

PASS information

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Research question and objectives	<p>This study aims to augment ongoing active and passive safety signal detection through signal refinement and, where warranted, evaluation of potential safety signals associated with the introduction of SARS-CoV-2 mRNA-1273 vaccine.</p> <p>The objectives of this study are to:</p> <ol style="list-style-type: none"> 1. Estimate crude and age/sex adjusted incidence rates (IR) and incidence rate ratios (IRR) at key time periods and among key populations <ol style="list-style-type: none"> a. Estimate background incidence rates of pre-defined AESIs during the pre-COVID and active-COVID but pre-vaccine COVID-19 EUA periods b. Estimate incidence rates for pre-defined AESIs among mRNA-1273-vaccinated individuals in post-EUA period. Estimate IRR by comparing post vaccine IR to background IR in two periods (pre-COVID, active- COVID) estimated in Objective 1(a) c. Estimate crude and age/sex adjusted incidence rates and incidence rate ratios for additionally-identified AESIs

	<ol style="list-style-type: none"> 2. Estimate age/sex adjusted observed to expected ratio for specific AESIs meeting pre-specified evaluation threshold from objective 1.b (completed as needed) 3. Estimate relative risk for specific AESIs meeting pre-specified evaluation threshold from objective 2 via self-controlled risk interval (SCRI) analyses (completed as needed)
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1. Abstract

Title

Post-marketing safety of SARS-CoV-2 mRNA-1273 vaccine in the US: Active surveillance, signal refinement and self-controlled risk interval (SCRI) signal evaluation in HealthVerity

Daina Esposito, MPH | Moderna Tx | Interim Report 3, Version 1.0, 27 October 2021

Keywords

Covid-19, Vaccine Safety, Adverse Events of Special Interest

Rationale and background

In the context of pandemic COVID-19 disease, Moderna has developed SARS-CoV-2 mRNA-1273 vaccine. The present study aims to augment ongoing active and passive signal detection by estimating background rates of Adverse Events of Special Interest (AESIs) prior to the first emergency use authorization (EUA) for any SARS-CoV-2 vaccine (11 December 2020) and then estimating rates of AESIs after vaccination subsequent to the EUA in an overall adult US population and in specific subgroups of interest.¹

Post-authorization data have demonstrated increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is highest among younger males.

This study will contextualize the risk of myocarditis and other potential safety signals and inform the need for further safety evaluation and signal refinement, notably using observed-to-expected (O/E) analyses where a safety concern has been raised from literature or medical reviews, disproportionate reporting or unexpected temporal relationship. In the event that O/E analysis results show observed values higher than expected, self-controlled risk interval (SCRI) analyses will be conducted to further evaluate the AESI or signal.

Research question and objectives

This study aims to augment ongoing active and passive safety signal detection through signal refinement and, where warranted, evaluation of potential safety signals associated with the introduction of SARS-CoV-2 mRNA-1273 vaccine.

The objectives of this study are to:

1. Estimate crude and age/sex adjusted incidence rates (IR) and incidence rate ratios (IRR) at key time periods and among key populations
 - a. Estimate background incidence rates of myocarditis and other AESIs during the pre-COVID and active-COVID but pre-vaccine COVID-19 EUA periods
 - i. *In the general population and influenza-vaccinated individuals during the pre-COVID period*
 - ii. *In the general population during the active-COVID but pre-vaccine COVID-19 EUA periods*

- b. Estimate incidence rates for myocarditis and other AESIs among mRNA-1273-vaccinated individuals in post-EUA period. Estimate IRR by comparing post vaccine IR to background IR in two periods (pre-COVID, active- COVID) estimated in Objective 1(a)
 - c. Estimate crude and age/sex adjusted incidence rates and incidence rate ratios for additionally-identified AESIs and potential safety signals if applicable.
2. Estimate an age/sex adjusted observed to expected ratio for myocarditis and other specific AESIs meeting pre-specified evaluation threshold from objective 1.b (completed as needed)
3. Estimate relative risk for myocarditis and other specific AESIs meeting pre-specified evaluation threshold from objective 2 via self-controlled risk interval (SCRI) analyses (completed as needed)

In this interim study update, cohort formation and estimated background incidence of selected AESI during the pre-COVID period and following mRNA-1273 vaccination are described, and these rates are compared (objectives 1a*i* and 1b). For myocarditis and pericarditis, age and sex adjusted observed to expected ratio is presented (objective 2).

Study design

Retrospective observational cohort study with active vaccine surveillance. Cohort analyses with historical comparators are used for signal detection. Upon approval of the proposed approach, self-controlled risk interval analyses will be used for signal refinement.

Setting

This retrospective observational cohort study will use secondary, de-identified individual-level medical and pharmacy claims data provided by HealthVerity. This data source includes more than 140 million patients insured under commercial, Medicare or Medicaid plans, and/or served by providers participating in several large US medical and pharmacy insurance claims submission systems. The data will be refreshed biweekly throughout the study period.

Subjects and study size

The analysis population for background rates will include a sample of patients from the HealthVerity database. The population for vaccinated individuals will be formed from the entirety of available HealthVerity data.

Variables and data sources

- **Exposures:** In this interim study report, exposure is defined based on receipt of at least dose of mRNA-1273. For the comparison group, no exposure is required as the historical cohort is used to derive estimates of incidence in a background population. Future interim reports will include analyses stratified by dose.
- **Outcomes:** Pre-defined AESI operationalized per published protocols from the EMA sponsored vACCine covid-19 monitoring readinESS (ACCESS) project and FDA CBER.

- **Key Covariates:** Stratification is shown by age group and sex.

Results

There were 140,122,236 individuals identified in the HealthVerity database at any time between 01 December 2017 and 10 December 2020. Of these individuals, 108.8 million were enrolled in a health plan providing information on enrollment during the same time frame. We excluded 134,778 individuals with missing information on sex, 6,096 individuals with missing information on age, and 15,157,248 individuals without continuous enrollment for at least 365 days at any time during the study period before sampling 50,015,708 individuals to mirror the distribution of the 2019 US census age and sex distribution. Of these individuals, 38,686,912 were at least 18 years of age.

Among 10,909,141 mRNA-1273 vaccine recipients meeting study entry criteria, 73.5% received a second dose with a median dosing interval of 28 days (IQR 28 – 28 days). Follow-up was censored due to receipt of a non-Moderna COVID-19 vaccine in 0.5% of cases. The median age of vaccinated individuals was higher than the historical cohort (55 vs 47 years) and a larger proportion of vaccine recipients were female (56.5% vs 52.3%). Most comorbidities were documented for similar proportions of the historical and vaccinated cohorts, respectively.

Myocarditis was observed in 2,186 patients in the historical cohort (IR 9.98 cases per 100,000 person-years 95% CI 9.47 – 10.30) and in 253 patients following vaccination (IR 9.94 cases per 100,000 person-years, 95% CI 8.72 – 11.17), producing an incidence rate ratio of 1.01 (95% CI 0.88 – 1.14). This small increase appears to be driven by a larger increase in young men, where the incidence following vaccination was 34.71 cases per 100,000 person-years (IRR 3.30, 95% CI 2.29 – 4.65). Although there were small numerical increases in men ages 30-39 and young women, these estimates are based on small numbers and lack precision. Observed vs expected analyses considering a 7-day risk window following vaccination produced findings with similar interpretation. An increase was observed in all individuals 18 to 29 years of age, where 9 events were observed and 2 expected (O/E ratio 4.93, 95% CI 2.25 – 9.36).

A smaller, numerical increase for men ages 18 to 29 was also observed for pericarditis. This outcome was observed in 5,418 patients in the historical cohort (IR 24.51, cases per 100,000 person-years 95% CI 23.86-25.16) and in 533 patients following vaccination (age and sex standardized IR 20.95 cases per 100,000 person-years, 95% CI 19.17 – 22.73), producing an incidence rate ratio of 0.85 (95% CI 0.78 – 0.93). In young males, 32 cases after vaccination produced an IR of 30.85 per 100,000 person-years (95% CI 20.16 – 41.54), corresponding to an IRR of 1.41 (95% CI 0.97 – 1.99). Overall observed to expected analyses and most age and sex specific analyses did not show an increase for the 7-day risk window, however an increase was observed in the 18 to 29-year age group (4 cases expected, 14 observed, OE ratio 3.31, 95% CI 1.81 – 5.56). This was again driven by young males, where 2 cases were expected and 10 observed (OE ratio 4.19, 95% CI 2.01 – 7.71).

Of the outcomes included in this interim analysis, incidence of Chilblain-like lesions and anosmia were meaningfully elevated following vaccination compared to historical data. For Chilblain-like lesions, 996 cases were observed in the historical cohort (IR 4.37, 95% CI 4.09-4.64) and 322 were observed following vaccination (IR 12.65, 95% CI 11.27 – 14.04),

producing a standardized incidence rate ratio of 2.90 (95% CI 2.55 – 3.28). Anosmia occurred in 10,800 cases in the historical cohort (IR 48.84 per 100,000 person-years, 95% CI 47.95 – 49.79) and in 2,774 cases following vaccination (IR 109.26 per 100,000 person-years, 95% CI 105.19 – 113.33), producing an IRR of 2.24 (95% CI 2.14 – 2.33). Other outcomes showed rates similar to or below the expected.

Discussion

Preliminary claims-based assessments of incidence and incidence rate ratios for AESI relevant to COVID-19 vaccine safety monitoring in a large, US cohort of adults are described.

Consistent with findings from the sponsor's review of the global safety database, an increase in the risk of myocarditis and pericarditis was identified for young men, with incidence rate ratio of 3.3 for myocarditis in this subgroup. This was similar to the increase observed for another available mRNA vaccine in Israel, and it is also aligned with increases in risk for this subgroup described in the literature. Age and sex adjusted observed-to-expected ratios focused on the 7-day period following vaccination suggest that the risk is greater proximate to vaccination.

Additionally, significant increases in the rate of anosmia and Chilblain-like lesions were identified following vaccination, especially in younger vaccine recipients. Of note, the historical incidence rates were calculated from the pre-COVID time period. It is unclear whether this may be influenced by increased incidence and/or increased recognition of these conditions in association with SARS CoV-2 infection and/or subsequent mRNA-1273 vaccination given secular trends. Additional analyses including crude and age/sex adjusted incidence rates (IR) and incidence rate ratios (IRR) calculated from the active-COVID but pre-vaccine COVID-19 EUA period will help characterize and refine these observed signals. Other outcomes did not show a meaningfully increased rate following receipt of mRNA-1273.

Marketing Authorisation Holder(s)

Moderna Tx

Names and affiliations of principal investigators

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2. List of abbreviations

Abbreviations	Definition
ACCESS	vACcine Covid-19 monitoring readinESS
AE	Adverse Event
AESI	Adverse Events of Special Interest
CI	Confidence Interval
CPT	Current Procedural Terminology
EMA	European Medicine Agency
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
GBS	Guillain-Barré Syndrome
GPP	Good Pharmacoepidemiological Practice
HIPAA	Health Insurance Portability and Accountability Act
ICD	International Classification of Disease
ICMJE	International Committee of Medical Journal Editors
IR	Incidence Rate
IRR	Incidence Rate Ratio
ICD-10	International Classification of Diseases, 10 th Revision
O/E	Observed to Expected
RMP	Risk Management Plan
SAP	Statistical Analysis Plan
SCRI	Self-controlled risk interval

US	United States
VAC4EU	Vaccine monitoring Collaboration for Europe
VAERS	Vaccine Adverse Event Reporting System
VSD	Vaccine Safety Datalink

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- Jennifer Hayden | Director of Science
- Sahar Syed | Scientific Analyst
- Christopher Bush | Scientist
- Jeremy Rassen | President

5. Milestones

Milestone	Planned date	Actual date	Comments
Final Protocol	31 January 2021	25 March 2021 *	Protocol revisions were required based on regulatory feedback
Protocol amendment	Not applicable	31 October 2021 *	Protocol revisions were required based on regulatory feedback

Interim Update #1	30 April 2021	30 April 2021	
Interim Update #2	31 July 2021	31 July 2021	
Interim Update #3	31 October 2021	31 October 2021	
Upcoming Interim Updates	Every 3 months through the end of the study period (31 December 2022)		
Final report	30 June 2023		

*Please note that additional protocol revisions were requested by the US FDA, resulting in an amendment to the study Protocol. This amendment is attached to the interim report.

6. Rationale and background

In the context of pandemic COVID-19 disease, Moderna has developed the SARS-CoV-2 mRNA-1273 vaccine. Phase 1 (NCT04283461) efficacy results were positive, notably in the elderly population (65 years old and above).^{2,3} A dose-confirmation phase 2a trial (NCT04405076) was then conducted followed by a phase 3 trial (NCT04470427) which has shown a vaccine efficacy rate of 94.1% in adults.⁴

Emergency use authorisation was obtained in the US on 18 December 2020 and other authorizations since been granted in Canada, Israel, the European Union, the United Kingdom, Switzerland, Singapore, Qatar, Brunei, Paraguay, Taiwan, Philippines, Thailand, South Korea, Japan, Jordan, Bhutan, United Arab Emirates, Columbia, Saudi Arabia, Vietnam, Sri Lanka, Haiti, Indonesia, Ukraine, Tunisia, Algeria, Nigeria, Ghana, Cambodia, Malaysia, Palestine, Egypt and Cabo Verde for active immunization to prevent COVID-19 in individuals 18 years of age and older. Use has been authorized in adolescents ages 12-17 in the Europe, Japan, Canada, Taiwan, Philippines, Saudi Arabia, the United Kingdom. The vaccine is licensed in those >12 years of age in Australia.

Myocarditis refers to inflammation of the myocardium and may be due to any one of numerous etiologies (e.g., infectious pathogens, toxins, drugs, and autoimmune disorders) that may resolve spontaneously, cause sudden cardiac death, or evolve into dilated cardiomyopathy. The most common etiology of myocarditis, especially among younger people, is viral infection (with numerous viruses, including SARS-CoV-2, implicated). Estimates of incidence vary substantially, with some sources describing a rate of 1-10 cases others 10-20 cases per 100,000 person-years. For reasons that are unclear, myocarditis tends to occur disproportionately among younger males (approximately 20-40 years of age). Reliable and accessible diagnostic tools for the early diagnosis of acute myocarditis are an unmet clinical need at this time (Blanco-Dominguez 2021). Rare cases of myocarditis and pericarditis have been observed following vaccination with mRNA vaccines targeting SARS-CoV-2, including SPIKEVAX. Most of these cases have occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men.

Anaphylaxis is also recognized as important identified risks. Other potential risks include vaccine-associated enhanced disease, which has not been clearly defined to date. Areas not assessed in the phase 3 trial included risks related to use in pregnant or lactating women, long-term safety, use in immunocompromised or frail subjects, use in populations with unstable health conditions and comorbidities, interaction with other vaccines, and long-term safety.

The Risk Management Plan (RMP) also prespecifies that adverse events of special interest (AESI) identified by regulatory agencies and vaccine expert groups will be monitored via routine and enhanced pharmacovigilance activities. The vaccine exposed population of the Phase 3 P301 study allowed the detection of rare events with a frequency of 1/10,000 persons or 0.01%. However, most rare adverse events of special interest (AESIs) for post-marketing safety surveillance have incidence rates lower than 2/10,000 persons or 0.02%. As such, additional safety surveillance and evaluation is needed in the post-marketing setting. This is especially critical as safety concerns have been raised in the past following mass vaccination campaigns either with existing or new vaccines.

The present study aims to augment ongoing active and passive signal detection by estimating background rates of AESIs prior to the first emergency use authorization (EUA) for any SARS-CoV-2

vaccine (11 December 2020) and then estimating rates of AESIs after vaccination subsequent to the EUA in an overall adult US population and in specific subgroups of interest.¹ This will contextualize AESI and potential safety signals and inform the need for further safety evaluation and signal refinement, notably using observed-to-expected (O/E) analyses where a safety concern has been raised from literature or medical reviews, disproportionate reporting, or unexpected temporal relationships. In the event that O/E analysis results indicate observed values higher than expected, self-controlled risk interval (SCRI) analyses will be conducted to further evaluate the AESI or signal.

7. Research question and objectives

This study aims to augment ongoing active and passive safety signal detection through signal refinement and, where warranted, evaluation of potential safety signals associated with the introduction of SARS-CoV-2 mRNA-1273 vaccine.

The objectives of this study are to:

1. Estimate crude and age/sex adjusted incidence rates (IR) and incidence rate ratios (IRR) at key time periods and among key populations
 - a. Estimate background incidence rates of myocarditis and other AESIs during the pre-COVID and active-COVID but pre-vaccine COVID-19 EUA periods
 - i. in the general population and influenza-vaccinated individuals during the pre-COVID period
 - ii. in the general population during the active-COVID but pre-vaccine COVID-19 EUA periods
 - b. Estimate incidence rates for myocarditis and other AESIs among mRNA-1273-vaccinated individuals in post-EUA period. Estimate IRR by comparing post vaccine IR to background IR in two periods (pre-COVID, active- COVID) estimated in Objective 1(a)
 - c. Estimate crude and age/sex adjusted incidence rates and incidence rate ratios for additionally-identified AESIs and potential safety signals if applicable.
2. Estimate age/sex adjusted observed to expected ratio for myocarditis and other specific AESIs meeting pre-specified evaluation threshold from objective 1.b (completed as needed)
3. Estimate relative risk for myocarditis and other specific AESIs meeting pre-specified evaluation threshold from objective 2 via self-controlled risk interval (SCRI) analyses (completed as needed).

In this interim study update, cohort formation and estimated background incidence of pre-defined AESI during the pre-COVID period are described (objective 1a). Subsequent quarterly study reports are expected to include analyses pertaining to the remaining study objectives.

8. Amendments and updates

The following amendments have been added to the study protocol after the start of analysis and interim reporting

Number	Date	Section of study protocol	Amendment or update	Reason
v3.0	26-08-2021	4	Abstract update for changes in Protocol v3.0	Alignment of the protocol to Version 3.0 changes

v3.0	26-08-2021	7	Update in current vaccine authorization status	Updated information available at time of protocol amendment.
v3.0	26-08-2021	8 & 9	The age range was expanded to capture individuals of all ages with subgroups for children, adolescents and adults.	Use of Spikevax has been observed in younger individuals, and indicated ages may change over the course of the study.
v3.0	26-08-2021	8 & 9	<ul style="list-style-type: none"> - Expanding beyond adult population - Adding a T1 flu vaccinated comparator group - Minor edits to analytic dataset 	<ul style="list-style-type: none"> - In anticipation of potential future use in younger age groups - per FDA CBER comment - More information on dataset available
v3.0	26-08-2021	8 & 9	<ul style="list-style-type: none"> - Expanding beyond adult population - Adding a T1 flu vaccinated comparator group - Minor edits to analytic dataset 	<ul style="list-style-type: none"> - In anticipation of potential future use in younger age groups - per FDA CBER comment - More information on dataset available
v3.0	26-08-2021	Annex 1	Update in references	Revisions were required based on regulatory feedback.
v3.0	26-08-2021	Annex 2	Addition of risk and control periods were specified and clarification of time varying covariates implemented	Revisions were required based on regulatory feedback.
v3.1	26-08-2021	9.5	Revised sample size estimates were included	Revisions were required based on regulatory feedback.
v3.1	26-08-2021	9.7	Additional sensitivity analyses were described	For potential considerations around healthcare utilization, heterologous vaccine schedule, and stratification by dose and/or immunocompromised status
V3.2	27-10-2021	Throughout	Myocarditis has been specified as primary outcomes, additional supporting background context has been included, and dose stratified analyses have been designated as mandatory regardless of sample size.	Revisions were required based on regulatory feedback.
V3.2	27-10-2021	9.5, 9.7	Revised sample size estimates were included based on the need to include myocarditis and reduce the proposed duration proposed control windows for SCRI analyses.	Revisions were required based on regulatory feedback.

V3.2	27-10-2021	9.7	<i>Additional analyses were described, including stratification by dose and inclusion of mild to moderate health states in analyses designed to characterize the potential impact of changes in healthcare utilization on study results.</i>	<i>Revisions were required based on regulatory feedback.</i>
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9. Research methods

9.1. Study design

This retrospective observational cohort study uses secondary, de-identified individual-level medical and pharmacy claims data provided by HealthVerity. This data source includes patients insured under commercial, Medicare or Medicaid plans, and/or served by providers participating in several large US medical and pharmacy insurance claims submission systems.

Individuals will be identified in three time periods corresponding to Pre-COVID (01 Dec 2018-30 Nov 2019), Active COVID (01 Dec 2019 – 10 Dec 2020), and Post-EUA (11 Dec 2020 – 31 Dec 2022). In the first two time periods, all individuals meeting enrollment requirements for the study cohort will be included. In the post-EUA time period, qualifying individuals will be followed starting on the date of the first claim for the mRNA-1273 vaccine. Analyses presented in this interim report include the Pre-COVID window and the Post-EUA period.

9.2. Setting

The study was conducted using secondary, de-identified individual level medical and pharmacy claims data provided by HealthVerity. The data represent more than 140 million patients insured under commercial, Medicare or Medicaid plans, and/or served by providers participating in several large US medical and pharmacy insurance claims submission systems.

9.3. Subjects

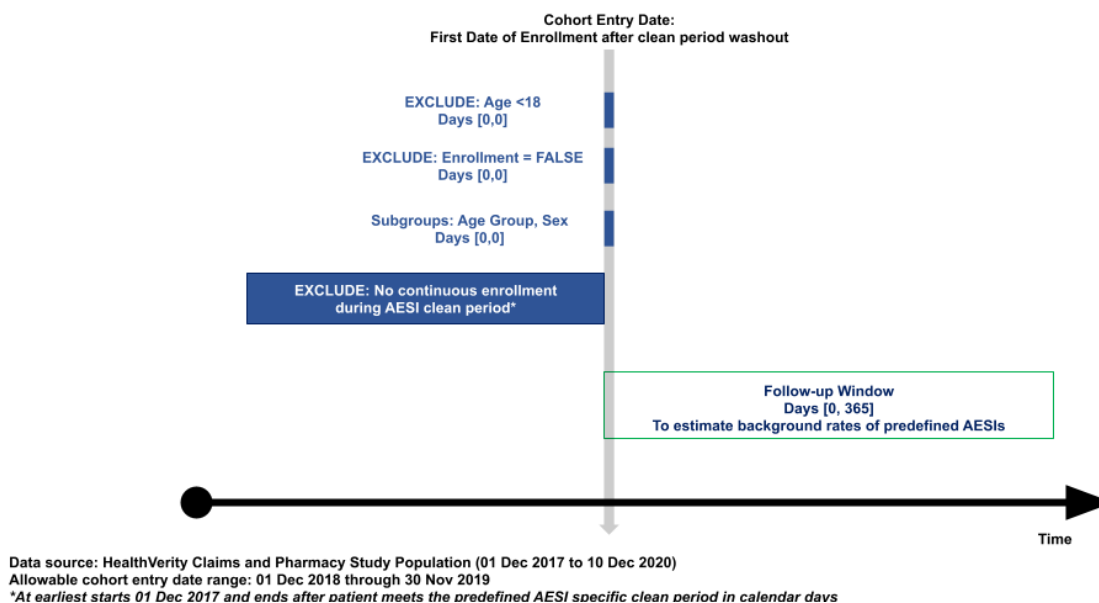
The currently presented analyses include individuals meeting the following study entry criteria:

Pre-COVID Historical Cohort:

- Included in a health plan covered by HealthVerity database ([see Section 9.2](#)) with capture of closed administrative healthcare claims
- Covered by a health plan during the pre-COVID-19 period
- For analysis of each outcomes, data includes an AESI specified clean period of continuous baseline enrollment or activity before the period of interest during which the patient is covered by continuous health plan eligibility
- Aged 18 years old or above at cohort entry date
 - Future analyses will include subpopulations of children and adolescents

Qualifying patients were then followed from the end of the clean period (for most outcomes, 365 days used to establish baseline characteristics and identify prevalence AESI diagnoses) through the end of the time period (i.e. 30 Nov 2019), the end of continuous health plan enrollment, or the first

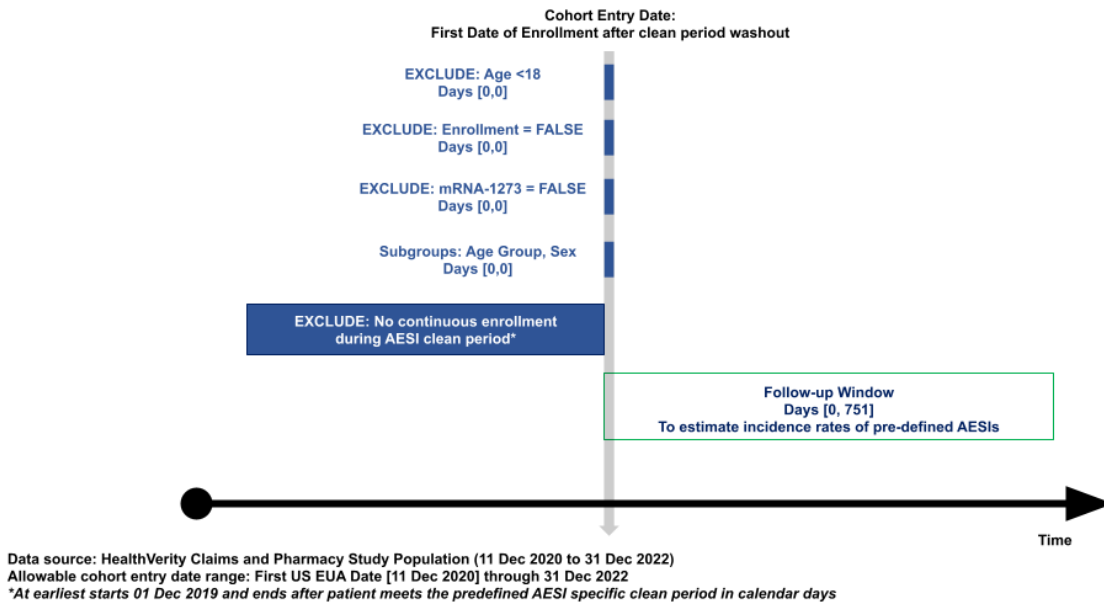
occurrence of the AESI considered in a given analysis. A summary of cohort selection is shown in [Figure 1](#).



Post-EUA Vaccinated Cohort

- Included the HealthVerity database ([see Section 9.2](#)) with capture of open or closed administrative healthcare claims
- At least one dose of mRNA-1273 vaccine
- For analysis of each outcomes, data includes an AESI specified clean period of continuous baseline enrollment or open claim activity before vaccination
- Aged 18 years old or above at cohort entry date
 - Future analyses will include subpopulations of children and adolescents

Qualifying patients were then followed from the date of the first vaccine dose administration through the end of data availability (20 June 2021), the end of HealthVerity data capture (defined as the end of continuous health plan enrollment for closed claims or 45 days after the last healthcare encounter for those with open claims), or the first occurrence of the AESI considered in a given analysis. A summary of cohort selection is shown in [Figure 2](#).



9.4. Variables

9.4.1. Exposures

The mRNA-1273 vaccination schedule consists of two 100 µg doses within a one month period, with the second dose between 28 and 31 days of the first. Exposure to mRNA-1273 vaccine was identified through specific CPT code 91301 and modifiers 0011A (1st dose) and 0012A (2nd dose) and 0013A (3rd dose) or NDC 10/11 code (80777-273-10, 80777-0273-10, 80777-273-15, 80777-273-99), noting that codes will be reviewed prior to execution of each interim analysis and updated to include newly identified entries. CPT codes and modifiers are expected to be fully reported as a result of insurance reimbursement requirements set by CMS and others. However, exposure status may be missed when vaccinations occur outside of conventional healthcare settings. This study considered a patient with evidence of at least one dose of mRNA-1273 as exposed (i.e., vaccinated), with exposure date determined as the first date of vaccination claim's date of service.

9.4.2. Outcomes

AESIs were identified in claims data and defined using ICD-10 and ATC codes. To the extent possible, were aligned with those used in protocols from FDA CBER, VAC4EU¹¹, and FDA Sentinel.

The [table](#) below provides the list of predefined AESIs for which Objective 1 IRs were estimated (see Annex 1 for corresponding code list). Several sources were considered to define this list: CDC/FDA's VAERS and VSD, and the ACCESS project endorsed by EMA. Additional AESIs may be added to future study reports.

Predefined AESIs
Acute aseptic arthritis
Acute disseminated encephalomyelitis (ADEM)
Acute kidney injury
Acute liver injury
Acute myocardial infarction (AMI)
Acute respiratory distress syndrome (ARDS)
Anaphylaxis

Anosmia, ageusia
Arrhythmia
Aseptic meningitis
Bell's palsy
Chilblain-like lesions
Chronic coronary heart disease
Coagulation disorders
Deep vein thrombosis (DVT)
Disseminated intravascular coagulation (DIC)
Encephalitis / Encephalomyelitis
Erythema multiforme
Gestational diabetes
Guillain-Barré Syndrome (GBS)
Heart failure
Kawasaki disease
Meningoencephalitis
Microangiopathy
Multisystem Inflammatory Syndrome in Adults (MIS-A)
Myocarditis, pericarditis
Narcolepsy / cataplexy
Pulmonary embolism (PE)
Seizures/convulsions
Single organ cutaneous vasculitis
Stroke, hemorrhagic
Stroke, non-hemorrhagic
Thrombocytopenia (immune and idiopathic)
Transverse myelitis
Type 1 Diabetes

In Interim Report #2, it was determined that several of the algorithms for these conditions produced inflated background rates in the historical period, which could imply poor specificity and result in the expectation of bias towards the null when comparing vaccinated vs. historical rates. These algorithms are currently under clinical review to determine whether modifications can improve performance, and updated estimates are expected in Interim Report #4. For outcomes presented in this analysis, revisions have included restriction of closed claims data to exclude denied and reversed claims as these may represent coding errors.

9.4.3.Subgroups

Present analyses include stratification by age, sex, and age by sex. When considering subgroups defined by age group and sex, values were identified at the index date and retained for the remainder of the follow-up period.

9.5. Data sources and measurement

HealthVerity data contains near real-time medical claims and outpatient pharmacy transactions, including drugs, diagnoses, and procedures. Data elements include provider-submitted claims, adjudicated insurance claims, and pharmacy billing manager claims submissions. They update in near real-time, with minimal lag between time of claim submission and time of inclusion in the database. Over 12 months of historical data is available for many patients. Hospitalizations are included in the

data at a summary level. Vaccinations will be captured via manufacturer-specific CPT codes. Drugs dispensed by a pharmacy are generally well captured, while OTC medications are not.

The medical claims used for this study will include open and closed medical claims. Open claims are adjudicated or unadjudicated claims submitted by providers or facilities for consideration for payment by payers. The claims are captured in clearing houses or practice management or revenue cycle management systems. Because they often are not yet associated with a particular insurer, there is no associated enrollment / eligibility file, the registry of who is and who is not covered under a plan. As such, with open claims, the total number of patients available for analysis (i.e. denominator) must be estimated. This is typically done by assuming coverage based on a patient's claims activity; however, as there is not an associated enrollment file, a complete record of a patient's activity with the healthcare system (observability) is not possible and there is the potential for missing information (diagnoses, procedures, or prescription fills). Open claims are processed and available in near real time. Closed claims data, sometimes referred to as payer data, represent claims accepted by and paid by health insurance companies. Because insurers generally pay for all of a patient's care, or at least record all care for payment decisions on future claims, closed claims present a fully complete view of services. The total number of patients available for analysis (i.e. denominator) is available from the enrollment file. Closed claims generally lag by 3-6 months.

To create linkages across databases to ensure de-identified, longitudinal, de-duplicated patient data, all data partners use the HealthVerity technology within their system to create a unique, secure, encrypted, and non-identifiable patient token. This token is then employed as a consistent linkage key across datasets. The linkage of patients has high accuracy: 99.7% of linkages made are made correctly (0.3% false positives), and 96% of possible linkages are made (4% false negative) and is done according to HIPAA regulations. With real-time assembly of data requiring the use of multiple sources, this approach appropriately balances timeliness with fidelity of linkage.

All data include key factors such as patient age, sex, and 3-digit zip level. Race and ethnicity information is not available. Use of data and the precise granularity available is controlled by HIPAA requirements or application of public health exemption. No PHI (protected health information) or PII (personal identifying information) leaves the data owner's possession, and all research data were certified HIPAA compliant by expert determination.

9.6. Bias

The principal validity threat relevant to the current analyses is information bias, as claims-based algorithms to identify incidence may overestimate or underestimate the absolute incidence of a given AESI through misclassification. To address this concern, outcomes are considered in the context of published estimates from other sources.

When considering comparative analyses, there are several sources of potential bias to consider. Differences in healthcare utilization prior to and following the pandemic may influence the sensitivity and specificity of event rates in the observed time periods, and open and closed claim environments have the potential to vary in performance. Further, the screening comparisons do not adjust for differences in the population receiving vaccination and their historical comparison other than age and gender – these confounders will be controlled in SCRI analyses where triggered.

Future analyses including comparative components will include use of alternative reference groups to capture changes in healthcare utilization related to the COVID-19 pandemic, and will include a combination of historical control-based and self-controlled analyses to facilitate triangulation across analytic approaches.

9.7. Study size

The analysis cohorts for background incidence rates in the Pre-COVID and Active COVID periods will be drawn from more than 50 million patients from the HealthVerity database. The cohort for vaccinated individuals will be formed from the entirety of available HealthVerity data from over 140 million patients.

9.8. Data transformation

Not applicable.

9.9. Statistical methods

9.9.1. Main summary measures

Standard descriptive statistics, such as counts and percentages for categorical variables, are used to characterize the patient cohort.

9.9.2. Main statistical methods

Incidence rates are calculated as the number of patients with an event divided by the sum of person-time at risk, where person-time is the total days from the index date through the date of the first instance of the applicable AESI or the end of observation (i.e., earliest of end of health plan enrollment, end of study period, or end of health plan enrollment). Incidence rates are presented per 100,000 person-years, and are shown with an associated confidence interval overall and for each age, sex, and age by sex specific stratum. Standardization to the age and sex distribution of the broad US population was also performed for males and females.

The incidence rate ratio (IRR) with 95% CI was then calculated to estimate the relative change in IRs pre/post mRNA-1273 vaccine EUA. IRRs were calculated overall and may be stratified as above.

For myocarditis and pericarditis, the observed vs expected event ratios (O/Es) and corresponding 95% CI were calculated as the ratio of the number of events among those vaccinated with mRNA-1273 to the number of events expected in this population from background rates as follows:

Number Expected (NE) = $\sum_s [\text{Background IR}_a]_s \times [\text{Exposed persons}]_s \times \text{time at risk}$

- Where a is the IR calculated in the historical pre-COVID-19 period
- Where s is the age group, sex, and calendar period stratum
- The time at risk is the cumulative sum of days for all persons exposed to the vaccine during which there is medical plausibility that there is a vaccine-associated increased risk of experiencing an event. The time at risk was calculated by summing the days after a dose was administered (risk interval). This considers the real-world implication that persons are not fully adherent and do not receive both doses of vaccine.

Time at risk for the analysis of myocarditis and pericarditis was specified as 7 days following vaccination.

9.9.3. Missing values

Administrative claims do not distinguish between absence of evidence and evidence of absence. As such, missing values are not identifiable.

9.9.4. Sensitivity analyses

Not applicable

9.9.5. Amendments to the statistical analysis plan

Changes to the study protocol have been described in [Section 8](#). The Statistical Analysis Plan will be updated accordingly up

9.10. Quality control

Data provided by HealthVerity were examined for completeness and consistency, including identifying any issues with missing files or variations in data structure. Standard data quality checks included:

- Generating statistics for each variable including the number of records observed, the number of unique values observed, the number of null values observed and percent fill, and the most frequently occurring values
- Comparing the schema of data received with the expected schema per vendor documentation
- Creating event density distributions for new datasets and data updates in order to explore event data over time and identify possible gaps or missing files
- Checking for variables with high proportions of missing data
- Cross-checking imported record counts against original data counts
- Cross-checking patient event dates against enrollment files (where available)
- Parallel coding for final validation of data transformation before platform deployment

All results were reviewed by the principal investigators to evaluate internal consistency of counts and totals. All calculated variables were checked against the component variables (crosstabulations) to ensure accuracy.

10. Results

10.1. Participants

There were 140,122,236 individuals identified in the HealthVerity database at any time between 01 December 2017 and 10 December 2020. Of these individuals, 108.8 million were enrolled in a health plan providing information on enrollment during the same time frame. We excluded 134,778 individuals with missing information on sex, 6,096 individuals with missing information on age, and 15,157,248 individuals without continuous enrollment for at least 365 days at any time during the study period before sampling 50,015,708 individuals to mirror the distribution of the 2019 US census age and sex distribution. Of these individuals, 38,686,912 were at least 18 years of age.

In the post-EUA period, there were 15,524,986 individuals receiving at least one dose of mRNA-1273 identified. Of these, 89,690 were excluded based on age <18 years of age, 1,656 were excluded due to missing age, 4,155,278 were excluded due to inadequate baseline data availability, and 338,928 were excluded based on conflicting values for gender. Further, 30,293 were excluded based on a prior COVID-19 vaccine; 10,909,141 individuals met all cohort entry criteria. Among these mRNA-1273 vaccine recipients, 73.5% received a second dose with a median dosing interval of 28 days (IQR 28 – 28 days). Follow-up was censored due to receipt of a non-Moderna COVID-19 vaccine in 0.5% of cases.

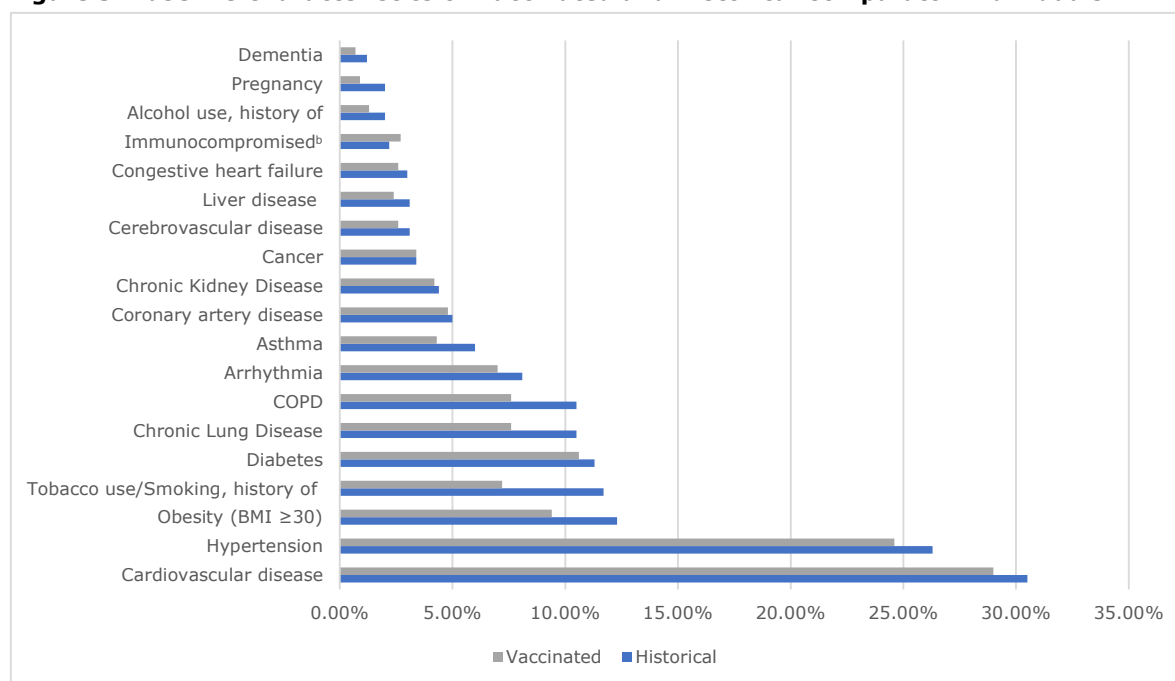
For analysis of each AESI, individuals with a diagnosis of the applicable outcome within the clean period required were excluded to remove prevalent cases from the incidence estimates. As such, the effective sample size used to calculate each incidence rate estimate varies as shown in [Table 1](#).

10.2. Descriptive data

Characteristics of the 26,813,190 cohort members in the pre-COVID-19 time period and the 10,909,141 mRNA-1273 vaccine recipients meeting study entry criteria are shown in [Table 2](#). The median age of vaccinated individuals was higher than the historical cohort (55 vs 47 years) and a larger proportion of vaccine recipients were female (56.5% vs 52.3%). All regions on the United States were represented, with 81.1% patients entering follow-up in the historical cohort during 2018Q4 (the start of the applicable time period) and 60.3% of vaccine recipients during Q12021. The populations varied in payer type; over half (55.5%) of the historical cohort was commercially insured, however individuals with Medicare (12.9%), Medicaid (28.4%), and other types of coverage were also included. By contrast, 67.1% of the vaccinated cohort had an unknown or other insurance type, which reflects inclusion of open claims data in this period.

As shown in [Figure 3](#), most comorbidities were documented for similar proportions of the historical and vaccinated cohorts, respectively. The historical cohort showed higher baseline rates of tobacco use, obesity, COPD, chronic lung disease, and asthma compared to the vaccinated group. For both groups, the most frequently observed comorbidity was cardiovascular disease followed by hypertension.

Figure 3: Baseline Characteristics of Vaccinated and Historical Comparator Individuals



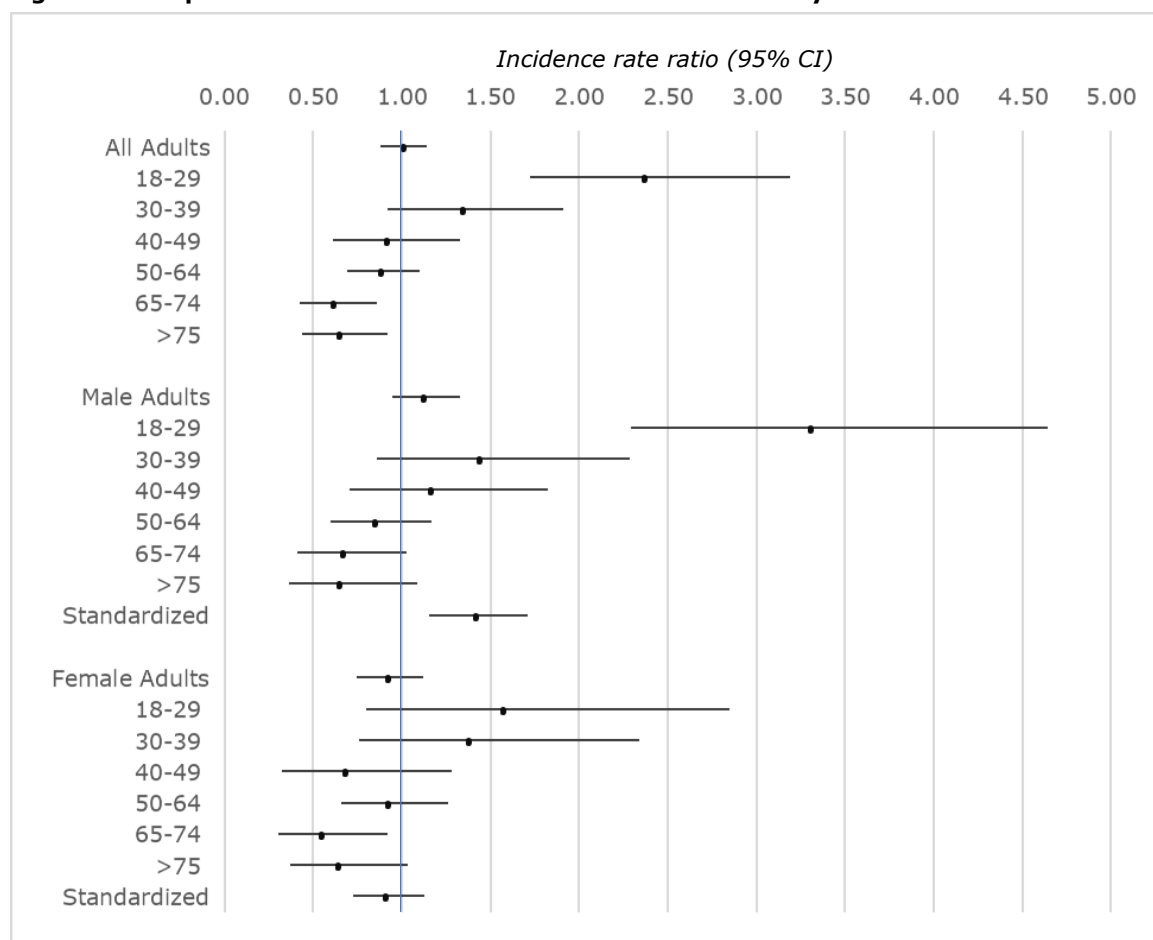
The most common classes of medications used at baseline included antibacterial medications (32.1% historical, 27.2% of vaccinated), analgesics/antipyretics (30.6% historical, 28.9% vaccinated) and hypotensive agents (24.7% historical, 32.6% vaccinated). Baseline use of vaccines, hypotensive agents, renin-aldosterone system inhibitors, antilipemic agents, and psychotherapeutic agents was more common in the vaccinated population than the historical group ([Table 2](#)).

10.3. Main results

10.3.1. Analysis of Myocarditis

Myocarditis was observed in 2,186 patients in the historical cohort (IR 9.98, cases per 100,000 person-years 95% CI 9.47 – 10.30) and in 253 patients following vaccination (IR 9.94 cases per 100,000 person-years, 95% CI 8.72 – 11.17), producing an incidence rate ratio of 1.01 (95% CI 0.88 – 1.14). This small increase appears to be driven by a larger increase in young men, where the incidence following vaccination was 34.71 cases per 100,000 person-years (IRR 3.30, 95% CI 2.29 – 4.65). Although there were small numerical increases in men ages 30-39 and young women, these estimates are based on small numbers and lack precision. No indication of an increased rate of myocarditis was observed for older individuals (Table 3), noting that small case counts limit precision as shown by the wide confidence intervals visualized in Figure 4.

Figure 4: Comparison of vaccinated vs historical incidence of myocarditis



Observed vs expected analyses considering a 7-day risk window following vaccination produced findings with similar interpretation. An increase was observed in all individuals 18 to 29 years of age, where 9 events were observed and 2 expected (O/E ratio 4.93, 95% CI 2.25 – 9.36). Upon stratification, this was driven by men for whom 8 events were observed and 1 expected (O/E ratio 6.97, 95% CI 3.01 – 13.74). For women in this age group, 1 case was expected and 1 was observed. Analyses in the 30 to 39-year age group included too few cases for interpretability, with 1 case expected and 2 cases observed for each gender.

A smaller, numerical increase for men ages 18 to 29 was also observed for pericarditis. This outcome was observed in 5,418 patients in the historical cohort (IR 24.51, cases per 100,000 person-years 95% CI 23.86-25.16) and in 533 patients following vaccination (age and sex standardized IR 20.95 cases per 100,000 person-years, 95% CI 19.17 – 22.73), producing an incidence rate ratio of 0.85 (95% CI 0.78 – 0.93). In young males, 32 cases after vaccination produced an IR of 30.85 per 100,000 person-years (95% CI 20.16 – 41.54), corresponding to an IRR of 1.41 (95% CI 0.97 – 1.99).

Although this subgroup specific or overall analysis did not meet the pre-specified threshold for observed vs. expected analyses, questions have been raised concerning a possible increased risk of pericarditis, especially given the possibility of myopericarditis. As such, these analyses were performed by request of the sponsor. Overall analyses and most age and sex specific analyses did not show an increase for the 7-day risk window, however an increase was observed in the 18 to 29-year age group (4 cases expected, 14 observed, OE ratio 3.31, 95% CI 1.81 – 5.56). This was again driven by young males, where 2 cases were expected and 10 observed (OE ratio 4.19, 95% CI 2.01 – 7.71). A smaller numerical increase was also observed for young women 2 cases expected, 4 cases observed for ages 18 to 29 and 30 to 39, however estimates were poorly precise given small event numbers.

The MAH proposes execution of SCRI analyses for each outcome, and a protocol appendix has been submitted for review as an appendix to this interim report.

10.3.2. Analysis of Other AESI

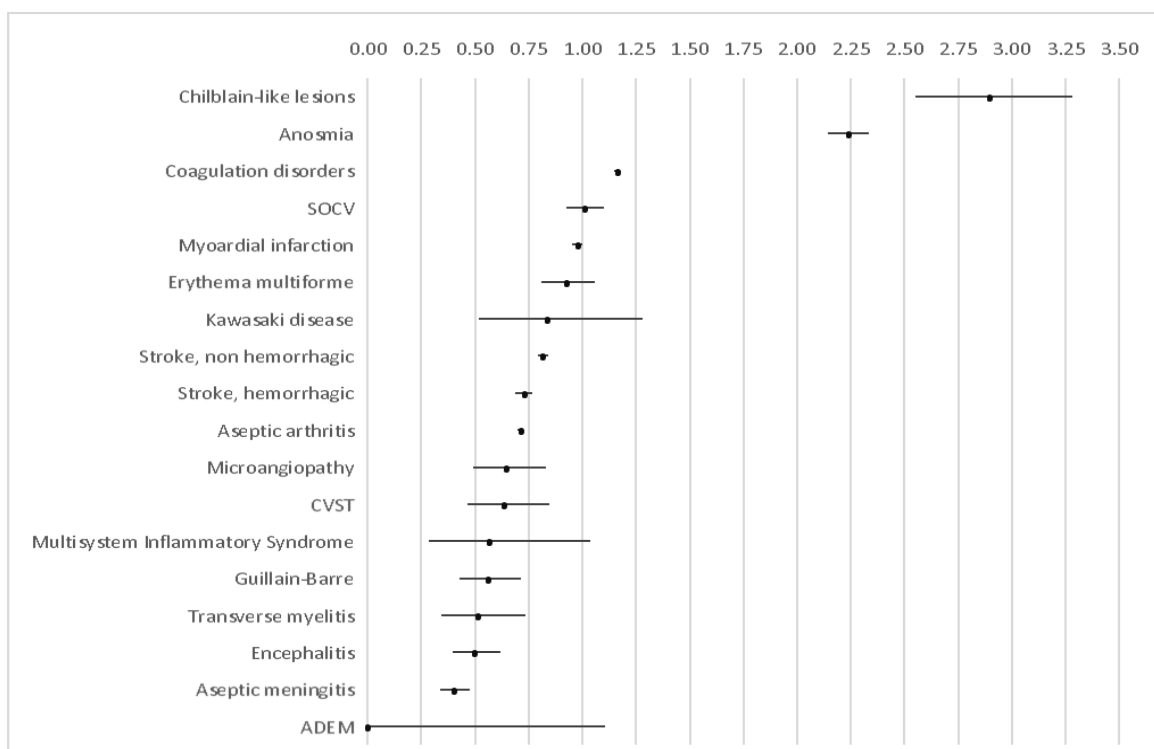
Consistent with expectations based on published literature, the incidence of study outcomes varied substantially across the AESI considered. Several outcomes were observed at rates that were higher than would have been expected based on population-based studies, which may be attributable to overly sensitive or poorly specific case definitions. Where case definitions were not considered suitable for progression to comparative analyses without additional review, the sponsor is considering potential modifications to algorithms. Analyses are presented for outcomes where the background incidence was similar to published rates, including those from the ACCESS project.

Of the outcomes included in this interim analysis, incidence of Chilblain-like lesions and anosmia was meaningfully elevated following vaccination compared to historical data. For Chilblain-like lesions, 996 cases were observed in the historical cohort (IR 4.37, 95% CI 4.09-4.64) and 322 were observed following vaccination (IR 12.65, 95% CI 11.27 – 14.04), producing a standardized incidence rate ratio of 2.90 (95% CI 2.55 – 3.28). The increase was higher in younger patients, with a peak incidence rate ratio of 6.45 (95% CI 3.35 – 11.97) in males ages 30-39 years. Elevation of the risk ratio decreased across categories of increasing age for both sexes.

Anosmia occurred in 10,800 cases in the historical cohort (IR 48.84 per 100,000 person-years, 95% CI 47.95 – 49.79) and in 2,774 cases following vaccination (IR 109.26 per 100,000 person-years, 95% CI 105.19 – 113.33), producing an IRR of 2.24 (95% CI 2.14 – 2.33). Like Chilblain-like lesions, the increase in the incidence following vaccination was stronger for younger vaccine recipients and declined with advancing age. The peak IRR occurred in women 18-29 years of age, however most age specific rates were comparable for men and women.

The extent to which these reflect increased awareness and diagnosis of these conditions given increased recognition emerging during the pandemic is uncertain. Further, no exclusion of anosmia cases based on presence of COVID-19 breakthrough infection has been applied. Regardless, observed vs expected analyses are in progress, and will be described along with relevant SCRI protocol appendices (if applicable per results from the observed vs expected analyses) and comparisons versus the historical active COVID-19 period (time period 2) in the next interim report.

Other AESI occurred following vaccination at rates that were similar to or lower than the incidence observed for the historical cohort ([Figure 5](#)).



When considering stratified analyses, coagulation disorders showed a small but statistically significant increase for males 18 to 29 years (IRR 1.38, 95% CI 1.22 – 1.56) that did not meet criteria for execution of observed versus expected analyses; no other age, sex, or age by sex group suggested an increase. Multisystem inflammatory syndrome, observed in 153 cases in the historical cohort (IR 0.66, 95% CI 0.56 – 0.78) and 10 cases in the vaccinated cohort (IR 0.45, 95% CI 0.19 – 0.99) produced stratum specific estimates that were questionably interpretable given the very low stratum specific case counts observed.

10.4. Other analyses

Not applicable

10.5. Adverse events/adverse reactions

The nature of the data used in this assessment preclude causality assessment at the individual case level. Given that only deidentified secondary data were used, adverse event reporting does not apply.

11. Discussion

11.1. Key results

This study described preliminary assessments of incidence and incidence rate ratios for AESI relevant to COVID-19 vaccine safety monitoring in a large, US cohort of adults. As expected, substantial variation was observed in the incidence estimates identified. Consistent with findings for MAH review of the global safety database, an increase in the risk of myocarditis and pericarditis was identified for young men, with incidence rate ratio of 3.3 for myocarditis in this subgroup. This was similar to the increase observed for other available mRNA vaccine in Israel, and is aligned with increases in risk for

this subgroup described in the literature. Age and sex adjusted observed-to-expected ratios focused on the 7-day period following vaccination suggest that the risk is stronger proximate to vaccination. Generally, these events appear to occur most often shortly after the second dose of vaccine, and dose-specific risk will be assessed in future reports. The MAH has proposed a Protocol Annex for execution of SCRI analyses for these outcomes, which will be conducted upon regulatory approval of the specified SCRI plan per the study protocol.

Additionally, significant increases in the rate of anosmia and Chilblain-like lesions were identified following vaccination, especially in younger vaccine recipients. It is unclear whether this may be influenced by increased recognition of these conditions in association with SARS CoV-2 infection given the use historical comparator data and resulting secular trends, however additional analyses will characterize and refine the observed signal. Other outcomes did not show a meaningfully increased rate following receive of mRNA-1273.

11.2. Limitations

In this study, administrative claims are used to identify diagnoses relevant to vaccine safety monitoring, however, estimated incidence in these settings may vary substantially based on the algorithm used. Algorithms that are overly sensitive may identify “rule out” or other tentative diagnoses, and this can inflate the apparent rate. By contrast, outcomes that are unlikely to come to medical attention or receive a diagnosis in a physician office, such as very early spontaneous abortion, are likely to be missed in a way that incidence will be underestimated. Algorithms must therefore balance the competing objectives of sensitivity and specificity based on the objectives of a given study.

Administrative claims collect data based on healthcare encounters, creating a longitudinal view of the patient on the basis of codes used primarily for billing. As such, conditions that do not affect reimbursement or come to medical attention can be missing. This type of data source also necessarily conflates absence of evidence with evidence of absence, which can be a source of bias. In our analysis, slightly lower rates of several comorbidities were observed following vaccination compared to the historical time frame regardless of an older age distribution. This may have multiple explanations. It is possible that individuals with substantial comorbidity were more likely to be vaccinated quickly in the campaign, which may have more often included mass vaccination centers not captured in integrated healthcare delivery systems or healthcare claims environments including HealthVerity . Alternatively, care seeking behavior during the baseline timeframe for this population could be reduced by the pandemic, producing less opportunity to capture baseline health status via medical encounters for individuals vaccinated early on in Time Period 3. In the former situation, a concern may arise for generalizability. In the latter, control of confounding by adjustment may become questionable. This would be addressed in SCRI analyses used to evaluate signals, however, given that this design efficiently manages time-invariant confounding.

11.3. Interpretation

Preliminary estimates of incidence for AESI relevant to vaccine safety monitoring show substantial variation in estimated incidence rates by outcome, age and gender. This was expected based on known epidemiology and published sources, and underscores the importance of subgroup analyses as planned in our ongoing assessments. Where estimates are meaningfully different from published rates in comparable settings, additional review of case definitions based on consideration of claims profiles is ongoing, and may support refinement of the case definitions applied. These updated results are anticipated in Interim Report 4.

An increased rate of myocarditis and possibly pericarditis was observed in young men, which is consistent with findings from surveillance and other published Real-World Evidence studies. This risk will be further characterized in SCRI analyses. Additional analyses to refine results for anosmia and Chilblain-like lesions are also being conducted.

11.4. Generalisability

Because these rates are assessed in US patients, the rates observed may be less generalizable to other countries or subpopulations where there are meaningful differences in the underlying risk of the AESI considered. Patient and population-based characteristics should be considered prior to use of these background rates. Further, as described in [Section 11.2](#), it is possible that vaccinated individuals captured in HealthVerity data may differ from other US vaccine recipients, particularly those who accessed mass vaccination sites or employer-sponsored vaccination sites. Likewise, vaccinated individuals captured in US claims may differ from vaccine recipients in other countries, especially where vaccination practice, indicated populations, and characteristics of the vaccine roll out have varied. A mechanism that would produce the expectation that these differences should change the relationship between vaccination and outcomes of interest is not presently clear, reducing the expected impact to interpretation.

12. Other information

Not applicable.

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Appendices

Annex 1. List of stand-alone documents

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[Table 3b: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Acute disseminated encephalomyelitis \(ADEM\)](#)

[Table 3c: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Acute myocardial infarction \(AMI\)](#)

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[Table 3o: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Myocarditis](#)

[Table 3p: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Pericarditis](#)

[Table 3q: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Single organ cutaneous vasculitis](#)

[Table 3r: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Stroke, hemorrhagic](#)

[Table 3s: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Stroke, non-hemorrhagic](#)

[Table 3t: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Transverse myelitis](#)

[Table 4a: Observed to Expected Analysis, mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Myocarditis](#)

[Table 4b: Observed to Expected Analysis, mRNA-1273 Recipients and Historical Controls Age \$\geq 18\$, Data through 20 June 2021: Pericarditis](#)

Table 1. Formation of the study cohort

ANALYTIC DATASET TIME PERIOD 1 & 2 Combined	N	Excluded
PATIENTS IN HEALTHVERITY DATABASE (DECEMBER 1, 2017 -	140,122,236	
PATIENTS WITH MEDICAL AND PHARMACY ENROLLMENT	108,860,504	31,261,732
PATIENTS WITH NON-MISSING DATA ON SEX	108,725,726	134,778
N -MISSING YEAR OF BIRTH	108,719,630	6,096
ENROLLMENT FOR 365 DAYS AT ANY POINT BETWEEN DECEMBER 1, 2017-DECEMBER 10, 2020 (60-DAY ALLOWABLE	93,562,382	15,157,248
STRATIFIED RANDOM SAMPLE TO MIRROR DISTRIBUTION OF THE 2019 US CENSUS AGE/SEX DISTRIBUTION	50,015,708	43,546,674
ADULT PATIENTS	38,686,912	
PEDIATRIC PATIENTS	11,328,796	

Patients in background random sample	50,015,708
Patients added to platform dataset as part of bi-weekly HV data	47,548,102
Patients in dataset	97,563,810

	N	Excluded (N)	Excluded (%)
T1: Adult Baseline 365-day Cohort	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,722	63,411,088	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,968	40,754	0.12%
Excluded based on Age < 18	27,237,043	6,874,925	20.15%
Excluded based on Age missing	27,236,505	538	0.00%
Excluded based on Conflicting genders	26,813,190	423,315	1.55%
Total Patients	26,813,190		

T1: Acute Aseptic Arthritis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,134,809	63,429,001	65.01%
Excluded: vaccinated patients not in the background random sample	34,093,851	40,958	0.12%
Excluded based on Age < 18	27,218,926	6,874,925	20.16%
Excluded based on Age missing	27,218,388	538	0.00%
Excluded based on Conflicting genders	26,795,073	423,315	1.56%
Excluded based on Acute Aseptic Arthritis in Washout	26,777,797	17,276	0.06%
Total Patients	26,777,797		

T1: Acute Myocardial Infarction	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,140,943	63,422,867	65.01%
Excluded: vaccinated patients not in the background random sample	34,100,032	40,911	0.12%
Excluded based on Age < 18	27,225,107	6,874,925	20.16%
Excluded based on Age missing	27,224,569	538	0.00%
Excluded based on Conflicting genders	26,801,254	423,315	1.55%
Excluded based on Acute Myocardial Infarction in Washout	26,793,742	7,512	0.03%
Total Patients	26,793,742		

T1: ADEM	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,712	63,411,098	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,958	40,754	0.12%
Excluded based on Age < 18	27,237,033	6,874,925	20.15%
Excluded based on Age missing	27,236,495	538	0.00%
Excluded based on Conflicting genders	26,813,180	423,315	1.55%
Excluded based on ADEM in Washout	26,813,166	14	0.00%
Total Patients	26,813,166		

T1: Anosmia, Aguesia	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,151,009	63,412,801	65.00%
Excluded: vaccinated patients not in the background random sample	34,110,245	40,764	0.12%
Excluded based on Age < 18	27,235,320	6,874,925	20.16%
Excluded based on Age missing	27,234,782	538	0.00%
Excluded based on Conflicting genders	26,811,467	423,315	1.55%
Excluded based on Anosmia, Ageusia in Washout	26,809,319	2,148	0.01%
Total Patients	26,809,319		

T1: Aseptic Meningitis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,178	63,411,632	65.00%

	N	Excluded (N)	Excluded (%)
T3: Adult Baseline 365-day Cohort			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Total Patients	10,909,141		

T3: Acute Aseptic Arthritis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Acute Aseptic Arthritis in Washout	10,876,923	32,218	0.30%
Total Patients	10,876,923		

T3: Acute Myocardial Infarction Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Acute myocardial infarction (AMI) in Wash	10,881,891	27,250	0.25%
Total Patients	10,881,891		

T3: ADEM Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Acute disseminated encephalomyelitis (ADEM)	10,909,132	9	0.00%
Total Patients	10,909,132		

T3: Anosmia, Aguesia Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%

Excluded: vaccinated patients not in the background random sample	34,111,418	40,760	0.12%
Excluded based on Age < 18	27,236,493	6,874,925	20.15%
Excluded based on Age missing	27,235,955	538	0.00%
Excluded based on Conflicting genders	26,812,640	423,315	1.55%
Excluded based on Aseptic Meningitis in Washout	26,812,320	320	0.00%
Total Patients	26,812,320		

T1: Chilblain-like Lesions	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,631	63,411,179	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,875	40,756	0.12%
Excluded based on Age < 18	27,236,950	6,874,925	20.15%
Excluded based on Age missing	27,236,412	538	0.00%
Excluded based on Conflicting genders	26,813,097	423,315	1.55%
Excluded based on Chilblain-like Lesions in Washout	26,812,929	168	0.00%
Total Patients	26,812,929		

T1: Coagulation Disorders	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,094,208	63,469,602	65.05%
Excluded: vaccinated patients not in the background random sample	34,052,679	41,529	0.12%
Excluded based on Age < 18	27,177,754	6,874,925	20.19%
Excluded based on Age missing	27,177,216	538	0.00%
Excluded based on Conflicting genders	26,753,901	423,315	1.56%
Excluded based on Coagulation Disorders in Washout	26,630,976	122,925	0.46%
Total Patients	26,630,976		

T1: CSVT	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,620	63,411,190	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,866	40,754	0.12%
Excluded based on Age < 18	27,236,941	6,874,925	20.15%
Excluded based on Age missing	27,236,403	538	0.00%
Excluded based on Conflicting genders	26,813,088	423,315	1.55%
Excluded based on CSVT in Washout	26,813,001	87	0.00%
Total Patients	26,813,001		

T1: Erythema multiforme	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,249	63,411,561	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,490	40,759	0.12%
Excluded based on Age < 18	27,236,565	6,874,925	20.15%
Excluded based on Age missing	27,236,027	538	0.00%
Excluded based on Conflicting genders	26,812,712	423,315	1.55%
Excluded based on Erythema multiforme in Washout	26,812,184	528	0.00%
Total Patients	26,812,184		

T1: GBS	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,547	63,411,263	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,793	40,754	0.12%
Excluded based on Age < 18	27,236,868	6,874,925	20.15%
Excluded based on Age missing	27,236,330	538	0.00%
Excluded based on Conflicting genders	26,813,015	423,315	1.55%
Excluded based on GBS in Washout	26,812,840	175	0.00%
Total Patients	26,812,840		

T1: Kawasaki Disease	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,661	63,411,149	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,907	40,754	0.12%
Excluded based on Age < 18	27,236,982	6,874,925	20.15%
Excluded based on Age missing	27,236,444	538	0.00%
Excluded based on Conflicting genders	26,813,129	423,315	1.55%
Excluded based on Kawasaki Disease in Washout	26,813,021	108	0.00%
Total Patients	26,813,021		

T1: Microangiopathy	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,505	63,411,305	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,749	40,756	0.12%
Excluded based on Age < 18	27,236,824	6,874,925	20.15%
Excluded based on Age missing	27,236,286	538	0.00%
Excluded based on Conflicting genders	26,812,971	423,315	1.55%

Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Anosmia, Ageusia in Washout	10,883,572	25,569	0.23%
Total Patients	10,883,572		

T3: Aseptic Meningitis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Aseptic meningitis in Washout	10,908,596	545	0.00%
Total Patients	10,908,596		

T3: Chilblain-like Lesions Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Chilblain-like lesions in Washout	10,907,967	1,174	0.01%
Total Patients	10,907,967		

T3: Coagulation Disorders Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Coagulation Disorders in Washout	10,769,938	139,203	1.28%
Total Patients	10,769,938		

T3: CSVT Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Central sinus venous thrombosis (CSVT) i	10,908,926	215	0.00%
Total Patients	10,908,926		

T3: Erythema multiforme Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Erythema multiforme in Washout	10,908,341	800	0.01%
Total Patients	10,908,341		

T3: GBS Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%

Excluded based on Microangiopathy in Washout	26,812,532	439	0.00%
Total Patients	26,812,532		

T1: MIS	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,693	63,411,117	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,939	40,754	0.12%
Excluded based on Age < 18	27,237,014	6,874,925	20.15%
Excluded based on Age missing	27,236,476	538	0.00%
Excluded based on Conflicting genders	26,813,161	423,315	1.55%
Excluded based on MIS in Washout	26,813,135	26	0.00%
Total Patients	26,813,135		

T1: Myocarditis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,334	63,411,476	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,576	40,758	0.12%
Excluded based on Age < 18	27,236,651	6,874,925	20.15%
Excluded based on Age missing	27,236,113	538	0.00%
Excluded based on Conflicting genders	26,812,798	423,315	1.55%
Excluded based on Myocarditis in Washout	26,812,260	538	0.00%
Total Patients	26,812,260		

T1: Pericarditis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,151,733	63,412,077	65.00%
Excluded: vaccinated patients not in the background random sample	34,110,972	40,761	0.12%
Excluded based on Age < 18	27,236,047	6,874,925	20.15%
Excluded based on Age missing	27,235,509	538	0.00%
Excluded based on Conflicting genders	26,812,194	423,315	1.55%
Excluded based on Pericarditis in Washout	26,811,080	1,114	0.00%
Total Patients	26,811,080		

T1: Single Organ Cutaneous Vasculitis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,151,746	63,412,064	65.00%
Excluded: vaccinated patients not in the background random sample	34,110,986	40,760	0.12%
Excluded based on Age < 18	27,236,061	6,874,925	20.15%
Excluded based on Age missing	27,235,523	538	0.00%
Excluded based on Conflicting genders	26,812,208	423,315	1.55%
Excluded based on Single Organ Cutaneous Vasculitis in Washout	26,810,879	1,329	0.00%
Total Patients	26,810,879		

T1: Stroke, hemorrhagic	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,149,639	63,414,171	65.00%
Excluded: vaccinated patients not in the background random sample	34,108,851	40,788	0.12%
Excluded based on Age < 18	27,233,926	6,874,925	20.16%
Excluded based on Age missing	27,233,388	538	0.00%
Excluded based on Conflicting genders	26,810,073	423,315	1.55%
Excluded based on Stroke, hemorrhagic in Washout	26,808,511	1,562	0.01%
Total Patients	26,808,511		

T1: Stroke, non-hemorrhagic	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,142,376	63,421,434	65.01%
Excluded: vaccinated patients not in the background random sample	34,101,516	40,860	0.12%
Excluded based on Age < 18	27,226,591	6,874,925	20.16%
Excluded based on Age missing	27,226,053	538	0.00%
Excluded based on Conflicting genders	26,802,738	423,315	1.55%
Excluded based on Stroke, non-hemorrhagic in Washout	26,795,753	6,985	0.03%
Total Patients	26,795,753		

T1: Transverse myelitis	97,563,810		
Excluded based on Insufficient enrollment in Time Period 1*	34,152,643	63,411,167	64.99%
Excluded: vaccinated patients not in the background random sample	34,111,889	40,754	0.12%
Excluded based on Age < 18	27,236,964	6,874,925	20.15%
Excluded based on Age missing	27,236,426	538	0.00%
Excluded based on Conflicting genders	26,813,111	423,315	1.55%
Excluded based on Transverse myelitis in Washout	26,813,023	88	0.00%
Total Patients	26,813,023		

T1: Encephalitis/encephalomyelitis	97,563,810		
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Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Guillain-Barre Syndrome (GBS) in Washout	10,908,895	246	0.00%
Total Patients	10,908,895		

T3: Kawasaki Disease Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Kawasaki Disease in Washout	10,909,043	98	0.00%
Total Patients	10,909,043		

T3: Microangiopathy Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Microangiopathy in Washout	10,908,741	400	0.00%
Total Patients	10,908,741		

T3: MIS Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Multisystem Inflammatory Syndrome (MIS)	10,909,093	48	0.00%
Total Patients	10,909,093		

T3: Myocarditis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Myocarditis in Washout	10,908,030	1,111	0.01%
Total Patients	10,908,030		

T3: Pericarditis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Pericarditis in Washout	10,906,803	2,338	0.02%
Total Patients	10,906,803		

T3: Single Organ Cutaneous Vasculitis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%

Excluded based on Insufficient enrollment in Time Period 1*	44,140,857	53,422,953	54.76%
Excluded: vaccinated patients not in the background random sample	38,012,580	6,128,277	13.88%
Excluded based on Age < 18	30,210,239	7,802,341	20.53%
Excluded based on Age missing	30,209,647	592	0.00%
Excluded based on Conflicting genders	29,727,751	481,896	1.60%
Excluded based on Encephalitis/encephalomyelitis in Washout	29,727,712	39	0.00%
Total Patients	29,727,712		

*Note: the number excluded for each criteria can change between AESI-cohorts given how the platform prioritizes exclusion criteria. For

Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Single Organ Cutaneous Vasculitis in Washout	10,906,822	2,319	0.02%
Total Patients	10,906,822		

T3: Stroke, hemorrhagic Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Stroke, hemorrhagic	10,904,748	4,393	0.04%
Total Patients	10,904,748		

T3: Stroke, non-hemorrhagic Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Stroke, non-hemorrhagic in Washout	10,890,062	19,079	0.17%
Total Patients	10,890,062		

T3: Transverse myelitis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	11,278,362	4,155,278	26.92%
Excluded based on Conflicting Genders	10,939,434	338,928	3.01%
Excluded based on any prior COVID-19 vaccine	10,909,141	30,293	0.28%
Excluded based on Transverse Myelitis in Washout	10,909,014	127	0.00%
Total Patients	10,909,014		

T3: Encephalitis/Encephalomyelitis Attrition			
Patients in dataset	97,563,810		
Excluded: not vaccinated with mRNA-1273	15,524,986	82,038,824	84.09%
Excluded based on Age <18	15,435,296	89,690	0.58%
Excluded based on Age Missing	15,433,640	1,656	0.01%
Excluded based on Medical or pharmacy claim	10,296,482	5,137,158	33.29%
Excluded based on Conflicting Genders	9,985,891	310,591	3.02%
Excluded based on any prior COVID-19 vaccine	9,955,622	30,269	0.30%
Excluded based on Encephalitis/encephalomyelitis in Washout	9,955,430	192	0.00%
Total Patients	9,955,430		

Table 2. Adult Baseline Characteristics

Characteristic	All Patients				Male				Female			
	Time period 1		Time period 3		Time period 1		Time period 3		Time period 1		Time period 3	
	N	%	N	%	N	%	N	%	N	%	N	%
All Patients	26,813,190	N/A	10,909,141	N/A	12,781,767	N/A	4,745,658	N/A	14,031,423	N/A	6,163,483	N/A
Age												
Mean (SD)	47.39 (18.26)		53.01 (18.00)		46.54 (17.96)		53.31 (17.57)		48.16 (18.50)		52.79 (18.32)	
Median (Q1, Q3)	47.00 [32.00, 62.00]		55.00 [39.00, 66.00]		46.00 [31.00, 61.00]		56.00 [40.00, 66.00]		48.00 [33.00, 62.00]		55.00 [38.00, 66.00]	
Min, Max	[18.00, 92.00]		[18.00, 93.00]		[18.00, 92.00]		[18.00, 93.00]		[18.00, 92.00]		[18.00, 93.00]	
Age Categories; n (%)												
18-29 years	5,646,635	21.1%	1,399,287	12.8%	2,827,712	22.1%	569,435	12.0%	2,818,923	20.1%	829,852	13.5%
30-39 years	4,447,548	16.6%	1,381,481	12.7%	2,162,955	16.9%	577,498	12.2%	2,284,593	16.3%	803,983	13.0%
40-49 years	4,331,321	16.2%	1,571,723	14.4%	2,102,134	16.4%	681,547	14.4%	2,229,187	15.9%	890,176	14.4%
50-64 years	7,334,491	27.4%	3,566,899	32.7%	3,480,457	27.2%	1,613,815	34.0%	3,854,034	27.5%	1,953,084	31.7%
65-74 years	3,237,213	12.1%	1,844,331	16.9%	1,473,025	11.5%	831,125	17.5%	1,764,188	12.6%	1,013,206	16.4%
≥75 years	1,815,982	6.8%	1,145,420	10.5%	735,484	5.8%	472,238	10.0%	1,080,498	7.7%	673,182	10.9%
Sex												
Male	12,781,767	47.7%	4,745,658	43.5%	12,781,767	100.0%	4,745,658	100.0%	0	0.0%	0	0.0%
Female	14,031,423	52.3%	6,163,483	56.5%	0	0.0%	0	0.0%	14,031,423	100.0%	6,163,483	100.0%
Geographic Region; n (%)												
Northeast	4,489,320	16.7%	2,022,560	18.5%	2,101,986	16.4%	874,797	18.4%	2,387,334	17.0%	1,147,763	18.6%
Midwest	6,729,063	25.1%	2,624,502	24.1%	3,305,026	25.9%	1,168,460	24.6%	3,424,037	24.4%	1,456,042	23.6%
South	8,615,749	32.1%	3,672,899	33.7%	3,976,772	31.1%	1,567,318	33.0%	4,638,977	33.1%	2,105,581	34.2%
West	6,734,954	25.1%	2,412,505	22.1%	3,287,333	25.7%	1,059,791	22.3%	3,447,621	24.6%	1,352,714	21.9%
US Territories	197,849	0.7%	56,479	0.5%	88,218	0.7%	23,360	0.5%	109,631	0.8%	33,119	0.5%
Missing	46,255	0.2%	120,196	1.1%	22,432	0.2%	51,932	1.1%	23,823	0.2%	68,264	1.1%
Calendar quarter of cohort entry ^a												
...Q4 2018	21,781,994	81.2%			10,356,282	81.0%			11,425,712	81.4%		
...Q1 2019	2,259,889	8.4%			1,098,093	8.6%			1,161,796	8.3%		
...Q2 2019	1,260,233	4.7%			612,021	4.8%			648,212	4.6%		
...Q3 2019	976,083	3.6%			461,048	3.6%			515,035	3.7%		
...Q4 2019	534,991	2.0%			254,323	2.0%			280,668	2.0%		
Q4 2020			88,369	0.8%			29,388	0.6%			58,981	1.0%
Q1 2021			6,575,765	60.3%			2,795,501	58.9%			3,780,264	61.3%
Q2 2021			4,245,007	38.9%			1,920,769	40.5%			2,324,238	37.7%
Q3 2021												
Q4 2021												
Payer Type; n (%)												
Commercial	14,888,965	55.5%	2,393,270	21.9%	7,629,411	59.7%	1,095,065	23.1%	7,259,554	51.7%	1,298,205	21.1%
Medicaid	7,608,601	28.4%	959,408	8.8%	3,291,194	25.7%	366,576	7.7%	4,317,407	30.8%	592,832	9.6%

Medicare	3,461,030	12.9%	251,224	2.3%	1,502,365	11.8%	109,086	2.3%	1,958,665	14.0%	142,138	2.3%
Other/Unknown	1,440,258	5.4%	7,324,376	67.1%	615,333	4.8%	3,182,908	67.1%	824,925	5.9%	4,141,468	67.2%
Charlson-Quan Index; n (%)												
Mean (SD)	0.65 (1.47)		0.55 (1.28)		0.63 (1.49)		0.61 (1.37)		0.66 (1.46)		0.51 (1.20)	
Median (Q1, Q3)	0.00 [0.00, 1.00]		0.00 [0.00, 1.00]		0.00 [0.00, 1.00]		0.00 [0.00, 1.00]		0.00 [0.00, 1.00]		0.00 [0.00, 0.00]	
Min, Max	[0.00, 27.00]		[0.00, 22.00]		[0.00, 27.00]		[0.00, 22.00]		[0.00, 27.00]		[0.00, 19.00]	
Categories; n(%)												
0	19,520,235	72.8%	8,163,137	74.8%	9,536,220	74.6%	3,493,957	73.6%	9,984,015	71.2%	4,669,180	75.8%
1	3,399,995	12.7%	1,299,737	11.9%	1,456,264	11.4%	557,833	11.8%	1,943,731	13.9%	741,904	12.0%
2+	3,892,960	14.5%	1,446,267	13.3%	1,789,283	14.0%	693,868	14.6%	2,103,677	15.0%	752,399	12.2%
Frailty												
Mean (SD)	0.12 (0.04)		0.12 (0.03)		0.12 (0.04)		0.11 (0.03)		0.12 (0.04)		0.12 (0.03)	
Median (Q1, Q3)	0.10 [0.10, 0.13]		0.10 [0.10, 0.12]		0.10 [0.10, 0.12]		0.10 [0.10, 0.12]		0.10 [0.10, 0.13]		0.10 [0.10, 0.12]	
Min, Max	[0.01, 0.69]		[0.00, 0.67]		[0.01, 0.66]		[0.00, 0.64]		[0.02, 0.69]		[0.01, 0.67]	
Categories; n(%)												
Robust (0-0.149)	23,016,170	85.8%	9,729,011	89.2%	11,244,376	88.0%	4,269,751	90.0%	11,771,794	83.9%	5,459,260	88.6%
Prefrail (0.15-0.249)	3,326,132	12.4%	1,094,650	10.0%	1,361,752	10.7%	442,993	9.3%	1,964,380	14.0%	651,657	10.6%
Mild frailty (0.25-0.349)	392,983	1.5%	75,761	0.7%	148,019	1.2%	29,138	0.6%	244,964	1.7%	46,623	0.8%
Moderate to severe frailty (>=0.35)	77,905	0.3%	9,719	0.1%	27,620	0.2%	3,776	0.1%	50,285	0.4%	5,943	0.1%
Clinical Characteristics; n (%)												
Alcohol use, history of	542,185	2.0%	145,407	1.3%	356,954	2.8%	92,302	1.9%	185,231	1.3%	53,105	0.9%
Arrhythmia	2,165,705	8.1%	765,930	7.0%	973,162	7.6%	355,380	7.5%	1,192,543	8.5%	410,550	6.7%
Asthma	1,613,635	6.0%	471,171	4.3%	542,074	4.2%	152,187	3.2%	1,071,561	7.6%	318,984	5.2%
Cancer	898,744	3.4%	374,664	3.4%	413,425	3.2%	180,151	3.8%	485,319	3.5%	194,513	3.2%
Cardiovascular disease	8,180,805	30.5%	3,160,504	29.0%	3,830,349	30.0%	1,503,538	31.7%	4,350,456	31.0%	1,656,966	26.9%
Coronary artery disease	1,335,823	5.0%	520,164	4.8%	777,350	6.1%	321,541	6.8%	558,473	4.0%	198,623	3.2%
Cerebrovascular disease	832,610	3.1%	286,262	2.6%	386,520	3.0%	137,321	2.9%	446,090	3.2%	148,941	2.4%
Chronic Kidney Disease	1,173,305	4.4%	456,425	4.2%	581,765	4.6%	230,223	4.9%	591,540	4.2%	226,202	3.7%
Chronic Lung Disease	2,821,874	10.5%	823,824	7.6%	1,097,788	8.6%	316,441	6.7%	1,724,086	12.3%	507,383	8.2%
Congestive heart failure	799,442	3.0%	286,234	2.6%	398,120	3.1%	152,340	3.2%	401,322	2.9%	133,894	2.2%
COPD	2,821,874	10.5%	823,824	7.6%	1,097,788	8.6%	316,441	6.7%	1,724,086	12.3%	507,383	8.2%
Dementia	313,054	1.2%	77,960	0.7%	113,842	0.9%	30,465	0.6%	199,212	1.4%	47,495	0.8%
Diabetes	3,042,538	11.3%	1,156,412	10.6%	1,428,358	11.2%	567,103	11.9%	1,614,180	11.5%	589,309	9.6%
Hypertension	7,060,064	26.3%	2,686,525	24.6%	3,356,377	26.3%	1,290,443	27.2%	3,703,687	26.4%	1,396,082	22.7%
Immunocompromised ^b	593,022	2.2%	292,818	2.7%	298,907	2.3%	140,274	3.0%	294,115	2.1%	152,544	2.5%
Liver disease	829,248	3.1%	263,040	2.4%	399,254	3.1%	124,201	2.6%	429,994	3.1%	138,839	2.3%
Obesity (BMI ≥30)	3,309,963	12.3%	1,024,635	9.4%	1,272,003	10.0%	412,568	8.7%	2,037,960	14.5%	612,067	9.9%
Pregnancy	532,679	2.0%	93,767	0.9%	4,983	0.0%	1,008	0.0%	527,696	3.8%	92,759	1.5%
Tobacco use/Smoking, history of	3,132,610	11.7%	783,421	7.2%	1,533,931	12.0%	385,370	8.1%	1,598,679	11.4%	398,051	6.5%
Drug Class (Most 30 Frequent in 365 Day Baseline Period) - T1^c												

Antibacterials	8,615,774	32.1%	2,971,177	27.2%	3,473,237	27.2%	1,169,718	24.6%	5,142,537	36.7%	1,801,459	29.2%
Analgesics and Antipyretics	8,215,585	30.6%	3,154,584	28.9%	3,347,511	26.2%	1,271,597	26.8%	4,868,074	34.7%	1,882,987	30.6%
Hypotensive Agents	6,631,489	24.7%	3,553,833	32.6%	3,100,028	24.3%	1,663,674	35.1%	3,531,461	25.2%	1,890,159	30.7%
Renin-Angiotensin-Aldosterone System Inhibitors	4,586,625	17.1%	2,447,918	22.4%	2,284,294	17.9%	1,225,113	25.8%	2,302,331	16.4%	1,222,805	19.8%
Antilipemic Agents	4,452,586	16.6%	2,517,898	23.1%	2,273,260	17.8%	1,288,404	27.1%	2,179,326	15.5%	1,229,494	19.9%
Psychotherapeutic Agents	4,241,600	15.8%	2,313,923	21.2%	1,446,543	11.3%	746,120	15.7%	2,795,057	19.9%	1,567,803	25.4%
Adrenals	3,705,761	13.8%	1,713,173	15.7%	1,471,226	11.5%	668,993	14.1%	2,234,535	15.9%	1,044,180	16.9%
Antilulcer Agents and Acid Suppressants	3,229,987	12.0%	1,530,910	14.0%	1,261,076	9.9%	606,478	12.8%	1,968,911	14.0%	924,432	15.0%
Anxiolytics, Sedatives, and Hypnotics	3,156,594	11.8%	1,506,930	13.8%	1,086,630	8.5%	501,218	10.6%	2,069,964	14.8%	1,005,712	16.3%
Sympatholytic (Adrenergic Blocking) Agents	3,045,356	11.4%	1,651,616	15.1%	1,629,790	12.8%	460,755	9.7%	1,415,566	10.1%	764,725	12.4%
Diuretics	3,005,836	11.2%	1,590,647	14.6%	1,234,251	9.7%	662,715	14.0%	1,771,585	12.6%	927,932	15.1%
Sympathomimetic (Adrenergic) Agents	2,937,695	11.0%	1,220,096	11.2%	1,123,739	8.8%	460,755	9.7%	1,813,956	12.9%	759,341	12.3%
Anticonvulsants	2,914,925	10.9%	1,403,371	12.9%	1,112,362	8.7%	513,432	10.8%	1,802,563	12.8%	889,939	14.4%
Bronchodilators	2,736,053	10.2%	1,135,582	10.4%	1,029,387	8.1%	422,324	8.9%	1,706,666	12.2%	713,258	11.6%
Cardiac Drugs	2,705,525	10.1%	1,478,971	13.6%	1,266,500	9.9%	699,002	14.7%	1,439,025	10.3%	779,969	12.7%
Anti-inflammatory Agents - Respiratory Tract Agents	2,635,267	9.8%	1,161,003	10.6%	985,027	7.7%	427,595	9.0%	1,650,240	11.8%	733,408	11.9%
beta-Adrenergic Blocking Agents	2,518,819	9.4%	1,375,528	12.6%	1,190,374	9.3%	655,684	13.8%	1,328,445	9.5%	719,844	11.7%
Vasodilating Agents	2,459,852	9.2%	1,427,494	13.1%	1,273,867	10.0%	820,226	17.3%	1,185,985	8.5%	607,268	9.9%
Vaccines	2,420,581	9.0%	2,667,639	24.5%	1,053,799	8.2%	1,146,279	24.2%	1,366,782	9.7%	1,521,360	24.7%
Anti-infectives - Skin and Mucous Membrane Agents	2,395,522	8.9%	941,744	8.6%	862,823	6.8%	339,337	7.2%	1,532,699	10.9%	602,407	9.8%
Anti-inflammatory Agents - Skin and Mucous Membrane Agents	2,382,556	8.9%	1,090,907	10.0%	909,580	7.1%	407,344	8.6%	1,472,976	10.5%	683,563	11.1%
Antidiabetic Agents	2,324,980	8.7%	1,257,955	11.5%	1,095,551	8.6%	610,994	12.9%	1,229,429	8.8%	646,961	10.5%
Anti-inflammatory Agents - Eye, Ear, Nose, and Throat (EENT) Preparations	2,322,487	8.7%	912,273	8.4%	872,619	6.8%	336,818	7.1%	1,449,868	10.3%	575,455	9.3%
Calcium-Channel Blocking Agents	2,114,243	7.9%	1,119,088	10.3%	1,015,699	7.9%	555,522	11.7%	1,098,544	7.8%	563,566	9.1%
Skeletal Muscle Relaxants	2,055,190	7.7%	922,422	8.5%	774,266	6.1%	332,535	7.0%	1,280,924	9.1%	589,887	9.6%
Antihistamines	2,032,664	7.6%	647,054	5.9%	677,765	5.3%	207,625	4.4%	1,354,899	9.7%	439,429	7.1%
Antitussives	1,714,464	6.4%	369,454	3.4%	629,134	4.9%	128,330	2.7%	1,085,330	7.7%	241,124	3.9%
Anti-infectives - Eye, Ear, Nose, and Throat (EENT) Preparations	1,650,863	6.2%	639,642	5.9%	681,896	5.3%	261,000	5.5%	968,967	6.9%	378,642	6.1%
First Generation Antihistamines	1,671,768	6.2%	629,626	5.8%	536,937	4.2%	192,709	4.1%	1,134,831	8.1%	436,917	7.1%
Thyroid and Antithyroid Agents	1,627,416	6.1%	972,301	8.9%	359,410	2.8%	214,954	4.5%	1,268,006	9.0%	757,347	12.3%
Vaccine Dose Received												
Dose 1			10,909,141				4,745,658				6,163,483	
Dose 2 (at least 7 days after Dose 1)			8,022,329 (73.5%)				3,504,662 (73.8%)				4,517,667 (73.3%)	
Receipt of Non-Moderna Vaccine During Follow-up			50,314 (0.5%)				23,394 (0.5%)				26,920 (0.4%)	
Interval between vaccine doses (Days)												
Mean (SD)			28.72 (4.23)				28.68 (4.07)				28.75 (4.35)	
Median (Q1, Q3)			28.00 [28.00, 28.00]				28.00 [28.00, 28.00]				28.00 [28.00, 28.00]	
Min, Max			[7.00, 170.00]				[7.00, 165.00]				[7.00, 170.00]	
Follow-up Time												
Mean (SD)	302.01 (105.13)		86.15 (35.40)		301.03 (105.51)		84.61 (34.51)		302.89 (104.77)		87.33 (36.03)	
Median (Q1, Q3)	366.00 [272.00, 366.00]		88.00 [61.00, 107.00]		366.00 [272.00, 366.00]		88.00 [61.00, 104.00]		366.00 [272.00, 366.00]		89.00 [61.00, 109.00]	

Min, Max	[1.00, 366.00]	[1.00, 192.00]	[1.00, 366.00]	[1.00, 192.00]	[1.00, 366.00]	[1.00, 191.00]
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^aT3 data are truncated to 6/20/2021

^bImmunocompromised patients were identified based upon the ICD-10-based algorithm defined in Polinski et al. (2021), which features medications and clinical conditions.

^cTop 30 medications were identified in the overall population for T1 and T3, respectively. The T3 overall population had an almost identical top 30, but would have included antithrombotic and antimigraine agents in lieu of first generation antihistamines and thyroid and antithyroid agents. Male and female subgroup counts are also described using the Top 30 medications identified in the T1 overall population.

Table 3a: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Acute Aseptic Arthritis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,777,797	-	-	21,999,247.73	103,587	470.87	468.00	473.73		10,876,923	-	-	2,535,593.55	8,491	334.87	327.75	342.00		0.71	0.70	0.73
18-29 years	5,646,147	21.09%	21.05%	4,289,494.28	1,070	24.94	23.45	26.44		1,399,109	12.86%	21.05%	267,823.00	28	10.45	6.58	14.33		0.42	0.28	0.60
30-39 years	4,445,982	16.60%	17.31%	3,581,726.79	3,652	101.96	98.66	105.27		1,380,807	12.69%	17.31%	290,530.00	138	47.50	39.57	55.42		0.47	0.39	0.55
40-49 years	4,327,808	16.16%	15.80%	3,627,003.96	8,775	241.94	236.87	247.00		1,569,818	14.43%	15.80%	337,829.00	376	111.30	100.05	122.55		0.46	0.41	0.51
50-64 years	7,320,587	27.34%	24.66%	6,251,672.95	36,396	582.18	576.20	588.16		3,555,977	32.69%	24.66%	811,340.00	2,300	283.48	271.90	295.07		0.49	0.47	0.51
65-74 years	3,229,040	12.06%	12.34%	2,698,287.35	26,269	973.54	961.77	985.32		1,836,105	16.88%	12.34%	501,029.00	2,274	453.87	435.21	472.52		0.47	0.45	0.49
>75 years	1,808,233	6.75%	8.85%	1,551,062.40	27,425	1,768.14	1,747.22	1,789.07		1,135,107	10.44%	8.85%	327,043.00	3,375	1,031.98	997.16	1,066.79		0.58	0.56	0.61
Crude																					
Male Adults	12,764,140	-	-	10,453,850.82	47,747	456.74	452.64	460.84		4,730,604	-	-	1,082,812.37	3,878	358.14	346.87	369.41		0.78	0.76	0.81
18-29 years	2,827,467	22.15%	22.10%	2,158,585.08	499	23.12	21.09	25.15		569,360	12.04%	22.10%	103,735.00	9	8.68	3.97	16.47		0.38	0.18	0.69
30-39 years	2,162,063	16.94%	17.90%	1,733,854.68	1,821	105.03	100.20	109.85		577,153	12.20%	17.90%	117,535.00	67	57.00	43.35	70.65		0.54	0.42	0.69
40-49 years	2,100,128	16.45%	16.10%	1,752,360.56	4,449	253.89	246.43	261.35		680,573	14.39%	16.10%	142,017.00	192	135.20	116.07	154.32		0.53	0.46	0.61
50-64 years	3,472,907	27.21%	24.60%	2,954,841.21	18,434	623.86	614.85	632.86		1,608,044	33.99%	24.60%	357,657.00	1,207	337.47	318.44	356.51		0.54	0.51	0.57
65-74 years	1,469,123	11.51%	11.80%	1,224,876.94	11,937	974.55	957.06	992.03		827,136	17.48%	11.80%	225,860.00	1,071	474.19	445.79	502.59		0.49	0.46	0.52
>75 years	732,452	5.74%	7.50%	629,332.35	10,607	1,685.44	1,653.36	1,717.51		468,338	9.90%	7.50%	136,009.00	1,332	979.35	926.76	1,031.94		0.58	0.55	0.62
Standardized																					
Male Adults	12,764,140	-	-	10,453,850.82	48,133	460.43	456.26	464.62		4,730,604	-	-	1,082,812.37	2,672	246.74	238.69	255.15		0.54	0.52	0.55
Crude																					
Female Adults	14,013,657	-	-	11,545,396.91	55,840	483.66	479.64	487.67		6,146,319	-	-	1,452,781.18	4,613	317.53	308.37	326.69		0.66	0.64	0.68
18-29 years	2,818,680	20.11%	20.10%	2,130,909.20	571	26.80	24.60	28.99		829,749	13.50%	20.10%	164,088.00	19	11.58	6.37	16.79		0.43	0.27	0.67
30-39 years	2,283,919	16.30%	16.80%	1,847,872.12	1,831	99.09	94.55	103.63		803,654	13.08%	16.80%	172,995.00	71	41.04	31.50	50.59		0.41	0.32	0.52
40-49 years	2,227,680	15.90%	15.50%	1,874,643.40	4,326	230.76	223.89	237.64		889,245	14.47%	15.50%	195,812.00	184	93.97	80.39	107.55		0.41	0.35	0.47
50-64 years	3,847,680	27.46%	24.70%	3,296,831.75	17,962	544.83	536.86	552.79		1,947,933	31.69%	24.70%	453,683.00	1,093	240.92	226.63	255.20		0.44	0.42	0.47
65-74 years	1,759,917	12.56%	12.80%	1,473,410.40	14,332	972.71	956.78	988.63		1,008,969	16.42%	12.80%	275,169.00	1,203	437.19	412.48	461.89		0.45	0.42	0.48
>75 years	1,075,781	7.68%	10.10%	921,730.05	16,818	1,824.61	1,797.04	1,852.19		666,769	10.85%	10.10%	191,034.00	2,043	1,069.44	1,023.07	1,115.82		0.59	0.56	0.61
Standardized																					
Female Adults	14,013,657	-	-	11,545,396.91	57,879	501.32	497.12	505.54		6,146,319	-	-	1,452,781.18	3,593	247.30	240.11	254.73		0.49	0.48	0.51

Table 3b: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Acute disseminated encephalomyelitis (ADEM)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,813,166	-	-	22,112,113.05	25	0.11	0.07	0.16	10,909,132	-	-	2,544,975.54	0	0.00	0.00	0.14	0.00	0.00	1.11		
18-29 years	5,646,625	21.06%	21.05%	4,290,642.75	8	0.19	0.08	0.37	1,399,286	12.83%	21.05%	267,859.00	0	0.00	0.00	1.38	0.00	0.00	7.28		
30-39 years	4,447,544	16.59%	17.31%	3,585,841.04	2	0.06	0.01	0.20	1,381,481	12.66%	17.31%	290,682.00	0	0.00	0.00	1.27	0.00	0.00	42.83		
40-49 years	4,331,319	16.15%	15.80%	3,636,942.45	6	0.16	0.06	0.36	1,571,720	14.41%	15.80%	338,253.00	0	0.00	0.00	1.09	0.00	0.00	6.96		
50-64 years	7,334,485	27.35%	24.66%	6,292,859.66	4	0.06	0.02	0.16	3,566,896	32.70%	24.66%	814,039.00	0	0.00	0.00	0.45	0.00	0.00	8.62		
65-74 years	3,237,212	12.07%	12.34%	2,726,684.60	3	0.11	0.02	0.32	1,844,330	16.91%	12.34%	503,582.00	0	0.00	0.00	0.73	0.00	0.00	9.28		
>75 years	1,815,981	6.77%	8.85%	1,579,142.54	2	0.13	0.02	0.46	1,145,419	10.50%	8.85%	330,561.00	0	0.00	0.00	1.12	0.00	0.00	16.59		
Crude																					
Male Adults	12,781,754	-	-	10,506,681.28	9	0.09	0.04	0.16	4,745,653	-	-	1,087,146.90	0	0.00	0.00	0.34	0.00	0.00	3.82		
18-29 years	2,827,707	22.12%	22.10%	2,159,121.86	3	0.14	0.03	0.41	569,434	12.00%	22.10%	103,748.00	0	0.00	0.00	3.56	0.00	0.00	35.68		
30-39 years	2,162,953	16.92%	17.90%	1,735,993.32	0	0.00	0.00	0.21	577,498	12.17%	17.90%	117,612.00	0	0.00	0.00	3.14	-	0.00	-		
40-49 years	2,102,133	16.45%	16.10%	1,757,575.18	3	0.17	0.04	0.50	681,545	14.36%	16.10%	142,234.00	0	0.00	0.00	2.59	0.00	0.00	21.19		
50-64 years	3,480,454	27.23%	24.60%	2,975,920.49	1	0.03	0.00	0.19	1,613,813	34.01%	24.60%	359,075.00	0	0.00	0.00	1.03	0.00	0.00	157.47		
65-74 years	1,473,024	11.52%	11.80%	1,237,983.84	1	0.08	0.00	0.45	831,125	17.51%	11.80%	227,112.00	0	0.00	0.00	1.62	0.00	0.00	103.57		
>75 years	735,483	5.75%	7.50%	640,086.60	1	0.16	0.00	0.87	472,238	9.95%	7.50%	137,365.00	0	0.00	0.00	2.69	0.00	0.00	88.54		
Standardized																					
Male Adults	12,781,754	-	-	10,506,681.28	9	0.09	0.04	0.17	4,745,653	-	-	1,087,146.90	0	0.00	-	0.79	0.00	-	6.24		
Crude																					
Female Adults	14,031,412	-	-	11,605,431.77	16	0.14	0.07	0.21	6,163,479	-	-	1,457,828.63	0	0.00	0.00	0.25	0.00	0.00	1.64		
18-29 years	2,818,918	20.09%	20.10%	2,131,520.90	5	0.23	0.08	0.55	829,852	13.46%	20.10%	164,111.00	0	0.00	0.00	2.25	0.00	0.00	10.66		
30-39 years	2,284,591	16.28%	16.80%	1,849,847.72	2	0.11	0.01	0.39	803,983	13.04%	16.80%	173,069.00	0	0.00	0.00	2.13	0.00	0.00	37.11		
40-49 years	2,229,186	15.89%	15.50%	1,879,367.27	3	0.16	0.03	0.47	890,175	14.44%	15.50%	196,019.00	0	0.00	0.00	1.88	0.00	0.00	16.44		
50-64 years	3,854,031	27.47%	24.70%	3,316,939.17	3	0.09	0.02	0.26	1,953,083	31.69%	24.70%	454,964.00	0	0.00	0.00	0.81	0.00	0.00	12.50		
65-74 years	1,764,188	12.57%	12.80%	1,488,700.77	2	0.13	0.02	0.49	1,013,205	16.44%	12.80%	276,470.00	0	0.00	0.00	1.33	0.00	0.00	18.70		
>75 years	1,080,498	7.70%	10.10%	939,055.94	1	0.11	0.00	0.59	673,181	10.92%	10.10%	193,196.00	0	0.00	0.00	1.91	0.00	0.00	92.35		
Standardized																					
Female Adults	14,031,412	-	-	11,605,431.77	16	0.14	0.08	0.23	6,163,479	-	-	1,457,828.63	0	0.00	-	0.45	0.00	-	2.34		

Table 3c: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Acute myocardial infarction (AMI)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,793,742	-	-	22,046,073.06	70,896	321.58	319.21	323.95		10,881,891	-	-	2,537,067.00	7,966	313.98	307.09	320.88		0.98	0.95	1.00
18-29 years	5,646,298	21.07%	21.05%	4,289,831.05	873	20.35	19.00	21.70		1,399,122	12.86%	21.05%	267,823.00	37	13.82	9.36	18.27		0.68	0.48	0.93
30-39 years	4,446,753	16.60%	17.31%	3,583,652.11	2,227	62.14	59.56	64.72		1,380,904	12.69%	17.31%	290,551.00	117	40.27	32.97	47.56		0.65	0.54	0.78
40-49 years	4,329,273	16.16%	15.80%	3,630,690.95	6,300	173.52	169.24	177.81		1,569,806	14.43%	15.80%	337,814.00	387	114.56	103.15	125.97		0.66	0.59	0.73
50-64 years	7,326,809	27.35%	24.66%	6,267,878.19	24,992	398.73	393.79	403.67		3,556,943	32.69%	24.66%	811,588.00	2,143	264.05	252.87	275.23		0.66	0.63	0.69
65-74 years	3,232,720	12.07%	12.34%	2,710,315.69	17,926	661.40	651.72	671.08		1,837,077	16.88%	12.34%	501,335.00	2,241	447.01	428.50	465.51		0.68	0.65	0.71
>75 years	1,811,889	6.76%	8.85%	1,563,705.07	18,578	1,188.08	1,170.99	1,205.16		1,138,039	10.46%	8.85%	327,957.00	3,041	927.26	894.30	960.21		0.78	0.75	0.81
Crude																					
Male Adults	12,770,445	-	-	10,468,994.59	39,781	379.99	376.25	383.72		4,729,701	-	-	1,082,569.19	4,430	409.21	397.16	421.26		1.08	1.04	1.11
18-29 years	2,827,523	22.14%	22.10%	2,158,654.23	516	23.90	21.84	25.97		569,331	12.04%	22.10%	103,725.00	23	22.17	13.11	31.24		0.93	0.60	1.38
30-39 years	2,162,450	16.93%	17.90%	1,734,675.14	1,290	74.37	70.31	78.42		577,171	12.20%	17.90%	117,541.00	56	47.64	35.16	60.12		0.64	0.49	0.83
40-49 years	2,100,851	16.45%	16.10%	1,753,737.20	3,829	218.33	211.42	225.25		680,359	14.38%	16.10%	141,962.00	237	166.95	145.69	188.20		0.76	0.67	0.87
50-64 years	3,475,601	27.22%	24.60%	2,960,339.48	15,391	519.91	511.69	528.12		1,607,426	33.99%	24.60%	357,511.00	1,318	368.66	348.76	388.56		0.71	0.67	0.75
65-74 years	1,470,526	11.52%	11.80%	1,228,809.51	10,018	815.26	799.30	831.23		826,838	17.48%	11.80%	225,777.00	1,281	567.37	536.30	598.44		0.70	0.66	0.74
>75 years	733,494	5.74%	7.50%	632,779.03	8,737	1,380.73	1,351.78	1,409.69		468,576	9.91%	7.50%	136,053.00	1,515	1,113.53	1,057.46	1,169.61		0.81	0.76	0.85
Standardized																					
Male Adults	12,770,445	-	-	10,468,994.59	39,995	382.03	378.25	385.84		4,729,701	-	-	1,082,569.19	3,052	281.96	273.31	290.96		0.74	0.71	0.76
Crude																					
Female Adults	14,023,297	-	-	11,577,078.46	31,115	268.76	265.78	271.75		6,152,190	-	-	1,454,497.82	3,536	243.11	235.10	251.12		0.90	0.87	0.94
18-29 years	2,818,775	20.10%	20.10%	2,131,176.82	357	16.75	15.01	18.49		829,791	13.49%	20.10%	164,098.00	14	8.53	4.06	13.00		0.51	0.29	0.84
30-39 years	2,284,303	16.29%	16.80%	1,848,976.97	937	50.68	47.43	53.92		803,733	13.06%	16.80%	173,010.00	61	35.26	26.41	44.11		0.70	0.53	0.90
40-49 years	2,228,422	15.89%	15.50%	1,876,953.75	2,471	131.65	126.46	136.84		889,447	14.46%	15.50%	195,851.00	150	76.59	64.33	88.85		0.58	0.49	0.68
50-64 years	3,851,208	27.46%	24.70%	3,307,538.72	9,601	290.28	284.47	296.08		1,949,517	31.69%	24.70%	454,077.00	825	181.69	169.29	194.09		0.63	0.58	0.67
65-74 years	1,762,194	12.57%	12.80%	1,481,506.17	7,908	533.78	522.02	545.55		1,010,239	16.42%	12.80%	275,558.00	960	348.38	326.35	370.42		0.65	0.61	0.70
>75 years	1,078,395	7.69%	10.10%	930,926.04	9,841	1,057.12	1,036.23	1,078.01		669,463	10.88%	10.10%	191,903.00	1,526	795.19	755.30	835.09		0.75	0.71	0.79
Standardized																					
Female Adults	14,023,297	-	-	11,577,078.46	32,319	279.16	276.03	282.31		6,152,190	-	-	1,454,497.82	2,754	189.33	183.04	195.85		0.68	0.65	0.70

Table 3d: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Anosmia, ageusia

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,809,319	-	-	22,099,851.62	10,800	48.87	47.95	49.79		10,883,572	-	-	2,538,879.67	2,774	109.26	105.19	113.33		2.24	2.14	2.33
18-29 years	5,646,292	21.06%	21.05%	4,289,874.50	721	16.81	15.58	18.03		1,394,203	12.81%	21.05%	266,845.00	404	151.40	136.64	166.16		9.01	7.97	10.17
30-39 years	4,447,121	16.59%	17.31%	3,584,596.77	1,136	31.69	29.85	33.53		1,376,931	12.65%	17.31%	289,659.00	381	131.53	118.33	144.74		4.15	3.69	4.66
40-49 years	4,330,744	16.15%	15.80%	3,635,050.69	1,743	47.95	45.70	50.20		1,566,987	14.40%	15.80%	337,171.00	459	136.13	123.68	148.59		2.84	2.56	3.14
50-64 years	7,332,887	27.35%	24.66%	6,287,863.02	4,332	68.89	66.84	70.95		3,558,889	32.70%	24.66%	812,082.00	905	111.44	104.18	118.70		1.62	1.51	1.74
65-74 years	3,236,601	12.07%	12.34%	2,724,481.44	1,881	69.04	65.92	72.16		1,842,194	16.93%	12.34%	502,915.00	383	76.16	68.53	83.78		1.10	0.99	1.23
>75 years	1,815,674	6.77%	8.85%	1,577,985.21	987	62.55	58.65	66.45		1,144,368	10.51%	8.85%	330,207.00	242	73.29	64.05	82.52		1.17	1.02	1.35
Crude																					
Male Adults	12,780,030	-	-	10,501,594.79	4,413	42.02	40.78	43.26		4,736,010	-	-	1,084,897.29	1,016	93.65	87.89	99.41		2.23	2.08	2.39
18-29 years	2,827,557	22.12%	22.10%	2,158,762.82	325	15.05	13.42	16.69		567,571	11.98%	22.10%	103,402.00	120	116.05	95.29	136.82		7.71	6.23	9.48
30-39 years	2,162,751	16.92%	17.90%	1,735,471.75	486	28.00	25.51	30.49		575,871	12.16%	17.90%	117,269.00	118	100.62	82.47	118.78		3.59	2.93	4.38
40-49 years	2,101,873	16.45%	16.10%	1,756,825.89	670	38.14	35.25	41.02		679,766	14.35%	16.10%	141,841.00	164	115.62	97.93	133.32		3.03	2.55	3.59
50-64 years	3,479,764	27.23%	24.60%	2,973,907.48	1,699	57.13	54.41	59.85		1,610,782	34.01%	24.60%	358,351.00	338	94.32	84.27	104.38		1.65	1.47	1.85
65-74 years	1,472,755	11.52%	11.80%	1,237,053.10	795	64.27	59.80	68.73		830,214	17.53%	11.80%	226,820.00	167	73.63	62.46	84.79		1.15	0.97	1.35
>75 years	735,330	5.75%	7.50%	639,573.73	438	68.48	62.07	74.90		471,806	9.96%	7.50%	137,215.00	109	79.44	64.52	94.35		1.16	0.94	1.43
Standardized																					
Male Adults	12,780,030	-	-	10,501,594.79	4,335	41.28	40.06	42.52		4,736,010	-	-	1,084,897.29	1,086	100.10	93.24	107.43		2.43	2.25	2.62
Crude																					
Female Adults	14,029,289	-	-	11,598,256.83	6,387	55.07	53.72	56.42		6,147,562	-	-	1,453,982.37	1,758	120.91	115.26	126.56		2.20	2.08	2.31
18-29 years	2,818,735	20.09%	20.10%	2,131,111.67	396	18.58	16.75	20.41		826,632	13.45%	20.10%	163,443.00	284	173.76	153.55	193.97		9.35	8.02	10.89
30-39 years	2,284,370	16.28%	16.80%	1,849,125.01	650	35.15	32.45	37.85		801,060	13.03%	16.80%	172,390.00	263	152.56	134.12	171.00		4.34	3.76	5.00
40-49 years	2,228,871	15.89%	15.50%	1,878,224.79	1,073	57.13	53.71	60.55		887,221	14.43%	15.50%	195,330.00	295	151.03	133.79	168.26		2.64	2.32	3.00
50-64 years	3,853,123	27.46%	24.70%	3,313,955.54	2,633	79.45	76.42	82.49		1,948,107	31.69%	24.70%	453,732.00	567	124.96	114.68	135.25		1.57	1.44	1.72
65-74 years	1,763,846	12.57%	12.80%	1,487,428.33	1,086	73.01	68.67	77.35		1,011,980	16.46%	12.80%	276,095.00	216	78.23	67.80	88.67		1.07	0.92	1.24
>75 years	1,080,344	7.70%	10.10%	938,411.48	549	58.50	53.61	63.40		672,562	10.94%	10.10%	192,992.00	133	68.91	57.20	80.63		1.18	0.97	1.42
Standardized																					
Female Adults	14,029,289	-	-	11,598,256.83	6,193	53.40	52.09	54.74		6,147,562	-	-	1,453,982.37	1,916	131.79	125.32	138.54		2.47	2.33	2.61

Table 3e: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Aseptic meningitis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,812,320	-	-	22,109,300.73	2,942	13.31	12.83	13.79		10,908,596	-	-	2,544,832.85	136	5.34	4.45	6.24		0.40	0.34	0.48
18-29 years	5,646,442	21.06%	21.05%	4,290,209.45	408	9.51	8.59	10.43		1,399,242	12.83%	21.05%	267,850.00	13	4.85	2.22	7.49		0.51	0.28	0.86
30-39 years	4,447,399	16.59%	17.31%	3,585,369.26	458	12.77	11.60	13.94		1,381,415	12.66%	17.31%	290,665.00	15	5.16	2.55	7.77		0.40	0.23	0.66
40-49 years	4,331,198	16.15%	15.80%	3,636,512.23	451	12.40	11.26	13.55		1,571,660	14.41%	15.80%	338,238.00	11	3.25	1.33	5.17		0.26	0.14	0.46
50-64 years	7,334,244	27.35%	24.66%	6,291,969.82	935	14.86	13.91	15.81		3,566,691	32.70%	24.66%	813,988.00	41	5.04	3.50	6.58		0.34	0.25	0.46
65-74 years	3,237,097	12.07%	12.34%	2,726,309.20	427	15.66	14.18	17.15		1,844,240	16.91%	12.34%	503,554.00	36	7.15	4.81	9.48		0.46	0.32	0.63
>75 years	1,815,940	6.77%	8.85%	1,578,930.77	263	16.66	14.64	18.67		1,145,348	10.50%	8.85%	330,537.00	20	6.05	3.40	8.70		0.36	0.22	0.56
Crude																					
Male Adults	12,781,335	-	-	10,505,375.10	1,407	13.39	12.69	14.09		4,745,400	-	-	1,087,079.73	58	5.34	3.96	6.71		0.40	0.30	0.51
18-29 years	2,827,620	22.12%	22.10%	2,158,932.53	176	8.15	6.95	9.36		569,414	12.00%	22.10%	103,744.00	4	3.86	1.05	9.87		0.47	0.15	1.16
30-39 years	2,162,885	16.92%	17.90%	1,735,784.06	209	12.04	10.41	13.67		577,467	12.17%	17.90%	117,605.00	4	3.40	0.93	8.71		0.28	0.09	0.69
40-49 years	2,102,071	16.45%	16.10%	1,757,375.28	218	12.40	10.76	14.05		681,516	14.36%	16.10%	142,227.00	8	5.62	2.43	11.08		0.45	0.21	0.87
50-64 years	3,480,330	27.23%	24.60%	2,975,495.51	466	15.66	14.24	17.08		1,613,722	34.01%	24.60%	359,053.00	19	5.29	2.91	7.67		0.34	0.21	0.52
65-74 years	1,472,966	11.52%	11.80%	1,237,804.49	216	17.45	15.12	19.78		831,086	17.51%	11.80%	227,100.00	15	6.61	3.26	9.95		0.38	0.22	0.62
>75 years	735,463	5.75%	7.50%	639,983.23	122	19.06	15.68	22.45		472,195	9.95%	7.50%	137,351.00	8	5.82	2.51	11.48		0.31	0.14	0.60
Standardized																					
Male Adults	12,781,335	-	-	10,505,375.10	1,397	13.30	12.61	14.02		4,745,400	-	-	1,087,079.73	53	4.89	3.56	6.69		0.37	0.30	0.51
Crude																					
Female Adults	14,030,985	-	-	11,603,925.63	1,535	13.23	12.57	13.89		6,163,196	-	-	1,457,753.12	78	5.35	4.16	6.54		0.40	0.32	0.50
18-29 years	2,818,822	20.09%	20.10%	2,131,276.92	232	10.89	9.48	12.29		829,828	13.46%	20.10%	164,106.00	9	5.48	2.51	10.41		0.50	0.24	0.94
30-39 years	2,284,514	16.28%	16.80%	1,849,585.20	249	13.46	11.79	15.13		803,948	13.04%	16.80%	173,061.00	11	6.36	2.60	10.11		0.47	0.25	0.83
40-49 years	2,229,127	15.89%	15.50%	1,879,136.95	233	12.40	10.81	13.99		890,144	14.44%	15.50%	196,012.00	3	1.53	0.32	4.47		0.12	0.03	0.34
50-64 years	3,853,914	27.47%	24.70%	3,316,474.32	469	14.14	12.86	15.42		1,952,969	31.69%	24.70%	454,935.00	22	4.84	2.82	6.86		0.34	0.22	0.51
65-74 years	1,764,131	12.57%	12.80%	1,488,504.71	211	14.18	12.26	16.09		1,013,154	16.44%	12.80%	276,454.00	21	7.60	4.35	10.85		0.54	0.33	0.82
>75 years	1,080,477	7.70%	10.10%	938,947.54	141	15.02	12.54	17.50		673,153	10.92%	10.10%	193,186.00	12	6.21	2.70	9.73		0.41	0.22	0.72
Standardized																					
Female Adults	14,030,985	-	-	11,603,925.63	1,532	13.20	12.54	13.88		6,163,196	-	-	1,457,753.12	76	5.20	4.04	6.66		0.39	0.30	0.50

Table 3f: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Chilblain-like lesions

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,812,929	-	-	22,111,129.39	966	4.37	4.09	4.64	10,907,967	-	-	2,544,625.47	322	12.65	11.27	14.04	2.90	2.55	3.28		
18-29 years	5,646,592	21.06%	21.05%	4,290,517.38	138	3.22	2.68	3.75	1,399,031	12.83%	21.05%	267,797.00	43	16.06	11.26	20.86	4.99	3.51	6.99		
30-39 years	4,447,499	16.59%	17.31%	3,585,692.89	140	3.90	3.26	4.55	1,381,257	12.66%	17.31%	290,618.00	52	17.89	13.03	22.76	4.58	3.31	6.27		
40-49 years	4,331,282	16.15%	15.80%	3,636,778.08	168	4.62	3.92	5.32	1,571,544	14.41%	15.80%	338,199.00	61	18.04	13.51	22.56	3.90	2.90	5.21		
50-64 years	7,334,417	27.35%	24.66%	6,292,535.03	314	4.99	4.44	5.54	3,566,570	32.70%	24.66%	813,942.00	93	11.43	9.10	13.75	2.29	1.81	2.88		
65-74 years	3,237,169	12.07%	12.34%	2,726,513.34	155	5.68	4.79	6.58	1,844,202	16.91%	12.34%	503,530.00	52	10.33	7.52	13.13	1.82	1.32	2.47		
>75 years	1,815,970	6.77%	8.85%	1,579,092.67	51	3.23	2.34	4.12	1,145,363	10.50%	8.85%	330,539.00	21	6.35	3.64	9.07	1.97	1.16	3.24		
Crude																					
Male Adults	12,781,687	-	-	10,506,380.88	305	2.90	2.58	3.23	4,745,232	-	-	1,087,022.71	107	9.84	7.98	11.71	3.39	2.71	4.22		
18-29 years	2,827,700	22.12%	22.10%	2,159,094.53	32	1.48	0.97	2.00	569,366	12.00%	22.10%	103,733.00	6	5.78	2.12	12.59	3.90	1.48	8.91		
30-39 years	2,162,947	16.92%	17.90%	1,735,965.75	32	1.84	1.20	2.48	577,432	12.17%	17.90%	117,594.00	14	11.91	5.67	18.14	6.46	3.35	11.97		
40-49 years	2,102,123	16.45%	16.10%	1,757,542.49	33	1.88	1.24	2.52	681,479	14.36%	16.10%	142,216.00	17	11.95	6.27	17.64	6.37	3.47	11.35		
50-64 years	3,480,426	27.23%	24.60%	2,975,791.95	122	4.10	3.37	4.83	1,613,675	34.01%	24.60%	359,035.00	34	9.47	6.29	12.65	2.31	1.56	3.35		
65-74 years	1,473,011	11.52%	11.80%	1,237,912.68	69	5.57	4.26	6.89	831,061	17.51%	11.80%	227,087.00	26	11.45	7.05	15.85	2.05	1.29	3.20		
>75 years	735,480	5.75%	7.50%	640,073.48	17	2.66	1.39	3.92	472,219	9.95%	7.50%	137,357.00	10	7.28	2.77	11.79	2.74	1.21	5.97		
Standardized																					
Male Adults	12,781,687	-	-	10,506,380.88	297	2.83	2.52	3.17	4,745,232	-	-	1,087,022.71	104	9.56	7.64	11.95	3.38	2.63	4.32		
Crude																					
Female Adults	14,031,242	-	-	11,604,748.51	661	5.70	5.26	6.13	6,162,735	-	-	1,457,602.76	215	14.75	12.78	16.72	2.59	2.22	3.02		
18-29 years	2,818,892	20.09%	20.10%	2,131,422.84	106	4.97	4.03	5.92	829,665	13.46%	20.10%	164,064.00	37	22.55	15.29	29.82	4.53	3.09	6.55		
30-39 years	2,284,552	16.28%	16.80%	1,849,727.13	108	5.84	4.74	6.94	803,825	13.04%	16.80%	173,023.00	38	21.96	14.98	28.95	3.76	2.57	5.41		
40-49 years	2,229,159	15.89%	15.50%	1,879,235.59	135	7.18	5.97	8.40	890,065	14.44%	15.50%	195,983.00	44	22.45	15.82	29.08	3.13	2.20	4.37		
50-64 years	3,853,991	27.47%	24.70%	3,316,743.08	192	5.79	4.97	6.61	1,952,895	31.69%	24.70%	454,907.00	59	12.97	9.66	16.28	2.24	1.66	2.99		
65-74 years	1,764,158	12.57%	12.80%	1,488,600.66	86	5.78	4.56	7.00	1,013,141	16.44%	12.80%	276,444.00	26	9.41	5.79	13.02	1.63	1.03	2.50		
>75 years	1,080,490	7.70%	10.10%	939,019.20	34	3.62	2.40	4.84	673,144	10.92%	10.10%	193,182.00	11	5.69	2.33	9.06	1.57	0.76	3.04		
Standardized																					
Female Adults	14,031,242	-	-	11,604,748.51	653	5.63	5.21	6.08	6,162,735	-	-	1,457,602.76	243	16.68	14.41	19.26	2.96	2.51	3.48		

Table 3h: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Coagulation disorders

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,630,976	-	-	21,780,463.46	229,990	1,055.95	1,051.63	1,060.26		10,769,938	-	-	2,503,715.06	30,734	1,227.54	1,213.81	1,241.26		1.16	1.15	1.18
18-29 years	5,636,133	21.16%	21.05%	4,273,040.47	12,724	297.77	292.60	302.95		1,394,480	12.95%	21.05%	266,779.00	820	307.37	286.33	328.41		1.03	0.96	1.11
30-39 years	4,434,699	16.65%	17.31%	3,561,742.90	17,042	478.47	471.29	485.66		1,373,023	12.75%	17.31%	288,609.00	1,406	487.16	461.70	512.63		1.02	0.96	1.07
40-49 years	4,314,367	16.20%	15.80%	3,605,558.28	22,091	612.69	604.61	620.77		1,560,067	14.49%	15.80%	335,396.00	1,806	538.47	513.63	563.30		0.88	0.84	0.92
50-64 years	7,282,849	27.35%	24.66%	6,197,324.25	69,183	1,116.34	1,108.02	1,124.66		3,525,978	32.74%	24.66%	803,432.00	7,615	947.81	926.52	969.10		0.85	0.83	0.87
65-74 years	3,190,639	11.98%	12.34%	2,642,265.75	57,737	2,185.13	2,167.31	2,202.96		1,809,301	16.80%	12.34%	492,195.00	8,645	1,756.42	1,719.39	1,793.44		0.80	0.79	0.82
>75 years	1,772,289	6.65%	8.85%	1,500,531.82	51,213	3,412.99	3,383.43	3,442.55		1,107,089	10.28%	8.85%	317,303.00	10,442	3,290.86	3,227.74	3,353.98		0.96	0.94	0.98
Crude																					
Male Adults	12,693,122	-	-	10,346,582.38	111,686	1,079.45	1,073.12	1,085.78		4,676,384	-	-	1,066,474.19	15,332	1,437.63	1,414.88	1,460.39		1.33	1.31	1.35
18-29 years	2,824,268	22.25%	22.10%	2,153,311.57	4,142	192.35	186.50	198.21		567,914	12.14%	22.10%	103,411.00	275	265.93	234.50	297.36		1.38	1.22	1.56
30-39 years	2,158,492	17.01%	17.90%	1,727,902.81	5,806	336.01	327.37	344.66		574,958	12.29%	17.90%	117,010.00	424	362.36	327.87	396.85		1.08	0.98	1.19
40-49 years	2,094,448	16.50%	16.10%	1,743,860.39	9,725	557.67	546.59	568.75		676,511	14.47%	16.10%	141,057.00	708	501.93	464.95	538.90		0.90	0.83	0.97
50-64 years	3,453,092	27.20%	24.60%	2,926,116.12	36,459	1,245.99	1,233.20	1,258.78		1,592,516	34.05%	24.60%	353,640.00	3,915	1,107.06	1,072.38	1,141.74		0.89	0.86	0.92
65-74 years	1,449,124	11.42%	11.80%	1,194,380.13	30,144	2,523.82	2,495.33	2,552.31		812,079	17.37%	11.80%	220,903.00	4,645	2,102.73	2,042.26	2,163.20		0.83	0.81	0.86
>75 years	713,698	5.62%	7.50%	601,011.36	25,410	4,227.87	4,175.89	4,279.86		452,406	9.67%	7.50%	130,454.00	5,365	4,112.55	4,002.51	4,222.60		0.97	0.94	1.00
Standardized																					
Male Adults	12,693,122	-	-	10,346,582.38	115,446	1,115.79	1,109.18	1,122.43		4,676,384	-	-	1,066,474.19	11,040	1,035.14	1,017.49	1,053.16		0.93	0.91	0.94
Crude																					
Female Adults	13,937,854	-	-	11,433,881.08	118,304	1,034.68	1,028.78	1,040.58		6,093,554	-	-	1,437,240.87	15,402	1,071.64	1,054.71	1,088.56		1.04	1.02	1.05
18-29 years	2,811,865	20.17%	20.10%	2,119,728.90	8,582	404.86	396.30	413.43		826,566	13.56%	20.10%	163,369.00	545	333.60	305.59	361.61		0.82	0.75	0.90
30-39 years	2,276,207	16.33%	16.80%	1,833,840.09	11,236	612.70	601.37	624.03		798,065	13.10%	16.80%	171,599.00	982	572.26	536.47	608.06		0.93	0.87	1.00
40-49 years	2,219,919	15.93%	15.50%	1,861,697.88	12,366	664.23	652.53	675.94		883,556	14.50%	15.50%	194,340.00	1,098	564.99	531.57	598.41		0.85	0.80	0.90
50-64 years	3,829,757	27.48%	24.70%	3,271,208.12	32,724	1,000.36	989.53	1,011.20		1,933,462	31.73%	24.70%	449,793.00	3,700	822.60	796.10	849.11		0.82	0.79	0.85
65-74 years	1,741,515	12.49%	12.80%	1,447,885.62	27,593	1,905.74	1,883.26	1,928.23		997,222	16.37%	12.80%	271,292.00	4,000	1,474.43	1,428.73	1,520.12		0.77	0.75	0.80
>75 years	1,058,591	7.60%	10.10%	899,520.47	25,803	2,868.53	2,833.53	2,903.53		654,683	10.74%	10.10%	186,849.00	5,077	2,717.17	2,642.43	2,791.91		0.95	0.92	0.98
Standardized																					
Female Adults	13,937,854	-	-	11,433,881.08	122,138	1,068.21	1,062.06	1,074.38		6,093,554	-	-	1,437,240.87	13,182	917.18	902.12	932.49		0.86	0.84	0.87

Table 3g: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Cerebral sinus venous thrombosis (CSVT)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,813,001	-	-	22,111,546.72	632	2.86	2.64	3.08	10,908,926	-	-	2,544,922.15	46	1.81	1.29	2.33	0.63	0.46	0.85		
18-29 years	5,646,601	21.06%	21.05%	4,290,571.39	94	2.19	1.75	2.63	1,399,255	12.83%	21.05%	267,853.00	2	0.75	0.09	2.70	0.34	0.06	1.15		
30-39 years	4,447,522	16.59%	17.31%	3,585,746.37	92	2.57	2.04	3.09	1,381,449	12.66%	17.31%	290,675.00	6	2.06	0.76	4.49	0.80	0.32	1.73		
40-49 years	4,331,289	16.15%	15.80%	3,636,841.03	106	2.91	2.36	3.47	1,571,694	14.41%	15.80%	338,245.00	8	2.37	1.02	4.66	0.81	0.37	1.59		
50-64 years	7,334,434	27.35%	24.66%	6,292,684.24	209	3.32	2.87	3.77	3,566,828	32.70%	24.66%	814,024.00	11	1.35	0.55	2.15	0.41	0.21	0.72		
65-74 years	3,237,187	12.07%	12.34%	2,726,612.55	80	2.93	2.29	3.58	1,844,296	16.91%	12.34%	503,572.00	2	0.40	0.05	1.43	0.14	0.02	0.46		
>75 years	1,815,968	6.77%	8.85%	1,579,091.14	51	3.23	2.34	4.12	1,145,404	10.50%	8.85%	330,553.00	17	5.14	2.70	7.59	1.59	0.90	2.72		
Crude																					
Male Adults	12,781,687	-	-	10,506,450.45	268	2.55	2.25	2.86	4,745,566	-	-	1,087,123.80	19	1.75	0.96	2.53	0.69	0.42	1.07		
18-29 years	2,827,696	22.12%	22.10%	2,159,099.75	28	1.30	0.82	1.78	569,428	12.00%	22.10%	103,747.00	0	0.00	0.00	3.56	0.00	0.00	2.35		
30-39 years	2,162,945	16.92%	17.90%	1,735,966.44	28	1.61	1.02	2.21	577,492	12.17%	17.90%	117,611.00	2	1.70	0.21	6.14	1.05	0.17	3.76		
40-49 years	2,102,123	16.45%	16.10%	1,757,533.89	48	2.73	1.96	3.50	681,534	14.36%	16.10%	142,231.00	3	2.11	0.43	6.16	0.77	0.19	2.21		
50-64 years	3,480,430	27.23%	24.60%	2,975,832.86	104	3.49	2.82	4.17	1,613,774	34.01%	24.60%	359,066.00	7	1.95	0.78	4.02	0.56	0.24	1.14		
65-74 years	1,473,013	11.52%	11.80%	1,237,953.79	35	2.83	1.89	3.76	831,105	17.51%	11.80%	227,107.00	0	0.00	0.00	1.62	0.00	0.00	0.49		
>75 years	735,480	5.75%	7.50%	640,063.72	25	3.91	2.37	5.44	472,233	9.95%	7.50%	137,362.00	7	5.10	2.05	10.50	1.30	0.52	2.92		
Standardized																					
Male Adults	12,781,687	-	-	10,506,450.45	263	2.50	2.21	2.83	4,745,566	-	-	1,087,123.80	16	1.51	0.87	2.66	0.60	0.34	1.01		
Crude																					
Female Adults	14,031,314	-	-	11,605,096.27	364	3.14	2.81	3.46	6,163,360	-	-	1,457,798.35	27	1.85	1.15	2.55	0.59	0.39	0.86		
18-29 years	2,818,905	20.09%	20.10%	2,131,471.64	66	3.10	2.35	3.84	829,827	13.46%	20.10%	164,106.00	2	1.22	0.15	4.40	0.39	0.07	1.34		
30-39 years	2,284,577	16.28%	16.80%	1,849,779.92	64	3.46	2.61	4.31	803,957	13.04%	16.80%	173,064.00	4	2.31	0.63	5.92	0.67	0.21	1.68		
40-49 years	2,229,166	15.89%	15.50%	1,879,307.14	58	3.09	2.29	3.88	890,160	14.44%	15.50%	196,015.00	5	2.55	0.83	5.95	0.83	0.29	1.92		
50-64 years	3,854,004	27.47%	24.70%	3,316,851.37	105	3.17	2.56	3.77	1,953,054	31.69%	24.70%	454,957.00	4	0.88	0.24	2.25	0.28	0.09	0.69		
65-74 years	1,764,174	12.57%	12.80%	1,488,658.76	45	3.02	2.14	3.91	1,013,191	16.44%	12.80%	276,465.00	2	0.72	0.09	2.61	0.24	0.04	0.83		
>75 years	1,080,488	7.70%	10.10%	939,027.42	26	2.77	1.70	3.83	673,171	10.92%	10.10%	193,191.00	10	5.18	1.97	8.38	1.87	0.86	3.81		
Standardized																					
Female Adults	14,031,314	-	-	11,605,096.27	363	3.13	2.82	3.47	6,163,360	-	-	1,457,798.35	27	1.86	1.20	2.83	0.59	0.38	0.90		

Table 3i: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Encephalitis/encephalomyelitis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	29,727,712	-	-	24,423,393.43	1,708	6.99	6.66	7.32	9,955,430	-	-	2,358,481.91	82	3.48	2.72	4.23	0.50	0.40	0.62		
18-29 years	6,389,128	21.49%	21.05%	4,900,002.06	178	3.63	3.10	4.17	1,215,971	12.21%	21.05%	236,972.00	5	2.11	0.69	4.92	0.58	0.21	1.31		
30-39 years	5,016,654	16.88%	17.31%	4,070,092.94	184	4.52	3.87	5.17	1,224,246	12.30%	17.31%	261,670.00	6	2.29	0.84	4.99	0.51	0.20	1.07		
40-49 years	4,819,161	16.21%	15.80%	4,025,854.06	204	5.07	4.37	5.76	1,419,873	14.26%	15.80%	309,676.00	8	2.58	1.12	5.09	0.51	0.23	0.98		
50-64 years	8,027,784	27.00%	24.66%	6,822,197.02	589	8.63	7.94	9.33	3,320,360	33.35%	24.66%	765,509.00	24	3.14	1.88	4.39	0.36	0.24	0.54		
65-74 years	3,525,544	11.86%	12.34%	2,934,729.50	334	11.38	10.16	12.60	1,704,680	17.12%	12.34%	471,669.00	23	4.88	2.88	6.87	0.43	0.27	0.64		
>75 years	1,949,441	6.56%	8.85%	1,670,517.86	219	13.11	11.37	14.85	1,070,300	10.75%	8.85%	312,987.00	16	5.11	2.61	7.62	0.39	0.23	0.63		
Crude																					
Male Adults	14,192,647	-	-	11,614,342.64	865	7.45	6.95	7.94	4,279,616	-	-	998,016.12	38	3.81	2.60	5.02	0.51	0.36	0.70		
18-29 years	3,185,164	22.44%	22.10%	2,447,599.61	97	3.96	3.17	4.75	474,022	11.08%	22.10%	88,131.00	1	1.13	0.03	6.32	0.29	0.01	1.44		
30-39 years	2,452,389	17.28%	17.90%	1,975,771.83	81	4.10	3.21	4.99	498,818	11.66%	17.90%	103,360.00	2	1.93	0.23	6.99	0.47	0.08	1.60		
40-49 years	2,346,080	16.53%	16.10%	1,950,279.88	109	5.59	4.54	6.64	605,894	14.16%	16.10%	128,222.00	3	2.34	0.48	6.84	0.42	0.11	1.17		
50-64 years	3,814,005	26.87%	24.60%	3,232,217.54	298	9.22	8.17	10.27	1,492,555	34.88%	24.60%	335,624.00	11	3.28	1.34	5.21	0.36	0.19	0.63		
65-74 years	1,606,599	11.32%	11.80%	1,333,114.42	170	12.75	10.84	14.67	766,938	17.92%	11.80%	212,542.00	13	6.12	2.79	9.44	0.48	0.26	0.82		
>75 years	788,410	5.56%	7.50%	675,359.35	110	16.29	13.24	19.33	441,389	10.31%	7.50%	130,136.00	8	6.15	2.65	12.11	0.38	0.17	0.74		
Standardized																					
Male Adults	14,192,647	-	-	11,614,342.64	872	7.51	7.01	8.03	4,279,616	-	-	998,016.12	30	2.97	2.00	4.49	0.39	0.26	0.57		
Crude																					
Female Adults	15,535,065	-	-	12,809,050.79	843	6.58	6.14	7.03	5,675,814	-	-	1,360,465.79	44	3.23	2.28	4.19	0.49	0.36	0.66		
18-29 years	3,203,964	20.62%	20.10%	2,452,402.45	81	3.30	2.58	4.02	741,949	13.07%	20.10%	148,841.00	4	2.69	0.73	6.88	0.81	0.25	2.03		
30-39 years	2,564,265	16.51%	16.80%	2,094,321.11	103	4.92	3.97	5.87	725,428	12.78%	16.80%	158,309.00	4	2.53	0.69	6.47	0.51	0.16	1.27		
40-49 years	2,473,081	15.92%	15.50%	2,075,574.18	95	4.58	3.66	5.50	813,979	14.34%	15.50%	181,454.00	5	2.76	0.89	6.43	0.60	0.22	1.38		
50-64 years	4,213,779	27.12%	24.70%	3,589,979.47	291	8.11	7.17	9.04	1,827,805	32.20%	24.70%	429,884.00	13	3.02	1.38	4.67	0.37	0.21	0.63		
65-74 years	1,918,945	12.35%	12.80%	1,601,615.08	164	10.24	8.67	11.81	937,742	16.52%	12.80%	259,127.00	10	3.86	1.47	6.25	0.38	0.19	0.69		
>75 years	1,161,031	7.47%	10.10%	995,158.51	109	10.95	8.90	13.01	628,911	11.08%	10.10%	182,851.00	8	4.38	1.89	8.62	0.40	0.18	0.78		
Standardized																					
Female Adults	15,535,065	-	-	12,809,050.79	848	6.62	6.18	7.09	5,675,814	-	-	1,360,465.79	42	3.07	2.18	4.29	0.46	0.33	0.64		

Table 3j: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Erythema multiforme

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,812,184	-	-	22,109,369.83	2,157	9.76	9.34	10.17	10,908,341	-	-	2,544,753.95	230	9.04	7.87	10.21	0.93	0.81	1.06		
18-29 years	5,646,426	21.06%	21.05%	4,290,229.81	315	7.34	6.53	8.15	1,399,177	12.83%	21.05%	267,835.00	26	9.71	5.98	13.44	1.32	0.87	1.94		
30-39 years	4,447,377	16.59%	17.31%	3,585,462.20	308	8.59	7.63	9.55	1,381,389	12.66%	17.31%	290,656.00	36	12.39	8.34	16.43	1.44	1.01	2.02		
40-49 years	4,331,157	16.15%	15.80%	3,636,471.91	371	10.20	9.16	11.24	1,571,600	14.41%	15.80%	338,223.00	25	7.39	4.49	10.29	0.72	0.47	1.07		
50-64 years	7,334,209	27.35%	24.66%	6,291,992.73	639	10.16	9.37	10.94	3,566,642	32.70%	24.66%	813,969.00	77	9.46	7.35	11.57	0.93	0.73	1.17		
65-74 years	3,237,100	12.07%	12.34%	2,726,294.49	317	11.63	10.35	12.91	1,844,191	16.91%	12.34%	503,537.00	40	7.94	5.48	10.41	0.68	0.49	0.94		
>75 years	1,815,915	6.77%	8.85%	1,578,918.69	207	13.11	11.32	14.90	1,145,342	10.50%	8.85%	330,534.00	26	7.87	4.84	10.89	0.60	0.39	0.89		
Crude																					
Male Adults	12,781,390	-	-	10,505,622.47	844	8.03	7.49	8.58	4,745,350	-	-	1,087,064.87	77	7.08	5.50	8.67	0.88	0.69	1.11		
18-29 years	2,827,625	22.12%	22.10%	2,158,966.66	108	5.00	4.06	5.95	569,395	12.00%	22.10%	103,740.00	6	5.78	2.12	12.59	1.16	0.46	2.47		
30-39 years	2,162,892	16.92%	17.90%	1,735,844.37	137	7.89	6.57	9.21	577,468	12.17%	17.90%	117,606.00	13	11.05	5.05	17.06	1.40	0.76	2.41		
40-49 years	2,102,073	16.45%	16.10%	1,757,404.68	134	7.62	6.33	8.92	681,503	14.36%	16.10%	142,224.00	8	5.62	2.43	11.08	0.74	0.34	1.44		
50-64 years	3,480,363	27.23%	24.60%	2,975,582.41	249	8.37	7.33	9.41	1,613,707	34.01%	24.60%	359,047.00	25	6.96	4.23	9.69	0.83	0.54	1.24		
65-74 years	1,472,976	11.52%	11.80%	1,237,821.45	135	10.91	9.07	12.75	831,067	17.51%	11.80%	227,093.00	12	5.28	2.29	8.27	0.48	0.26	0.85		
>75 years	735,461	5.75%	7.50%	640,002.91	81	12.66	9.90	15.41	472,210	9.95%	7.50%	137,355.00	13	9.46	4.32	14.61	0.75	0.40	1.31		
Standardized																					
Male Adults	12,781,390	-	-	10,505,622.47	845	8.04	7.51	8.61	4,745,350	-	-	1,087,064.87	78	7.21	5.50	9.40	0.90	0.68	1.16		
Crude																					
Female Adults	14,030,794	-	-	11,603,747.36	1,313	11.32	10.70	11.93	6,162,991	-	-	1,457,689.08	153	10.50	8.83	12.16	0.93	0.78	1.09		
18-29 years	2,818,801	20.09%	20.10%	2,131,263.15	207	9.71	8.39	11.04	829,782	13.46%	20.10%	164,095.00	20	12.19	6.85	17.53	1.25	0.77	1.95		
30-39 years	2,284,485	16.28%	16.80%	1,849,617.83	171	9.25	7.86	10.63	803,921	13.04%	16.80%	173,050.00	23	13.29	7.86	18.72	1.44	0.91	2.19		
40-49 years	2,229,084	15.89%	15.50%	1,879,067.23	237	12.61	11.01	14.22	890,097	14.44%	15.50%	195,999.00	17	8.67	4.55	12.80	0.69	0.41	1.10		
50-64 years	3,853,846	27.47%	24.70%	3,316,410.33	390	11.76	10.59	12.93	1,952,935	31.69%	24.70%	454,922.00	52	11.43	8.32	14.54	0.97	0.72	1.29		
65-74 years	1,764,124	12.57%	12.80%	1,488,473.05	182	12.23	10.45	14.00	1,013,124	16.44%	12.80%	276,444.00	28	10.13	6.38	13.88	0.83	0.55	1.22		
>75 years	1,080,454	7.70%	10.10%	938,915.78	126	13.42	11.08	15.76	673,132	10.92%	10.10%	193,180.00	13	6.73	3.07	10.39	0.50	0.27	0.86		
Standardized																					
Female Adults	14,030,794	-	-	11,603,747.36	1,310	11.29	10.68	11.92	6,162,991	-	-	1,457,689.08	158	10.82	9.07	12.87	0.96	0.80	1.15		

Table 3k: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Guillain-Barre Syndrome (GBS)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,812,840	-	-	22,111,145.25	980	4.43	4.15	4.71	10,908,895	-	-	2,544,912.51	63	2.48	1.86	3.09	0.56	0.43	0.72		
18-29 years	5,646,590	21.06%	21.05%	4,290,564.79	93	2.17	1.73	2.61	1,399,266	12.83%	21.05%	267,856.00	3	1.12	0.23	3.27	0.52	0.13	1.44		
30-39 years	4,447,493	16.59%	17.31%	3,585,723.69	105	2.93	2.37	3.49	1,381,459	12.66%	17.31%	290,677.00	5	1.72	0.56	4.01	0.59	0.21	1.34		
40-49 years	4,331,270	16.15%	15.80%	3,636,794.57	155	4.26	3.59	4.93	1,571,691	14.41%	15.80%	338,246.00	7	2.07	0.83	4.26	0.49	0.21	0.98		
50-64 years	7,334,371	27.35%	24.66%	6,292,515.38	326	5.18	4.62	5.74	3,566,805	32.70%	24.66%	814,016.00	25	3.07	1.87	4.28	0.59	0.39	0.88		
65-74 years	3,237,169	12.07%	12.34%	2,726,513.59	181	6.64	5.67	7.61	1,844,284	16.91%	12.34%	503,568.00	11	2.18	0.89	3.48	0.33	0.17	0.58		
>75 years	1,815,947	6.77%	8.85%	1,579,033.23	120	7.60	6.24	8.96	1,145,390	10.50%	8.85%	330,551.00	12	3.63	1.58	5.68	0.48	0.25	0.84		
Crude																					
Male Adults	12,781,587	-	-	10,506,187.92	511	4.86	4.44	5.29	4,745,548	-	-	1,087,117.22	32	2.94	1.92	3.96	0.61	0.42	0.85		
18-29 years	2,827,695	22.12%	22.10%	2,159,090.81	44	2.04	1.44	2.64	569,430	12.00%	22.10%	103,747.00	1	0.96	0.02	5.37	0.47	0.02	2.44		
30-39 years	2,162,934	16.92%	17.90%	1,735,947.21	41	2.36	1.64	3.08	577,492	12.17%	17.90%	117,610.00	3	2.55	0.53	7.45	1.08	0.27	3.12		
40-49 years	2,102,110	16.45%	16.10%	1,757,503.56	80	4.55	3.55	5.55	681,533	14.36%	16.10%	142,232.00	1	0.70	0.02	3.92	0.15	0.01	0.78		
50-64 years	3,480,385	27.23%	24.60%	2,975,731.13	175	5.88	5.01	6.75	1,613,768	34.01%	24.60%	359,064.00	13	3.62	1.65	5.59	0.62	0.34	1.05		
65-74 years	1,473,000	11.52%	11.80%	1,237,886.67	107	8.64	7.01	10.28	831,098	17.51%	11.80%	227,103.00	5	2.20	0.71	5.14	0.25	0.09	0.58		
>75 years	735,463	5.75%	7.50%	640,028.55	64	10.00	7.55	12.45	472,227	9.95%	7.50%	137,361.00	9	6.55	3.00	12.44	0.66	0.31	1.27		
Standardized																					
Male Adults	12,781,587	-	-	10,506,187.92	507	4.83	4.41	5.27	4,745,548	-	-	1,087,117.22	26	2.43	1.58	3.76	0.50	0.32	0.75		
Crude																					
Female Adults	14,031,253	-	-	11,604,957.33	469	4.04	3.68	4.41	6,163,347	-	-	1,457,795.29	31	2.13	1.38	2.88	0.53	0.36	0.75		
18-29 years	2,818,895	20.09%	20.10%	2,131,473.98	49	2.30	1.66	2.94	829,836	13.46%	20.10%	164,108.00	2	1.22	0.15	4.40	0.53	0.09	1.83		
30-39 years	2,284,559	16.28%	16.80%	1,849,776.48	64	3.46	2.61	4.31	803,967	13.04%	16.80%	173,067.00	2	1.16	0.14	4.17	0.33	0.06	1.14		
40-49 years	2,229,160	15.89%	15.50%	1,879,291.01	75	3.99	3.09	4.89	890,158	14.44%	15.50%	196,014.00	6	3.06	1.12	6.66	0.77	0.30	1.66		
50-64 years	3,853,986	27.47%	24.70%	3,316,784.25	151	4.55	3.83	5.28	1,953,037	31.69%	24.70%	454,952.00	12	2.64	1.15	4.13	0.58	0.31	1.01		
65-74 years	1,764,169	12.57%	12.80%	1,488,626.92	74	4.97	3.84	6.10	1,013,186	16.44%	12.80%	276,464.00	6	2.17	0.80	4.72	0.44	0.17	0.95		
>75 years	1,080,484	7.70%	10.10%	939,004.69	56	5.96	4.40	7.53	673,163	10.92%	10.10%	193,190.00	3	1.55	0.32	4.54	0.26	0.06	0.74		
Standardized																					
Female Adults	14,031,253	-	-	11,604,957.33	468	4.03	3.67	4.41	6,163,347	-	-	1,457,795.29	29	2.00	1.33	2.97	0.50	0.33	0.73		

Table 3I: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Kawasaki Disease

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,813,021	-	-	22,111,837.36	219	0.99	0.86	1.12	10,909,043	-	-	2,544,951.44	21	0.83	0.47	1.18	0.83	0.52	1.28		
18-29 years	5,646,547	21.06%	21.05%	4,290,502.78	119	2.77	2.28	3.27	1,399,247	12.83%	21.05%	267,851.00	5	1.87	0.61	4.36	0.67	0.24	1.53		
30-39 years	4,447,523	16.59%	17.31%	3,585,783.02	48	1.34	0.96	1.72	1,381,460	12.66%	17.31%	290,676.00	5	1.72	0.56	4.01	1.29	0.45	3.02		
40-49 years	4,331,308	16.15%	15.80%	3,636,914.70	22	0.60	0.35	0.86	1,571,707	14.41%	15.80%	338,250.00	2	0.59	0.07	2.14	0.98	0.16	3.56		
50-64 years	7,334,465	27.35%	24.66%	6,292,830.58	17	0.27	0.14	0.40	3,566,883	32.70%	24.66%	814,034.00	2	0.25	0.03	0.89	0.91	0.14	3.41		
65-74 years	3,237,199	12.07%	12.34%	2,726,669.52	8	0.29	0.13	0.58	1,844,329	16.91%	12.34%	503,581.00	3	0.60	0.12	1.74	2.03	0.44	7.42		
>75 years	1,815,979	6.77%	8.85%	1,579,136.77	5	0.32	0.10	0.74	1,145,417	10.50%	8.85%	330,559.00	4	1.21	0.33	3.10	3.82	0.91	15.09		
Crude																					
Male Adults	12,781,676	-	-	10,506,515.82	125	1.19	0.98	1.40	4,745,597	-	-	1,087,131.45	12	1.10	0.48	1.73	0.93	0.49	1.63		
18-29 years	2,827,669	22.12%	22.10%	2,159,043.17	65	3.01	2.28	3.74	569,413	12.00%	22.10%	103,743.00	3	2.89	0.60	8.45	0.96	0.24	2.71		
30-39 years	2,162,941	16.92%	17.90%	1,735,953.70	30	1.73	1.11	2.35	577,485	12.17%	17.90%	117,610.00	1	0.85	0.02	4.74	0.49	0.02	2.58		
40-49 years	2,102,125	16.45%	16.10%	1,757,557.96	12	0.68	0.30	1.07	681,538	14.36%	16.10%	142,233.00	2	1.41	0.17	5.08	2.06	0.31	8.15		
50-64 years	3,480,441	27.23%	24.60%	2,975,900.75	9	0.30	0.14	0.57	1,613,802	34.01%	24.60%	359,071.00	2	0.56	0.07	2.01	1.84	0.27	7.73		
65-74 years	1,473,016	11.52%	11.80%	1,237,975.52	6	0.48	0.18	1.05	831,124	17.51%	11.80%	227,112.00	2	0.88	0.11	3.18	1.82	0.25	8.58		
>75 years	735,484	5.75%	7.50%	640,084.72	3	0.47	0.10	1.37	472,235	9.95%	7.50%	137,363.00	2	1.46	0.18	5.26	3.11	0.37	20.89		
Standardized																					
Male Adults	12,781,676	-	-	10,506,515.82	131	1.25	1.04	1.49	4,745,597	-	-	1,087,131.45	15	1.37	0.63	2.70	1.09	0.49	2.09		
Crude																					
Female Adults	14,031,345	-	-	11,605,321.54	94	0.81	0.65	0.97	6,163,446	-	-	1,457,819.99	9	0.62	0.28	1.17	0.76	0.36	1.45		
18-29 years	2,818,878	20.09%	20.10%	2,131,459.61	54	2.53	1.86	3.21	829,834	13.46%	20.10%	164,108.00	2	1.22	0.15	4.40	0.48	0.08	1.65		
30-39 years	2,284,582	16.28%	16.80%	1,849,829.33	18	0.97	0.52	1.42	803,975	13.04%	16.80%	173,067.00	4	2.31	0.63	5.92	2.38	0.69	6.62		
40-49 years	2,229,183	15.89%	15.50%	1,879,356.74	10	0.53	0.20	0.86	890,169	14.44%	15.50%	196,017.00	0	0.00	0.00	1.88	0.00	0.00	3.35		
50-64 years	3,854,024	27.47%	24.70%	3,316,929.82	8	0.24	0.10	0.48	1,953,081	31.69%	24.70%	454,963.00	0	0.00	0.00	0.81	0.00	0.00	3.31		
65-74 years	1,764,183	12.57%	12.80%	1,488,693.99	2	0.13	0.02	0.49	1,013,205	16.44%	12.80%	276,469.00	1	0.36	0.01	2.02	2.69	0.09	35.40		
>75 years	1,080,495	7.70%	10.10%	939,052.05	2	0.21	0.03	0.77	673,182	10.92%	10.10%	193,196.00	2	1.04	0.13	3.74	4.86	0.51	46.69		
Standardized																					
Female Adults	14,031,345	-	-	11,605,321.54	99	0.85	0.69	1.05	6,163,446	-	-	1,457,819.99	11	0.78	0.34	1.58	0.92	0.39	1.83		

Table 3m: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Microangiopathy

	Pre-COVID (12/01/2018-11/30/2019)								Post-vaccination (12/18/2020 - 06/20/2021)								Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL
Crude																			
All Adults	26,812,532	-	-	22,110,956.46	798	3.61	3.36	3.86	10,908,741	-	-	2,544,873.16	59	2.32	1.73	2.91	0.64	0.49	0.83
18-29 years	5,646,558	21.06%	21.05%	4,290,526.95	80	1.86	1.46	2.27	1,399,251	12.83%	21.05%	267,851.00	2	0.75	0.09	2.70	0.40	0.07	1.36
30-39 years	4,447,448	16.59%	17.31%	3,585,680.60	102	2.84	2.29	3.40	1,381,428	12.66%	17.31%	290,670.00	3	1.03	0.21	3.02	0.36	0.09	1.01
40-49 years	4,331,209	16.15%	15.80%	3,636,754.20	126	3.46	2.86	4.07	1,571,660	14.41%	15.80%	338,238.00	10	2.96	1.12	4.79	0.85	0.42	1.57
50-64 years	7,334,276	27.35%	24.66%	6,292,491.35	286	4.55	4.02	5.07	3,566,742	32.70%	24.66%	814,001.00	21	2.58	1.48	3.68	0.57	0.36	0.87
65-74 years	3,237,114	12.07%	12.34%	2,726,487.53	126	4.62	3.81	5.43	1,844,272	16.91%	12.34%	503,563.00	10	1.99	0.76	3.22	0.43	0.21	0.79
>75 years	1,815,927	6.77%	8.85%	1,579,015.82	78	4.94	3.84	6.04	1,145,388	10.50%	8.85%	330,549.00	13	3.93	1.79	6.07	0.80	0.43	1.40
Crude																			
Male Adults	12,781,556	-	-	10,506,279.44	292	2.78	2.46	3.10	4,745,512	-	-	1,087,111.38	18	1.66	0.89	2.42	0.60	0.36	0.94
18-29 years	2,827,691	22.12%	22.10%	2,159,088.09	19	0.88	0.48	1.28	569,426	12.00%	22.10%	103,746.00	0	0.00	0.00	3.56	0.00	0.00	3.55
30-39 years	2,162,926	16.92%	17.90%	1,735,939.43	31	1.79	1.16	2.41	577,471	12.17%	17.90%	117,607.00	0	0.00	0.00	3.14	0.00	0.00	1.50
40-49 years	2,102,102	16.45%	16.10%	1,757,513.24	45	2.56	1.81	3.31	681,524	14.36%	16.10%	142,230.00	2	1.41	0.17	5.08	0.55	0.09	1.90
50-64 years	3,480,380	27.23%	24.60%	2,975,782.33	128	4.30	3.56	5.05	1,613,764	34.01%	24.60%	359,063.00	8	2.23	0.96	4.39	0.52	0.24	1.01
65-74 years	1,472,993	11.52%	11.80%	1,237,913.06	46	3.72	2.64	4.79	831,103	17.51%	11.80%	227,105.00	4	1.76	0.48	4.51	0.47	0.15	1.21
>75 years	735,464	5.75%	7.50%	640,043.29	23	3.59	2.12	5.06	472,224	9.95%	7.50%	137,360.00	4	2.91	0.79	7.46	0.81	0.24	2.19
Standardized																			
Male Adults	12,781,556	-	-	10,506,279.44	283	2.69	2.39	3.03	4,745,512	-	-	1,087,111.38	13	1.20	0.70	2.21	0.45	0.26	0.76
Crude																			
Female Adults	14,030,976	-	-	11,604,677.02	506	4.36	3.98	4.74	6,163,229	-	-	1,457,761.77	41	2.81	1.95	3.67	0.65	0.46	0.88
18-29 years	2,818,867	20.09%	20.10%	2,131,438.86	61	2.86	2.14	3.58	829,825	13.46%	20.10%	164,105.00	2	1.22	0.15	4.40	0.43	0.07	1.46
30-39 years	2,284,522	16.28%	16.80%	1,849,741.17	71	3.84	2.95	4.73	803,957	13.04%	16.80%	173,063.00	3	1.73	0.36	5.07	0.45	0.11	1.27
40-49 years	2,229,107	15.89%	15.50%	1,879,240.95	81	4.31	3.37	5.25	890,136	14.44%	15.50%	196,009.00	8	4.08	1.76	8.04	0.95	0.43	1.87
50-64 years	3,853,896	27.47%	24.70%	3,316,709.03	158	4.76	4.02	5.51	1,952,978	31.69%	24.70%	454,937.00	13	2.86	1.30	4.41	0.60	0.33	1.03
65-74 years	1,764,121	12.57%	12.80%	1,488,574.47	80	5.37	4.20	6.55	1,013,169	16.44%	12.80%	276,459.00	6	2.17	0.80	4.72	0.40	0.16	0.87
>75 years	1,080,463	7.70%	10.10%	938,972.53	55	5.86	4.31	7.41	673,164	10.92%	10.10%	193,189.00	9	4.66	2.13	8.84	0.80	0.37	1.55
Standardized																			
Female Adults	14,030,976	-	-	11,604,677.02	505	4.35	3.97	4.75	6,163,229	-	-	1,457,761.77	38	2.62	1.85	3.69	0.60	0.42	0.84

Table 3n: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Multisystem Inflammatory Syndrome (MIS)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,813,135	-	-	22,111,976.55	153	0.69	0.58	0.80	10,909,093	-	-	2,544,963.50	10	0.39	0.15	0.64	0.57	0.28	1.04		
18-29 years	5,646,625	21.06%	21.05%	4,290,634.69	15	0.35	0.17	0.53	1,399,282	12.83%	21.05%	267,859.00	2	0.75	0.09	2.70	2.14	0.33	8.15		
30-39 years	4,447,542	16.59%	17.31%	3,585,831.50	11	0.31	0.13	0.49	1,381,480	12.66%	17.31%	290,681.00	2	0.69	0.08	2.49	2.24	0.34	9.02		
40-49 years	4,331,314	16.15%	15.80%	3,636,914.15	24	0.66	0.40	0.92	1,571,717	14.41%	15.80%	338,252.00	1	0.30	0.01	1.65	0.45	0.02	2.39		
50-64 years	7,334,468	27.35%	24.66%	6,292,801.24	69	1.10	0.84	1.36	3,566,882	32.70%	24.66%	814,035.00	0	0.00	0.00	0.45	0.00	0.00	0.34		
65-74 years	3,237,207	12.07%	12.34%	2,726,666.03	21	0.77	0.44	1.10	1,844,325	16.91%	12.34%	503,580.00	2	0.40	0.05	1.43	0.52	0.08	1.89		
>75 years	1,815,979	6.77%	8.85%	1,579,128.93	13	0.82	0.38	1.27	1,145,407	10.50%	8.85%	330,557.00	3	0.91	0.19	2.65	1.10	0.25	3.60		
Crude																					
Male Adults	12,781,760	-	-	10,506,652.14	49	0.47	0.34	0.60	4,745,636	-	-	1,087,141.42	4	0.37	0.10	0.94	0.79	0.24	2.01		
18-29 years	2,827,712	22.12%	22.10%	2,159,125.24	3	0.14	0.03	0.41	569,431	12.00%	22.10%	103,747.00	1	0.96	0.02	5.37	6.94	0.26	65.09		
30-39 years	2,162,954	16.92%	17.90%	1,735,991.09	4	0.23	0.06	0.59	577,497	12.17%	17.90%	117,612.00	0	0.00	0.00	3.14	0.00	0.00	16.45		
40-49 years	2,102,132	16.45%	16.10%	1,757,567.76	9	0.51	0.23	0.97	681,545	14.36%	16.10%	142,234.00	1	0.70	0.02	3.92	1.37	0.06	8.36		
50-64 years	3,480,455	27.23%	24.60%	2,975,904.79	21	0.71	0.40	1.01	1,613,808	34.01%	24.60%	359,074.00	0	0.00	0.00	1.03	0.00	0.00	1.27		
65-74 years	1,473,023	11.52%	11.80%	1,237,980.33	6	0.48	0.18	1.05	831,125	17.51%	11.80%	227,112.00	0	0.00	0.00	1.62	0.00	0.00	3.53		
>75 years	735,484	5.75%	7.50%	640,082.94	6	0.94	0.34	2.04	472,230	9.95%	7.50%	137,362.00	2	1.46	0.18	5.26	1.55	0.22	7.34		
Standardized																					
Male Adults	12,781,760	-	-	10,506,652.14	48	0.46	0.34	0.61	4,745,636	-	-	1,087,141.42	5	0.44	0.09	1.44	0.96	0.19	2.84		
Crude																					
Female Adults	14,031,375	-	-	11,605,324.40	104	0.90	0.72	1.07	6,163,457	-	-	1,457,822.08	6	0.41	0.15	0.90	0.46	0.18	0.98		
18-29 years	2,818,913	20.09%	20.10%	2,131,509.45	12	0.56	0.24	0.88	829,851	13.46%	20.10%	164,111.00	1	0.61	0.02	3.40	1.08	0.05	6.25		
30-39 years	2,284,588	16.28%	16.80%	1,849,840.42	7	0.38	0.15	0.78	803,983	13.04%	16.80%	173,069.00	2	1.16	0.14	4.17	3.05	0.43	13.72		
40-49 years	2,229,182	15.89%	15.50%	1,879,346.39	15	0.80	0.39	1.20	890,172	14.44%	15.50%	196,018.00	0	0.00	0.00	1.88	0.00	0.00	2.12		
50-64 years	3,854,013	27.47%	24.70%	3,316,896.44	48	1.45	1.04	1.86	1,953,074	31.69%	24.70%	454,962.00	0	0.00	0.00	0.81	0.00	0.00	0.47		
65-74 years	1,764,184	12.57%	12.80%	1,488,685.70	15	1.01	0.50	1.52	1,013,200	16.44%	12.80%	276,468.00	2	0.72	0.09	2.61	0.72	0.11	2.74		
>75 years	1,080,495	7.70%	10.10%	939,045.99	7	0.75	0.30	1.54	673,177	10.92%	10.10%	193,195.00	1	0.52	0.01	2.88	0.69	0.03	4.49		
Standardized																					
Female Adults	14,031,375	-	-	11,605,324.40	100	0.86	0.70	1.05	6,163,457	-	-	1,457,822.08	7	0.46	0.15	1.13	0.53	0.17	1.24		

Table 3o: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Myocarditis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,812,260	-	-	22,109,577.92	2,186	9.89	9.47	10.30	10,908,030	-	-	2,544,670.87	253	9.94	8.72	11.17	1.01	0.88	1.14		
18-29 years	5,646,436	21.06%	21.05%	4,290,239.90	318	7.41	6.60	8.23	1,399,118	12.83%	21.05%	267,821.00	47	17.55	12.53	22.57	2.37	1.73	3.19		
30-39 years	4,447,411	16.59%	17.31%	3,585,507.17	294	8.20	7.26	9.14	1,381,355	12.66%	17.31%	290,649.00	32	11.01	7.20	14.82	1.34	0.92	1.91		
40-49 years	4,331,160	16.15%	15.80%	3,636,545.67	329	9.05	8.07	10.02	1,571,586	14.41%	15.80%	338,217.00	28	8.28	5.21	11.35	0.92	0.61	1.33		
50-64 years	7,334,228	27.35%	24.66%	6,292,093.10	697	11.08	10.26	11.90	3,566,510	32.70%	24.66%	813,935.00	79	9.71	7.57	11.85	0.88	0.69	1.10		
65-74 years	3,237,103	12.07%	12.34%	2,726,307.73	310	11.37	10.10	12.64	1,844,169	16.91%	12.34%	503,530.00	35	6.95	4.65	9.25	0.61	0.43	0.86		
>75 years	1,815,922	6.77%	8.85%	1,578,884.36	238	15.07	13.16	16.99	1,145,292	10.50%	8.85%	330,519.00	32	9.68	6.33	13.04	0.64	0.44	0.92		
Crude																					
Male Adults	12,781,223	-	-	10,505,220.56	1,266	12.05	11.39	12.71	4,745,072	-	-	1,086,986.95	147	13.52	11.34	15.71	1.12	0.94	1.33		
18-29 years	2,827,566	22.12%	22.10%	2,158,828.08	227	10.51	9.15	11.88	569,342	12.00%	22.10%	103,726.00	36	34.71	23.37	46.04	3.30	2.29	4.65		
30-39 years	2,162,865	16.92%	17.90%	1,735,775.23	185	10.66	9.12	12.19	577,429	12.17%	17.90%	117,594.00	18	15.31	8.24	22.38	1.44	0.86	2.28		
40-49 years	2,102,038	16.45%	16.10%	1,757,333.35	202	11.49	9.91	13.08	681,476	14.36%	16.10%	142,216.00	19	13.36	7.35	19.37	1.16	0.71	1.82		
50-64 years	3,480,324	27.23%	24.60%	2,975,526.71	372	12.50	11.23	13.77	1,613,598	34.01%	24.60%	359,020.00	38	10.58	7.22	13.95	0.85	0.60	1.17		
65-74 years	1,472,975	11.52%	11.80%	1,237,784.21	172	13.90	11.82	15.97	831,040	17.51%	11.80%	227,083.00	21	9.25	5.29	13.20	0.67	0.41	1.03		
>75 years	735,455	5.75%	7.50%	639,972.98	108	16.88	13.69	20.06	472,187	9.95%	7.50%	137,348.00	15	10.92	5.39	16.45	0.65	0.36	1.09		
Standardized																					
Male Adults	12,781,223	-	-	10,505,220.56	1,268	12.07	11.41	12.76	4,745,072	-	-	1,086,986.95	186	17.07	14.07	20.59	1.41	1.16	1.71		
Crude																					
Female Adults	14,031,037	-	-	11,604,357.36	920	7.93	7.42	8.44	6,162,958	-	-	1,457,683.92	106	7.27	5.89	8.66	0.92	0.75	1.12		
18-29 years	2,818,870	20.09%	20.10%	2,131,411.81	91	4.27	3.39	5.15	829,776	13.46%	20.10%	164,094.00	11	6.70	2.74	10.66	1.57	0.80	2.85		
30-39 years	2,284,546	16.28%	16.80%	1,849,731.94	109	5.89	4.79	7.00	803,926	13.04%	16.80%	173,055.00	14	8.09	3.85	12.33	1.37	0.76	2.34		
40-49 years	2,229,122	15.89%	15.50%	1,879,212.32	127	6.76	5.58	7.93	890,110	14.44%	15.50%	196,001.00	9	4.59	2.10	8.72	0.68	0.32	1.28		
50-64 years	3,853,904	27.47%	24.70%	3,316,566.39	325	9.80	8.73	10.86	1,952,912	31.69%	24.70%	454,915.00	41	9.01	6.25	11.77	0.92	0.66	1.26		
65-74 years	1,764,128	12.57%	12.80%	1,488,523.52	138	9.27	7.72	10.82	1,013,129	16.44%	12.80%	276,447.00	14	5.06	2.41	7.72	0.55	0.30	0.92		
>75 years	1,080,467	7.70%	10.10%	938,911.38	130	13.85	11.47	16.23	673,105	10.92%	10.10%	193,171.00	17	8.80	4.62	12.98	0.64	0.37	1.03		
Standardized																					
Female Adults	14,031,037	-	-	11,604,357.36	917	7.90	7.40	8.44	6,162,958	-	-	1,457,683.92	105	7.18	5.80	8.85	0.91	0.73	1.12		

Table 3p: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Pericarditis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,811,080	-	-	22,105,989.81	5,418	24.51	23.86	25.16		10,906,803	-	-	2,544,311.81	533	20.95	19.17	22.73		0.85	0.78	0.93
18-29 years	5,646,273	21.06%	21.05%	4,289,812.83	719	16.76	15.54	17.99		1,399,063	12.83%	21.05%	267,808.00	45	16.80	11.89	21.71		1.00	0.73	1.34
30-39 years	4,447,273	16.59%	17.31%	3,585,095.01	688	19.19	17.76	20.62		1,381,235	12.66%	17.31%	290,621.00	44	15.14	10.67	19.61		0.79	0.58	1.06
40-49 years	4,331,018	16.15%	15.80%	3,636,073.26	742	20.41	18.94	21.87		1,571,419	14.41%	15.80%	338,174.00	56	16.56	12.22	20.90		0.81	0.61	1.06
50-64 years	7,333,813	27.35%	24.66%	6,290,831.97	1,805	28.69	27.37	30.02		3,566,070	32.70%	24.66%	813,814.00	172	21.14	17.98	24.29		0.74	0.63	0.86
65-74 years	3,236,923	12.07%	12.34%	2,725,697.51	907	33.28	31.11	35.44		1,843,903	16.91%	12.34%	503,442.00	121	24.03	19.75	28.32		0.72	0.60	0.87
>75 years	1,815,780	6.77%	8.85%	1,578,479.23	557	35.29	32.36	38.22		1,145,113	10.50%	8.85%	330,451.00	95	28.75	22.97	34.53		0.81	0.65	1.01
Crude																					
Male Adults	12,780,561	-	-	10,503,327.98	2,979	28.36	27.34	29.38		4,744,452	-	-	1,086,812.37	279	25.67	22.66	28.68		0.91	0.80	1.02
18-29 years	2,827,463	22.12%	22.10%	2,158,548.33	472	21.87	19.89	23.84		569,300	12.00%	22.10%	103,718.00	32	30.85	20.16	41.54		1.41	0.97	1.99
30-39 years	2,162,790	16.92%	17.90%	1,735,561.99	406	23.39	21.12	25.67		577,359	12.17%	17.90%	117,580.00	24	20.41	12.25	28.58		0.87	0.57	1.30
40-49 years	2,101,964	16.45%	16.10%	1,757,096.45	431	24.53	22.21	26.84		681,397	14.36%	16.10%	142,196.00	28	19.69	12.40	26.98		0.80	0.54	1.16
50-64 years	3,480,084	27.23%	24.60%	2,974,851.72	947	31.83	29.81	33.86		1,613,393	34.01%	24.60%	358,961.00	100	27.86	22.40	33.32		0.88	0.71	1.07
65-74 years	1,472,890	11.52%	11.80%	1,237,488.88	466	37.66	34.24	41.08		830,903	17.51%	11.80%	227,041.00	60	26.43	19.74	33.11		0.70	0.53	0.91
>75 years	735,370	5.75%	7.50%	639,780.61	257	40.17	35.26	45.08		472,100	9.95%	7.50%	137,317.00	35	25.49	17.04	33.93		0.63	0.44	0.89
Standardized																					
Male Adults	12,780,561	-	-	10,503,327.98	2,969	28.27	27.25	29.31		4,744,452	-	-	1,086,812.37	277	25.53	22.19	29.33		0.90	0.78	1.04
Crude																					
Female Adults	14,030,519	-	-	11,602,661.84	2,439	21.02	20.19	21.86		6,162,351	-	-	1,457,499.44	254	17.43	15.28	19.57		0.83	0.73	0.94
18-29 years	2,818,810	20.09%	20.10%	2,131,264.50	247	11.59	10.14	13.03		829,763	13.47%	20.10%	164,090.00	13	7.92	3.62	12.23		0.68	0.38	1.16
30-39 years	2,284,483	16.28%	16.80%	1,849,533.02	282	15.25	13.47	17.03		803,876	13.04%	16.80%	173,042.00	20	11.56	6.49	16.62		0.76	0.47	1.17
40-49 years	2,229,054	15.89%	15.50%	1,878,976.82	311	16.55	14.71	18.39		890,022	14.44%	15.50%	195,978.00	28	14.29	9.00	19.58		0.86	0.58	1.25
50-64 years	3,853,729	27.47%	24.70%	3,315,980.25	858	25.87	24.14	27.61		1,952,677	31.69%	24.70%	454,854.00	72	15.83	12.17	19.49		0.61	0.48	0.77
65-74 years	1,764,033	12.57%	12.80%	1,488,208.62	441	29.63	26.87	32.40		1,013,000	16.44%	12.80%	276,401.00	61	22.07	16.53	27.61		0.74	0.57	0.97
>75 years	1,080,410	7.70%	10.10%	938,698.62	300	31.96	28.34	35.58		673,013	10.92%	10.10%	193,134.00	60	31.07	23.21	38.93		0.97	0.73	1.28
Standardized																					
Female Adults	14,030,519	-	-	11,602,661.84	2,421	20.87	20.05	21.73		6,162,351	-	-	1,457,499.44	228	15.62	13.67	17.85		0.75	0.65	0.86

Table 3q: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Single organ cutaneous vasculitis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL	
Crude																					
All Adults	26,810,879	-	-	22,106,113.16	4,882	22.08	21.46	22.70		10,906,822	-	-	2,544,305.48	568	22.32	20.49	24.16	1.01	0.93	1.10	
18-29 years	5,646,351	21.06%	21.05%	4,290,095.03	424	9.88	8.94	10.82		1,399,081	12.83%	21.05%	267,813.00	33	12.32	8.12	16.53	1.25	0.86	1.76	
30-39 years	4,447,267	16.59%	17.31%	3,585,199.93	526	14.67	13.42	15.93		1,381,260	12.66%	17.31%	290,625.00	40	13.76	9.50	18.03	0.94	0.67	1.28	
40-49 years	4,330,962	16.15%	15.80%	3,636,097.91	696	19.14	17.72	20.56		1,571,402	14.41%	15.80%	338,173.00	60	17.74	13.25	22.23	0.93	0.71	1.20	
50-64 years	7,333,687	27.35%	24.66%	6,290,713.79	1,725	27.42	26.13	28.72		3,566,050	32.70%	24.66%	813,803.00	209	25.68	22.20	29.16	0.94	0.81	1.08	
65-74 years	3,236,833	12.07%	12.34%	2,725,592.57	877	32.18	30.05	34.31		1,843,923	16.91%	12.34%	503,445.00	116	23.04	18.85	27.23	0.72	0.59	0.87	
>75 years	1,815,779	6.77%	8.85%	1,578,413.93	634	40.17	37.04	43.29		1,145,106	10.50%	8.85%	330,447.00	110	33.29	27.07	39.51	0.83	0.67	1.01	
Crude																					
Male Adults	12,780,914	-	-	10,504,503.27	1,823	17.35	16.56	18.15		4,744,834	-	-	1,086,910.04	224	20.61	17.91	23.31	1.19	1.03	1.36	
18-29 years	2,827,614	22.12%	22.10%	2,158,924.85	153	7.09	5.96	8.21		569,373	12.00%	22.10%	103,735.00	7	6.75	2.71	13.90	0.95	0.41	1.92	
30-39 years	2,162,850	16.92%	17.90%	1,735,752.21	196	11.29	9.71	12.87		577,431	12.17%	17.90%	117,595.00	10	8.50	3.23	13.77	0.75	0.38	1.37	
40-49 years	2,102,005	16.45%	16.10%	1,757,271.70	256	14.57	12.78	16.35		681,441	14.36%	16.10%	142,209.00	23	16.17	9.56	22.78	1.11	0.71	1.67	
50-64 years	3,480,154	27.23%	24.60%	2,975,158.85	611	20.54	18.91	22.17		1,613,506	34.01%	24.60%	358,993.00	82	22.84	17.90	27.79	1.11	0.88	1.39	
65-74 years	1,472,875	11.52%	11.80%	1,237,577.42	355	28.69	25.70	31.67		830,951	17.51%	11.80%	227,053.00	59	25.99	19.35	32.62	0.91	0.68	1.19	
>75 years	735,416	5.75%	7.50%	639,818.25	252	39.39	34.52	44.25		472,132	9.95%	7.50%	137,326.00	43	31.31	21.95	40.67	0.80	0.57	1.09	
Standardized																					
Male Adults	12,780,914	-	-	10,504,503.27	1,821	17.34	16.55	18.16		4,744,834	-	-	1,086,910.04	181	16.66	14.34	19.41	0.96	0.82	1.12	
Crude																					
Female Adults	14,029,965	-	-	11,601,609.89	3,059	26.37	25.43	27.30		6,161,988	-	-	1,457,395.44	344	23.60	21.11	26.10	0.90	0.80	1.00	
18-29 years	2,818,737	20.09%	20.10%	2,131,170.18	271	12.72	11.20	14.23		829,708	13.46%	20.10%	164,078.00	26	15.85	9.76	21.94	1.25	0.82	1.84	
30-39 years	2,284,417	16.28%	16.80%	1,849,447.73	330	17.84	15.92	19.77		803,829	13.04%	16.80%	173,030.00	30	17.34	11.13	23.54	0.97	0.66	1.39	
40-49 years	2,228,957	15.89%	15.50%	1,878,826.21	440	23.42	21.23	25.61		889,961	14.44%	15.50%	195,964.00	37	18.88	12.80	24.96	0.81	0.57	1.12	
50-64 years	3,853,533	27.47%	24.70%	3,315,554.95	1,114	33.60	31.63	35.57		1,952,544	31.69%	24.70%	454,810.00	127	27.92	23.07	32.78	0.83	0.69	1.00	
65-74 years	1,763,958	12.57%	12.80%	1,488,015.15	522	35.08	32.07	38.09		1,012,972	16.44%	12.80%	276,393.00	57	20.62	15.27	25.98	0.59	0.44	0.77	
>75 years	1,080,363	7.70%	10.10%	938,595.68	382	40.70	36.62	44.78		672,974	10.92%	10.10%	193,121.00	67	34.69	26.39	43.00	0.85	0.65	1.10	
Standardized																					
Female Adults	14,029,965	-	-	11,601,609.89	3,027	26.09	25.17	27.04		6,161,988	-	-	1,457,395.44	322	22.07	19.67	24.73	0.85	0.75	0.95	

Table 3r: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Stroke, hemorrhagic

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,808,511	-	-	22,097,512.39	16,957	76.74	75.58	77.89		10,904,748	-	-	2,543,680.52	1,419	55.79	52.88	58.69		0.73	0.69	0.77
18-29 years	5,646,382	21.06%	21.05%	4,290,025.58	608	14.17	13.05	15.30		1,399,146	12.83%	21.05%	267,829.00	21	7.84	4.49	11.19		0.55	0.35	0.84
30-39 years	4,447,250	16.59%	17.31%	3,585,036.36	845	23.57	21.98	25.16		1,381,284	12.67%	17.31%	290,642.00	30	10.32	6.63	14.02		0.44	0.30	0.62
40-49 years	4,330,826	16.15%	15.80%	3,635,600.50	1,436	39.50	37.46	41.54		1,571,363	14.41%	15.80%	338,170.00	64	18.93	14.29	23.56		0.48	0.37	0.61
50-64 years	7,332,848	27.35%	24.66%	6,287,998.12	5,430	86.35	84.06	88.65		3,565,358	32.70%	24.66%	813,652.00	344	42.28	37.81	46.75		0.49	0.44	0.55
65-74 years	3,236,240	12.07%	12.34%	2,723,452.37	3,957	145.29	140.77	149.82		1,843,351	16.90%	12.34%	503,263.00	369	73.32	65.84	80.80		0.50	0.45	0.56
>75 years	1,814,965	6.77%	8.85%	1,575,399.47	4,681	297.13	288.62	305.64		1,144,246	10.49%	8.85%	330,125.00	591	179.02	164.59	193.46		0.60	0.55	0.66
Crude																					
Male Adults	12,779,036	-	-	10,498,567.99	9,248	88.09	86.29	89.88		4,743,163	-	-	1,086,418.17	764	70.32	65.34	75.31		0.80	0.74	0.86
18-29 years	2,827,540	22.13%	22.10%	2,158,737.00	378	17.51	15.75	19.28		569,344	12.00%	22.10%	103,728.00	11	10.60	4.34	16.87		0.61	0.32	1.06
30-39 years	2,162,789	16.92%	17.90%	1,735,525.63	478	27.54	25.07	30.01		577,378	12.17%	17.90%	117,589.00	14	11.91	5.67	18.14		0.43	0.24	0.71
40-49 years	2,101,843	16.45%	16.10%	1,756,811.00	812	46.22	43.04	49.40		681,329	14.36%	16.10%	142,186.00	33	23.21	15.29	31.13		0.50	0.35	0.70
50-64 years	3,479,445	27.23%	24.60%	2,973,051.44	3,140	105.62	101.92	109.31		1,612,913	34.01%	24.60%	358,844.00	222	61.87	53.73	70.00		0.59	0.51	0.67
65-74 years	1,472,467	11.52%	11.80%	1,236,175.60	2,177	176.11	168.71	183.51		830,535	17.51%	11.80%	226,920.00	205	90.34	77.97	102.71		0.51	0.44	0.59
>75 years	734,952	5.75%	7.50%	638,267.32	2,263	354.55	339.95	369.16		471,664	9.94%	7.50%	137,151.00	279	203.42	179.55	227.29		0.57	0.51	0.65
Standardized																					
Male Adults	12,779,036	-	-	10,498,567.99	9,422	89.75	87.91	91.62		4,743,163	-	-	1,086,418.17	537	49.43	45.74	53.50		0.55	0.51	0.60
Crude																					
Female Adults	14,029,475	-	-	11,598,944.41	7,709	66.46	64.98	67.95		6,161,585	-	-	1,457,262.36	655	44.95	41.51	48.39		0.68	0.62	0.73
18-29 years	2,818,842	20.09%	20.10%	2,131,288.58	230	10.79	9.40	12.19		829,802	13.47%	20.10%	164,101.00	10	6.09	2.32	9.87		0.56	0.28	1.02
30-39 years	2,284,461	16.28%	16.80%	1,849,510.73	367	19.84	17.81	21.87		803,906	13.05%	16.80%	173,053.00	16	9.25	4.72	13.78		0.47	0.27	0.75
40-49 years	2,228,983	15.89%	15.50%	1,878,789.50	624	33.21	30.61	35.82		890,034	14.44%	15.50%	195,984.00	31	15.82	10.25	21.39		0.48	0.33	0.67
50-64 years	3,853,403	27.47%	24.70%	3,314,946.67	2,290	69.08	66.25	71.91		1,952,445	31.69%	24.70%	454,808.00	122	26.82	22.06	31.58		0.39	0.32	0.46
65-74 years	1,763,773	12.57%	12.80%	1,487,276.77	1,780	119.68	114.12	125.24		1,012,816	16.44%	12.80%	276,342.00	164	59.35	50.26	68.43		0.50	0.42	0.58
>75 years	1,080,013	7.70%	10.10%	937,132.15	2,418	258.02	247.74	268.31		672,582	10.92%	10.10%	192,973.00	312	161.68	143.74	179.62		0.63	0.56	0.70
Standardized																					
Female Adults	14,029,475	-	-	11,598,944.41	8,015	69.10	67.55	70.68		6,161,585	-	-	1,457,262.36	521	35.78	33.02	38.78		0.52	0.48	0.56

Table 3s: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Stroke, non-hemorrhagic
Pre-COVID (12/01/2018-11/30/2019)

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL		IRR	95% CI LL	95% CI UL
Crude																					
All Adults	26,795,753	-	-	22,055,303.40	60,394	273.83	271.65	276.01		10,890,062	-	-	2,539,459.84	5,674	223.43	217.62	229.25		0.82	0.79	0.84
18-29 years	5,646,345	21.07%	21.05%	4,289,950.52	721	16.81	15.58	18.03		1,399,154	12.85%	21.05%	267,830.00	26	9.71	5.98	13.44		0.58	0.38	0.84
30-39 years	4,446,904	16.60%	17.31%	3,584,088.16	1,774	49.50	47.19	51.80		1,381,083	12.68%	17.31%	290,594.00	77	26.50	20.58	32.42		0.54	0.42	0.67
40-49 years	4,329,725	16.16%	15.80%	3,632,468.88	4,467	122.97	119.37	126.58		1,570,375	14.42%	15.80%	337,953.00	241	71.31	62.31	80.31		0.58	0.51	0.66
50-64 years	7,328,039	27.35%	24.66%	6,273,307.06	19,941	317.87	313.46	322.28		3,560,210	32.69%	24.66%	812,413.00	1,494	183.90	174.57	193.22		0.58	0.55	0.61
65-74 years	3,233,021	12.07%	12.34%	2,712,006.66	15,751	580.79	571.72	589.86		1,839,552	16.89%	12.34%	502,108.00	1,511	300.93	285.76	316.10		0.52	0.49	0.55
>75 years	1,811,719	6.76%	8.85%	1,563,482.12	17,740	1,134.65	1,117.95	1,151.34		1,139,688	10.47%	8.85%	328,562.00	2,325	707.63	678.86	736.39		0.62	0.60	0.65
Crude																					
Male Adults	12,772,891	-	-	10,478,823.74	29,294	279.55	276.35	282.76		4,735,860	-	-	1,084,351.19	2,756	254.16	244.67	263.65		0.91	0.87	0.95
18-29 years	2,827,580	22.14%	22.10%	2,158,818.60	320	14.82	13.20	16.45		569,369	12.02%	22.10%	103,735.00	10	9.64	3.67	15.61		0.65	0.33	1.17
30-39 years	2,162,653	16.93%	17.90%	1,735,235.20	775	44.66	41.52	47.81		577,313	12.19%	17.90%	117,570.00	27	22.96	14.30	31.63		0.51	0.34	0.74
40-49 years	2,101,308	16.45%	16.10%	1,755,416.35	2,086	118.83	113.73	123.93		680,902	14.38%	16.10%	142,090.00	116	81.64	66.78	96.49		0.69	0.57	0.83
50-64 years	3,476,851	27.22%	24.60%	2,965,290.94	10,833	365.33	358.45	372.21		1,610,050	34.00%	24.60%	358,162.00	814	227.27	211.66	242.88		0.62	0.58	0.67
65-74 years	1,470,863	11.52%	11.80%	1,230,552.14	7,953	646.30	632.09	660.50		828,557	17.50%	11.80%	226,330.00	761	336.23	312.35	360.12		0.52	0.48	0.56
>75 years	733,636	5.74%	7.50%	633,510.51	7,327	1,156.57	1,130.09	1,183.05		469,669	9.92%	7.50%	136,463.00	1,028	753.32	707.27	799.37		0.65	0.61	0.69
Standardized																					
Male Adults	12,772,891	-	-	10,478,823.74	29,741	283.82	280.55	287.13		4,735,860	-	-	1,084,351.19	1,863	171.80	165.19	178.77		0.61	0.58	0.63
Crude																					
Female Adults	14,022,862	-	-	11,576,479.66	31,100	268.65	265.66	271.63		6,154,202	-	-	1,455,108.65	2,918	200.53	193.26	207.81		0.75	0.72	0.78
18-29 years	2,818,765	20.10%	20.10%	2,131,131.92	401	18.82	16.97	20.66		829,785	13.48%	20.10%	164,095.00	16	9.75	4.97	14.53		0.52	0.30	0.83
30-39 years	2,284,251	16.29%	16.80%	1,848,852.96	999	54.03	50.68	57.38		803,770	13.06%	16.80%	173,023.00	50	28.90	20.89	36.91		0.53	0.40	0.70
40-49 years	2,228,417	15.89%	15.50%	1,877,052.53	2,381	126.85	121.75	131.94		889,473	14.45%	15.50%	195,863.00	125	63.82	52.63	75.01		0.50	0.42	0.60
50-64 years	3,851,188	27.46%	24.70%	3,308,016.12	9,108	275.33	269.68	280.99		1,950,160	31.69%	24.70%	454,251.00	680	149.70	138.45	160.95		0.54	0.50	0.59
65-74 years	1,762,158	12.57%	12.80%	1,481,454.52	7,798	526.37	514.69	538.06		1,010,995	16.43%	12.80%	275,778.00	750	271.96	252.49	291.42		0.52	0.48	0.56
>75 years	1,078,083	7.69%	10.10%	929,971.61	10,413	1,119.71	1,098.21	1,141.22		670,019	10.89%	10.10%	192,099.00	1,297	675.17	638.43	711.92		0.60	0.57	0.64
Standardized																					
Female Adults	14,022,862	-	-	11,576,479.66	32,537	281.06	277.91	284.24		6,154,202	-	-	1,455,108.65	2,280	156.71	150.97	162.67		0.56	0.54	0.58

Table 3t: Incidence and Incidence Rate Ratios among mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Transverse myelitis

	Pre-COVID (12/01/2018-11/30/2019)									Post-vaccination (12/18/2020 - 06/20/2021)									Incidence Rate Ratio		
	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	Number of patients	Age Distribution	U.S. Census Age Distribution - 2019	Number of person years	Number of patients with an event*	IR per 100,000 person-years	95% CI LL	95% CI UL	IRR	95% CI LL	95% CI UL		
Crude																					
All Adults	26,813,023	-	-	22,111,645.68	493	2.23	2.03	2.43	10,909,014	-	-	2,544,942.11	29	1.14	0.72	1.55	0.51	0.35	0.73		
18-29 years	5,646,612	21.06%	21.05%	4,290,596.58	54	1.26	0.92	1.59	1,399,281	12.83%	21.05%	267,859.00	0	0.00	0.00	1.38	0.00	0.00	0.91		
30-39 years	4,447,527	16.59%	17.31%	3,585,770.49	72	2.01	1.54	2.47	1,381,465	12.66%	17.31%	290,678.00	2	0.69	0.08	2.49	0.34	0.06	1.17		
40-49 years	4,331,282	16.15%	15.80%	3,636,857.85	73	2.01	1.55	2.47	1,571,707	14.41%	15.80%	338,249.00	4	1.18	0.32	3.03	0.59	0.18	1.47		
50-64 years	7,334,438	27.35%	24.66%	6,292,686.82	183	2.91	2.49	3.33	3,566,846	32.70%	24.66%	814,025.00	11	1.35	0.55	2.15	0.46	0.24	0.82		
65-74 years	3,237,199	12.07%	12.34%	2,726,619.17	78	2.86	2.23	3.50	1,844,310	16.91%	12.34%	503,576.00	6	1.19	0.44	2.59	0.42	0.16	0.90		
>75 years	1,815,965	6.77%	8.85%	1,579,114.75	33	2.09	1.38	2.80	1,145,405	10.50%	8.85%	330,555.00	6	1.82	0.67	3.95	0.87	0.33	1.98		
Crude																					
Male Adults	12,781,694	-	-	10,506,498.18	193	1.84	1.58	2.10	4,745,607	-	-	1,087,133.20	15	1.38	0.68	2.08	0.75	0.43	1.24		
18-29 years	2,827,702	22.12%	22.10%	2,159,105.52	23	1.07	0.63	1.50	569,432	12.00%	22.10%	103,748.00	0	0.00	0.00	3.56	0.00	0.00	2.90		
30-39 years	2,162,944	16.92%	17.90%	1,735,965.40	23	1.32	0.78	1.87	577,493	12.17%	17.90%	117,611.00	1	0.85	0.02	4.74	0.64	0.03	3.44		
40-49 years	2,102,122	16.45%	16.10%	1,757,547.92	26	1.48	0.91	2.05	681,541	14.36%	16.10%	142,233.00	2	1.41	0.17	5.08	0.95	0.15	3.41		
50-64 years	3,480,431	27.23%	24.60%	2,975,846.38	71	2.39	1.83	2.94	1,613,793	34.01%	24.60%	359,070.00	7	1.95	0.78	4.02	0.82	0.35	1.69		
65-74 years	1,473,017	11.52%	11.80%	1,237,955.85	34	2.75	1.82	3.67	831,116	17.51%	11.80%	227,109.00	1	0.44	0.01	2.45	0.16	0.01	0.84		
>75 years	735,478	5.75%	7.50%	640,077.12	16	2.50	1.27	3.72	472,232	9.95%	7.50%	137,362.00	4	2.91	0.79	7.46	1.16	0.33	3.30		
Standardized																					
Male Adults	12,781,694	-	-	10,506,498.18	190	1.81	1.56	2.09	4,745,607	-	-	1,087,133.20	12	1.13	0.68	2.08	0.62	0.33	1.12		
Crude																					
Female Adults	14,031,329	-	-	11,605,147.49	300	2.59	2.29	2.88	6,163,407	-	-	1,457,808.92	14	0.96	0.46	1.46	0.37	0.21	0.62		
18-29 years	2,818,910	20.09%	20.10%	2,131,491.07	31	1.45	0.94	1.97	829,849	13.46%	20.10%	164,111.00	0	0.00	0.00	2.25	0.00	0.00	1.32		
30-39 years	2,284,583	16.28%	16.80%	1,849,805.09	49	2.65	1.91	3.39	803,972	13.04%	16.80%	173,067.00	1	0.58	0.01	3.22	0.22	0.01	1.12		
40-49 years	2,229,160	15.89%	15.50%	1,879,309.94	47	2.50	1.79	3.22	890,166	14.44%	15.50%	196,016.00	2	1.02	0.12	3.69	0.41	0.07	1.41		
50-64 years	3,854,007	27.47%	24.70%	3,316,840.45	112	3.38	2.75	4.00	1,953,053	31.69%	24.70%	454,956.00	4	0.88	0.24	2.25	0.26	0.08	0.64		
65-74 years	1,764,182	12.57%	12.80%	1,488,663.32	44	2.96	2.08	3.83	1,013,194	16.44%	12.80%	276,466.00	5	1.81	0.59	4.22	0.61	0.21	1.45		
>75 years	1,080,487	7.70%	10.10%	939,037.63	17	1.81	0.95	2.67	673,173	10.92%	10.10%	193,193.00	2	1.04	0.13	3.74	0.57	0.09	2.15		
Standardized																					
Female Adults	14,031,329	-	-	11,605,147.49	292	2.52	2.24	2.83	6,163,407	-	-	1,457,808.92	12	0.81	0.43	1.09	0.32	0.17	0.57		

Table 4a: Observed to Expected Analysis, mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Myocarditis

Observed vs Expected (OE) assessed time period 3 (12/11/2020 - 06/20/2021) vs time period 1 (12/01/2018- 11/30/2019)	O/E	95% CI LL	95% CI UL	Observed No. of Events	95% CI LL	95% CI UL	Expected No. of Events	Background IR per 100,000 Person- Years (Standardized to Vaccinated Population)	No. Exposed (Vaccinated) Patients*	Time at Risk (Days)
All ages	0.89	0.53	1.38	19	11.13	28.98	21	9.45	10,903,250	7
18-29 years	4.93	2.25	9.36	9	4.50	18.72	2	6.81	1,397,901	7
30-39 years	1.92	0.52	4.91	4	1.04	9.82	2	7.88	1,380,480	7
40-49 years	1.13	0.23	3.30	3	0.69	9.90	3	8.81	1,570,726	7
50-64 years	0.27	0.03	0.96	2	0.24	7.68	8	11.02	3,565,069	7
65-74 years	0.00	0.00	0.92	0	0.00	3.68	4	11.36	1,843,900	7
≥75 years	0.30	0.01	1.68	1	0.03	5.04	3	15.10	1,145,174	7
Males, all ages	1.22	0.67	2.05	14	7.37	22.55	11	12.66	4,742,897	7
18-29 years	6.97	3.01	13.74	8	3.01	13.74	1	10.51	568,832	7
30-39 years	1.70	0.21	6.13	2	0.21	6.13	1	10.66	577,048	7
40-49 years	2.00	0.41	5.84	3	0.82	11.68	2	11.49	681,078	7
50-64 years	0.26	0.01	1.44	1	0.04	5.76	4	12.50	1,612,887	7
65-74 years	0.00	0.00	1.67	0	0.00	3.34	2	13.90	830,914	7
≥75 years	0.00	0.00	2.41	0	0.00	4.82	2	16.88	472,138	7
Females, all ages	0.50	0.16	1.17	5	1.60	11.70	10	8.31	6,160,353	7
18-29 years	1.47	0.04	8.21	1	0.04	8.21	1	4.27	829,069	7
30-39 years	2.20	0.27	7.96	2	0.27	7.96	1	5.89	803,432	7
40-49 years	0.00	0.00	3.20	0	0.00	3.20	1	6.76	889,648	7
50-64 years	0.27	0.01	1.52	1	0.04	6.08	4	9.80	1,952,182	7
65-74 years	0.00	0.00	2.05	0	0.00	4.10	2	9.27	1,012,986	7
≥75 years	0.56	0.01	3.12	1	0.02	6.24	2	13.85	673,036	7

*Number of vaccinated individuals included in the 1-7 day risk window

Table 4b: Observed to Expected Analysis, mRNA-1273 Recipients and Historical Controls Age ≥18, Data through 20 June 2021: Pericarditis

Observed vs Expected (OE) assessed time period 3 (12/11/2020 - 06/20/2021) vs time period 1 (12/01/2018- 11/30/2019)	O/E	95% CI LL	95% CI UL	Observed No. of Events	95% CI LL	95% CI UL	Expected No. of Events	Background IR per 100,000 Person- Years (Standardized to Vaccinated Population)	No. Exposed (Vaccinated) Patients*	Time at Risk
All ages	0.96	0.72	1.26	52	38.88	68.04	54	29.35	10,902,023	7
18-29 years	3.31	1.81	5.56	14	7.24	22.24	4	15.77	1,397,846	7
30-39 years	1.01	0.33	2.36	5	1.65	11.80	5	18.65	1,380,360	7
40-49 years	1.16	0.47	2.39	7	2.82	14.34	6	20.01	1,570,559	7
50-64 years	0.82	0.47	1.33	16	9.40	26.60	20	28.57	3,564,629	7
65-74 years	0.68	0.29	1.34	8	3.48	16.08	12	33.25	1,843,634	7
≥75 years	0.26	0.03	0.93	2	0.24	7.44	8	35.34	1,144,995	7
Males, all ages	1.05	0.7	1.51	29	19.60	42.28	28	29.91	4,742,277	7
18-29 years	4.19	2.01	7.71	10	4.02	15.42	2	21.87	568,790	7
30-39 years	0.39	0.01	2.15	1	0.03	6.45	3	23.39	576,978	7
40-49 years	1.25	0.34	3.20	4	1.02	9.60	3	24.53	680,999	7
50-64 years	1.12	0.56	2.00	11	5.60	20.00	10	31.83	1,612,682	7
65-74 years	0.50	0.10	1.46	3	0.60	8.76	6	37.66	830,777	7
≥75 years	0.00	0.00	1.01	0	0.00	4.04	4	40.17	472,051	7
Females, all ages	0.87	0.55	1.3	23	14.85	35.1	27	21.81	6,159,746	7
18-29 years	2.17	0.59	5.56	4	1.18	11.12	2	11.59	829,056	7
30-39 years	1.70	0.46	4.36	4	0.92	8.72	2	15.25	803,382	7
40-49 years	1.06	0.22	3.10	3	0.66	9.3	3	16.55	889,560	7
50-64 years	0.52	0.17	1.20	5	1.7	12	10	25.87	1,951,947	7
65-74 years	0.87	0.28	2.03	5	1.68	12.18	6	29.63	1,012,857	7
≥75 years	0.48	0.06	1.75	2	0.24	7	4	31.96	672,944	7

*Number of vaccinated individuals included in the 1-7 day risk window