined. For those with suggestions of imbalance with either exposure or outcome, the association between exposure and outcome will be stratified by categories of the potential confounder to look for differences across strata (potential effect modification) and influence on summary estimates of association (confounding). The variables will ultimately be selected based on a combination of the a priori decisions and a qualitative assessment of the empirical relationships. Sensitivity analyses will assess the robustness of cut-point selections and groupings and consider tightly confounded variables and their collinearity. The results of the multivariable model should corroborate the knowledge gained from the stratified analyses. We will control for calendar week in all models. Robust variance will be computed to account for clustering introduced by neighborhood level variables. Vaccine effectiveness (VE) will be estimated as (1 – adjusted HR)*100%, and the hazard ratio (HR) will be estimated using Cox proportional hazard model with corresponding 95% CIs calculated.

8.3. Additional Analytic Elements for Test Negative and Full Cohort Design

1. Provide descriptive statistics and determine VE stratified by virus variants determined to be important or prevalent based on sequencing analyses.

2. Determine VE of BNT162b2 stratified by various patient characteristics (e.g., age, sex, chronic medical conditions, receipt of influenza vaccine). Table 2 has the full list of proposed stratified analyses

9. LIST OF TABLES AND TABLE SHELLS

Please see separate Excel document which outlines proposed table shells for these analyses.

10. APPENDICES

Appendix 1. Diagnosis and Procedure Codes used in the three protocols

Acute Respiratory Infection Diagnosis codes

ICD-10 code	ICD-10 definition
J12.0	Adenoviral pneumonia
J12.1	Respiratory syncytial virus pneumonia
J12.2	Parainfluenza virus pneumonia
J12.81	Pneumonia due to SARS-associated coronavirus
J12.82	Pneumonia due to coronavirus disease 2019
J12.3	Human metapneumovirus pneumonia
J12.89	Other viral pneumonia
J12.9	Viral pneumonia, unspecified
J13	Pneumonia due to Streptococcus pneumoniae
J18.1	Lobar pneumonia, unspecified organism
J15.0	Pneumonia due to Klebsiella pneumoniae
J15.1	Pneumonia due to Pseudomonas
J14	Pneumonia due to Hemophilus influenzae
J15.4	Pneumonia due to other streptococci
J15.4	Pneumonia due to other streptococci
J15.3	Pneumonia due to streptococcus, group B
J15.4	Pneumonia due to other streptococci
J15.20	Pneumonia due to staphylococcus, unspecified
J15.211	Pneumonia due to Methicillin susceptible Staphylococcus aureus
J15.212	Pneumonia due to Methicillin resistant Staphylococcus aureus
J15.29	Pneumonia due to other staphylococcus
J15.8	Pneumonia due to other specified bacteria
J15.5	Pneumonia due to Escherichia coli
J15.6	Pneumonia due to other Gram-negative bacteria
A48.1	Legionnaires' disease
J15.8	Pneumonia due to other specified bacteria
J15.9	Unspecified bacterial pneumonia
J15.7	Pneumonia due to Mycoplasma pneumoniae
J16.0	Chlamydial pneumonia
J16.8	Pneumonia due to other specified infectious organisms
B25.0	Cytomegaloviral pneumonitis
A37.01	Whooping cough due to Bordetella pertussis with pneumonia
A37.11	Whooping cough due to Bordetella parapertussis with pneumonia

ICD-10 code	ICD-10 definition
A37.81	Whooping cough due to other Bordetella species with pneumonia
A37.91	Whooping cough, unspecified species with pneumonia
A22.1	Pulmonary anthrax
B44.0	Invasive pulmonary aspergillosis
J17	Pneumonia in diseases classified elsewhere
B77.81	Ascariasis pneumonia
J17	Pneumonia in diseases classified elsewhere
J18.0	Bronchopneumonia, unspecified organism
J18.8	Other pneumonia, unspecified organism
J18.9	Pneumonia, unspecified organism
J10.00	Influenza due to other identified influenza virus with unspecified type of pneumonia
J10.01	Influenza due to other identified influenza virus with the same other identified influenza virus pneumonia
J10.08	Influenza due to other identified influenza virus with other specified pneumonia
J11.00	Influenza due to unidentified influenza virus with unspecified type of pneumonia
J11.08	Influenza due to unidentified influenza virus with specified pneumonia
J12.9	Viral pneumonia, unspecified
J10.1	Influenza due to other identified influenza virus with other respiratory manifestations
J11.1	Influenza due to unidentified influenza virus with other respiratory manifestations
J10.2	Influenza due to other identified influenza virus with gastrointestinal manifestations
J10.81	Influenza due to other identified influenza virus with encephalopathy
J10.82	Influenza due to other identified influenza virus with myocarditis
J10.83	Influenza due to other identified influenza virus with otitis media
J10.89	Influenza due to other identified influenza virus with other manifestations
J11.2	Influenza due to unidentified influenza virus with gastrointestinal manifestations
J11.81	Influenza due to unidentified influenza virus with encephalopathy
J11.82	Influenza due to unidentified influenza virus with myocarditis
J11.83	Influenza due to unidentified influenza virus with otitis media
J11.89	Influenza due to unidentified influenza virus with other manifestations
J09.X1	Influenza due to identified novel influenza A virus with pneumonia
J09.X2	Influenza due to identified novel influenza A virus with other respiratory manifestations
J09.X3	Influenza due to identified novel influenza A virus with gastrointestinal manifestations
J09.X9	Influenza due to identified novel influenza A virus with other manifestations
J10.08	Influenza due to other identified influenza virus with other specified pneumonia

ICD-10 code	ICD-10 definition
J10.1	Influenza due to other identified influenza virus with other respiratory manifestations
J09.X9	Influenza due to identified novel influenza A virus with other manifestations
J09.X1	Influenza due to identified novel influenza A virus with pneumonia
J09.X2	Influenza due to identified novel influenza A virus with other respiratory manifestations
J09.X3	Influenza due to identified novel influenza A virus with gastrointestinal manifestations
J09.X9	Influenza due to identified novel influenza A virus with other manifestations