Non-Interventional Study Protocol
B1971066

Effect of Trumenba on Gonococcal Infections in Adolescents and Young Adults in the United States: A Retrospective Cohort Study

Statistical Analysis Plan
(SAP)

Version: 1.0

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1 AMENDMENTS FROM PREVIOUS VERSION(S)

This is an initial SAP

2 INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study B1971066. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment. Note that any text taken directly from the protocol is *italicized*, with exceptions note where it appears.

This study is not a post-authorization safety study (PASS) and is not a commitment to any regulatory authority. This aim of this study is to evaluate the effect of Trumenba (fHbp) vaccine on gonococcal infection among 15-30 years in the United States.

2.1 STUDY DESIGN

This is a retrospective cohort study including individuals 15 to 30 years of age enrolled in a health plan covered by IQVIA PharMetrics® Plus during 1 Jan 2016 to until the latest release of the data (October 2022). The study is to estimate the effect of Trumenba vaccination on the disease of interest, in particular, the gonococcal incidences will be compared between the recipients of Trumenba + MenACWY vaccines and the recipients of MenACWY vaccine.

The exposure cohort will be the individuals who have received at least one dose of Trumenba and at least one dose of MenACWY between 1 January 2016 and 31 December 2021. The non–exposure or reference cohort will be the individuals with no dose of Trumenba but at least one dose of MenACWY vaccine received during the same time period.

The date of index vaccination (zero time) for the exposed cohort is the date of the last dose of Trumenba vaccination, after at least one dose of MenACWY. Trumemba and MenAWCY will be identified by Current Procedural Terminology® (CPT) codes and National Drug Codes (NDC) listed in Appendix Tables 4 and 3, respectively. The index date of the unexposed cohort is the first date of MenACWY vaccination. The diseases of interest are gonococcal infection and chlamydia infections occurring at least 14 days after the zero time. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes listed in Appendix Table 1 and 2 will identify gonococcal and chlamydia infections, respectively. Only the first episode will be considered as the event in case of repeated infections. Individuals will be followed until the earliest occurrence of the following: outcome, at death date (if known), at plan disenrollment or end of study period.

Study population

This is a retrospective cohort study and the study population are adolescents and young adults approximately 15 to 30 years of age at their date of vaccination (calculated based on birth year) and will be identified from administrative claims during 01 January 2016 and 31 December 2021.

Data source

This source of the data for this study will be the health care administrative claims data obtained from the IQVIA PharMetrics® Plus, which is a longitudinal health plan database of adjudicated medical and pharmacy claims, including patient enrollment data for national and sub-national health plans and self-insured employer groups in the United States. Data contributors to the database are largely commercial health plans. It is representative of the commercially insured US national population for patients under 65 years of age. It contains a longitudinal view of inpatient and outpatient services, prescription and office/outpatient administered drugs, costs, and detailed enrollment information. All data are compliant to the Health Insurance Portability and Accountability Act (HIPAA) to protect patient privacy. The database is used in a variety

of life sciences and commercial effectiveness studies. Over 250 peer reviewed publications have used PharMetrics Plus data. There will be more than 500,000 subjects for conducting this study.

2.2 STUDY OBJECTIVES

2.2.1 Primary Objectives

- *To examine the effect of at least one dose of Trumenba on gonococcal infection in adolescents and young adults of 15-30 years in the United States*

2.2.2 Secondary Objectives

- *To examine the effect of at least two doses of Trumenba on gonococcal infection in adolescents and young adults of 15-30 years in the United States*
- *To examine the effect of at least one dose of Trumenba on chlamydial infection in adolescents and young adults of 15-30 years in the United States*
- *To examine the effect of at least two doses of Trumenba on chlamydial infection in adolescents and young adults of 15-30 years in the United States*

2.2.3 Exploratory Objectives

- *To examine the effect of at least one dose of Trumenba on gonococcal infection in adolescents and young adults of 16-23 years in the United States*
- *To examine the effect of at least one dose of Trumenba on gonococcal infection in adolescents and young adults of 15-30 years in the United States at 12 months, 24 months, 36 months and 48 months following the index vaccination*

3 HYPOTHESES AND DECISION RULES

This is an exploratory study, thus no hypothesis will be tested. There will be more than 500,000 individuals in which approximately 15% will be the experimental group. Assming a total of 500,000 subjects, and the probability of failure in the experimental group over the maximum time period of the study is 0.0036 and the probability of failure in the control group over the maximum time period of the study is 0.0048. This provides a power of 94% assuming a hazard ratio of 80% (20% vaccine effectiveness) and at an alpha of 0.05. The calculation was made using "powerSurvEPI" package under RStudio (Version 1.1.453).

3.1 STATISTICAL HYPOTHESES

Not Applicable

3.2 STATISTICAL DECISION RULES

The alpha level will be 0.05, 2-sided. No adjustments for multiple comparisons will be made.

4 ANALYSIS SETS/POPULATIONS

The analysis population will include adolescents and young adults 15 to 30 years of age during 01 January 2016 – 31 December 2021

4.1 FULL ANALYSIS SET

The full analysis data set will consists of all subjects who met all inclusion/exclusion criteria. Any participant who will not meet the inclusion/exclusion criteria will be excluded from the full analysis set.

Inclusion criteria

1. Individuals of approximately 15-30 years old (using July 1 of birth year) enrolled in a health plan available in PharMetrics Plus database during 01 January 2016 and 31 December 2021

2. Individuals having at least one dose of MenACWY during 01 January 2016 and 31 December 2021. MenACWY vaccination will be identified using CPT codes and NDCs listed in Appendix Table 3.

Exclusion criteria

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

1. Individuals having a dose of Trumemba before their first dose of MenACWY during 01 January 2016 and 31 December 2021
2. Individuals having any dose of Bexsero at any time during 01 January 2016 and 31 December 2021. Bexsero vaccination will be identified using CPT codes and NDCs listed in Appendix Table 5.
3. Individuals with missing demographic variables or dates of outcome diagnoses or vaccine administration.

4.2 SAFETY ANALYSIS SET

There are no safety endpoints in this study.

4.3 OTHER ANALYSIS SET

Not applicable

4.4 SUBGROUPS

No subgroup analysis will be performed. However, the vaccine effectiveness will be assessed using several different time points as described in Section 7 (refer to Section 7.2.3.5.1).

5 ENDPOINTS AND COVARIATES

5.1 EFFICACY/EFFECTIVENESS ENDPOINT(S)

5.1.1 Primary Endpoint

- VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients of both Trumenba (at least one dose) and MenACWY (at least one

dose) vaccines and the reciepients of MenACWY vaccine only multiplied by 100, adjusted for age, sex, and US region.

In this analysis, the cases are those who have at least one diagnosis code for gonococcal infection (Appendix Table 1) during follow-up. Each individual will be followed for the outcome from 14 days after their zero time until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

5.2 SAFETY ENDPOINT(S)

No safety endpoints in this study

5.3 OTHER ENDPOINTS

5.3.1 Secondary Endpoint(s)

1. VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 15-30 years) of both Trumenba (at least two doses) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100, adjusted for (age, sex, and US region, as appropriate).

   In this analysis, the cases are those who had at least one diagnosis code of gonococcal infection during follow-up. Each individual will be followed for the outcome from 14 days after their zero time until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

2. VE calculated as 1 minus the hazard ratio for chlamydial infection between the recipients (aged 15-30 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of

MenACWY vaccine only multiplied by 100, adjusted for (age, sex, and US region).

In this analysis, the cases are those who had at least one claim of chlamydial infection in the database. Each individual will be followed for the outcome from 14 days after their zero time until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

3. VE calculated as 1 minus the hazard ratio for chlamydial infection between the recipients (aged 15-30 years) of both Trumenba (at least two doses) and MenACWY (at least one dose) vaccines and the reciepients (aged 15-30 years) of MenACWY vaccine only multiplied by 100, adjusted for age, sex, US region.

   In this analysis, the cases are those who had at least one claim of chlamydial infection in the database. Each individual will be followed for the outcome from 14 days after their zero time until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

5.3.2 Exploratory Endpoints

1. VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 16-23 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 16-23 years) of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables (age, sex, and US region, as appropriate).

   In this analysis, the cases are those who had at least one claim of gonococcal infection in the database. Each individual will be followed until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

2. VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 15-30 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables (age,sex, and US region).

   In this analysis, the cases are those who had at least one claim of gonococcal infection in the database. Each individual will be followed for the outcome from 14 days after their zero time until the end of the follow-up period, censoring the follow-up at death date (if known) or plan disenrollment (if known).

   The analysis will be carried out by different periods of study (zero time to 12 months post zero time, zero time to 24 months post zero time, zero time to 36 months post zero time, and zero time to 48 months post zero time)

5.4 COVARIATES

Variable	Role	Operational definition
Age (years)	Baseline characteristic and potential confounder	Age will be calculated based on the 1st date of Trumenba vaccination for the exposed cohort and the date of the 1st dose of MenACWY for the unexposed cohort
Sex	Baseline characteristic and potential confounder	Sex will be categorized as female and male
US region	Baseline characteristic and potential confounder	US region which is categorized as : E=Northeast S=South MW=Midwest W=West

Variable	Role	Operational definition
		O=Unknown

6 HANDLING OF MISSING VALUES

Analyses will be based on all available data. Participants who have data missing for a certain analysis will be excluded only from that analysis. No imputation for missing values will be performed.

7 STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

7.1 STATISTICAL METHODS

Means, medians, and standard deviations will be provided for continuous variables when performing descriptive analysis of continuous data. Numbers and percentages will be provided for dichotomous and polychotomous variables when performing descriptive analysis of categorical data. Bivariate comparisons of baseline characteristics and outcomes measures will be provided. Appropriate tests (e.g., t-test, chi-square test) will be used based on the distribution of the measure. The cumulative incidence rate for clinical outcomes will be calculated. The incidence rate will be calculated as the number of patients who experience the event divided by the observed time at risk. An unadjusted Kaplan Meier curve will be drawn to illustrate time-to-event.

7.2 STATISTICAL ANALYSES

7.2.1 Primary Endpoint - Effectiveness of trumenba against gonococcal infection.

The primary endpoint is the vaccine effectiveness (VE), to be calculated as 1 minus the hazard ratio for gonococcal infection between the recipients of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables (age, sex and US region, as appropriate).

7.2.1.1 Primary Endpoint - Main Analysis

Vaccination Status

If a participant received at least one dose of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess gonococcal infection that occurred between 14 days after zero time and till end of the study period. We will censor the data at death date (if known), plan disenrollment, or the end of the study period, whichever comes first. In descriptive analyses, we will fit Kaplan-Meier curves. We will also create unadjusted and covariate adjusted Cox proportional hazard regression models with time varying approach verifying first that the proportionality assumption was satisfied for all independent variables. Since the individuals entered into the surveillance at different points of time, we will employ the computing process algorithm of the proportional hazard model where the date of entry and the date of end of follow-up will be used in the model instead of time contribution to compute the hazard ratios.

Hazard ratios (HRs) will be estimated by exponentiation of the coefficient for the vaccine variable in these models, with vaccine effectiveness estimated as (1–HR)×100%. Standard errors (SEs) for the coefficients will be used to estimate p-values and 95% CIs for the HRs. If a covariate does not satisfy the assumption of proportionality, we will exclude the variable for the multivariable model and will perform the stratified analysis using the covariate. Both crude and adjusted VE with its corresponding 95% CI will be calculated.

7.2.1.2 Primary Endpoint – Sensitivity Analysis

In a sensitivity analysis, we will exclude coinfection cases, i.e., individuals with diagnosis codes for gonorrhea and chlamydia within 30 days of one another. Although the case definition will differ from the main analysis, the method of evaluation will be same as the main analysis.

7.3 SAFETY ENDPOINTS

Not applicable

7.4 OTHER ENDPOINTS

7.4.1 Safety Analyses

Not Applicable

7.4.2 Analyses of other endpoints

7.4.2.1 Secondary Endpoint 1 - Effectiveness of trumenba against gonococcal infection.

VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 15-30 years) of both Trumenba (at least two doses) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables.

[redacted]

7.4.2.1.1 Secondary Endpoint 1 - Main Analysis

Vaccination Status

If a participant received at least two doses of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess gonococcal infection that occurred between 14 days after zero time and till end of the study period. The analysis will be performed as written in the Section 7.2.1.1.

7.4.2.2 Secondary Endpoint 2 - Effectiveness of trumenba against chlamydial infection

VE calculated as 1 minus the hazard ratio for chlamydial infection between the recipients (aged 15-30 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables.

7.4.2.2.1. Secondary Endpoint 2 - Main Analysis

Vaccination Status

If a participant received at least one dose of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess chlamydial infection that occurred between 14 days after zero time and till end of the study period. The analysis will be performed same as in Section 7.2.1.1.

7.4.2.3 Secondary Endpoint 3 - Effectiveness of Trumenba against chlamydial infection.

VE calculated as 1 minus the hazard ratio for chlamydial infection between the recipients (aged 15-30 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100 adjusted for potentially confounding variables.

7.4.2.3.1. Secondary Endpoint 3 - Main Analysis

Vaccination Status

If a participant received at least two doses of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess chlamydial infection that occurred between 14 days after zero time and till end of the study period. The analysis will be performed as written in the Section 7.2.1.1.

7.2.3.4. Exploratory Endpoint 1 – Effectiveness of Trumenba against gonococcal infection.

VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 16-23 years) of both Trumenba (at least two doses) and MenACWY (at least one dose) vaccines and the recipients (aged 16-23 years) of MenACWY vaccine only multiplied by 100, adjusted for potentially confounding variables.

7.2.3.4.1. Exploratory Endpoint 1 - Main Analysis

Vaccination Status

If a participant received at least one dose of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess gonococcal infection that occurred between 14 days after zero time and till end of the study period. The analysis will be performed as written in the Section 7.2.1.1.

7.2.3.5. Exploratory Endpoint 2 – Effectiveness of trumenba against gonococcal infection.

VE calculated as 1 minus the hazard ratio for gonococcal infection between the recipients (aged 15-30 years) of both Trumenba (at least one dose) and MenACWY (at least one dose) vaccines and the recipients (aged 15-30 years) of MenACWY vaccine only multiplied by 100 adjusted for potentially confounding variables.

7.2.3.5.1. Exploratory Endpoint 2 - Main Analysis

Vaccination Status

If a participant received at least one dose of Trumenba and at least one dose of MenACWY vaccine will be considered as vaccinated (exposed population).

Analysis

We will assess gonococcal infection that occurred between i) 14 days after zero time and 365 days ii) 14 days after zero time and 730 days, iii) 14 days after zero time and 1095 days, and iv) 14 days after zero time and till end of the study period. The analysis will be performed as written in the Section 7.2.1.1.

7.4.3 Summary of Analyses

Outcome	Analysis Set	Supports Protocol Objective Number	Subgroup	Statistical Method	Covariates/Strata	Missing Data
Gonococcal and chlamydial infections	All patients	All	Gender, age group, and US region, if required	Cox proportional hazard regression	Demographic characteristics, if required.	Excluded
Time to event, days	All patients	All	Same as above	Cox proportional hazard regression	Same as above	Excluded

8 LIST OF TABLES AND TABLE SHELLS

8.1 GENERAL TABLES

Table 1.1 Characteristics of the study population – 15-30 years old

	Total	Group 1			Group 2		
		Exposed cohort with ≥1 dose of Trumemba	Non exposed	P value	Exposed cohort with ≥2 doses of Trumemba	Non exposed	P value
All samples							
Age at vaccination (in years) Mean (SD) Median (Q1, Q3) Min, Max							
Age group (years) 15-17 18-19 20-24 25-30							
US region Northeast South Midwest West Unknown							
Gender Male Female							
Infection Gonococcal only Chlamydia only Co-infection*							

*Both the diseases occurred within 30 days of one another.

The p-values for the continuous variables were determined using Student's t-test (when the data were normally distributed as determined by Shapiro-Wilk test) or Wilcoxon-Mann-Whitney test (when the data were not normally distributed). For the normally distributed data, the p-values were derived from pooled method when the variance was equal and from Satterthwaite approximation when the variance was unequal. For the categorical variables, the p-values were determined by chi-square test (when all the cell values=10) or Fisher's exact test (when any of the cell values <10).

Table 1.2 Characteristics of the study population – 16-23 years old

	Total	Group 1			Group 2		
		Exposed cohort (≥1 dose of Trumemba)	Non exposed	P value	Exposed cohort (≥2 doses of Trumemba	Non exposed	P value
Age at vaccination (in years) Mean (SD) Median (Q1, Q3) Min, Max							
Age group (years) 16-19 20-23							
US region Northeast South Midwest West Unknown							
Gender Male Female							
Infection Gonococcal only Chlamydia only Co-infection*							

*Both the diseases occurred within 30 days of one another.

The p-values for the continuous variables were determined using Student's t-test (when the data were normally distributed as determined by Shapiro-Wilk test) or Wilcoxon-Mann-Whitney test (when the data were not normally distributed). For the normally distributed data, the p-values were derived from pooled method when the variance was equal and from Satterthwaite approximation when the variance was unequal. For the categorical variables, the p-values were determined by chi-square test (when all the cell values=10) or Fisher's exact test (when any of the cell values <10).

8.2 TABLES – PRIMARY AND SECONDARY ENDPOINTS

Table 2.1. Effectiveness of Trumenba in 15-30 Years Old

	Exposed cohort				Non-Exposed cohort				Unadjusted	Adjusted
	No. of persons	Person years	Cases	Incidence/ 100,000/year	No. of persons	Person years	Cases	Incidence/ 100,000/year	VE (95% CI)	VE (95% CI)
≥1 dose of Trumenba										
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Gonococcal infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
≥2 doses of Trumenba										
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Gonococcal infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)

VE calculated as 1 minus the hazard ratio for gonococcal infection between exposed and non-exposed cohort, multiplied by 100

8.3 TABLES – EXPLORATORY ENDPOINTS

Table 3.1. Effectiveness of Trumenba in 16-23 Years Old

	Exposed cohort				Non-Exposed cohort				Unadjusted	Adjusted
	No. of persons	No. of cases	Person-years	Incidence/ 100,000/year	No. of persons	No. of cases	Person-years	Incidence/ 100,000/year	VE (95% CI)	VE (95% CI)
≥1 dose of Trumenba										
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Gonococcal infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
≥2 doses of Trumenba										
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Gonococcal infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)
Chlamydial infection only	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx (xx, xx)	xx (xx, xx)

VE calculated as 1 minus the hazard ratio for gonococcal infection between exposed and non-exposed cohort, multiplied by 100

Table 3.2 Effectiveness of Trumenba in 15-30 Years by Year of Follow-up Among Participants received ≥1 dose of Truumenba

	MenACWY only				TRUMENBA and MenACWY				Unadjusted VE		Adjusted VE	
	No. of persons	No. of cases	Person-years	Incidence/ 100,000/year	No. of persons	No. of cases	Person-years	Incidence/ 100,000/year	VE	95% CI	VE	95% CI
At 12 months of follow-up												
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
At 24 months of follow-up												
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
At 36 months of follow-up												
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
At 48 months of follow-up												
Gonococcal infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx
Chlamydial infection	xx	xx	xxxx	xx.xx	xx	xx	xxxx	xx.xx	xx	xx, xx	xx	xx, xx

VE calculated as 1 minus the hazard ratio for gonococcal infection between exposed and non-exposed cohort, multiplied by 100

9 LIST OF FIGURES

10 APPENDICES

10.1 APPENDIX 1: DATA DERIVATION DETAILS

Age in years will be calculated in years as integer ((Date of vaccination - Date of Birth + 1) /365.25). Since the date of birth is written in year only, we will add July 1 of the year as the data of birth of the individuals.

10.2 APPENDIX 2: ADDITIONAL STATISTICAL METHODOLOGY DETAILS

10.2.1 Procudure for producing the KM Curve

```
Proc lifetest data=ana outtest=test maxtime=2500 outsurv=surv noprint;
time time*event(0); strata exposure/test=logrank;run;
symbol1 i=join c=black v=none;
symbol2 i=join c=red v=none;
title h=1 "Kaplan-Meier Survival Curve of Not Having Gonoccoal Infection";
proc gplot data=surv;
plot survival*time=exposure;
run;
```

10.3 APPENDIX 3: DIAGNOSIS AND PROCEDURE CODES USED IN THE STUDY

Table 1. Diagnosis Codes for Identifying Gonococcal Infections

Code	Type
A540	ICD-10-CM
A5400	ICD-10-CM
A5401	ICD-10-CM

A5402	ICD-10-CM
A5403	ICD-10-CM
A5409	ICD-10-CM
A541	ICD-10-CM
A542	ICD-10-CM
A5421	ICD-10-CM
A5422	ICD-10-CM
A5423	ICD-10-CM
A5424	ICD-10-CM
A5429	ICD-10-CM
A543	ICD-10-CM
A5430	ICD-10-CM
A5431	ICD-10-CM
A5432	ICD-10-CM
A5433	ICD-10-CM
A5439	ICD-10-CM
A544	ICD-10-CM
A5440	ICD-10-CM
A5441	ICD-10-CM
A5442	ICD-10-CM
A5443	ICD-10-CM
A5449	ICD-10-CM
A545	ICD-10-CM
A546	ICD-10-CM
A548	ICD-10-CM
A5481	ICD-10-CM
A5482	ICD-10-CM

A5483	ICD-10-CM
A5484	ICD-10-CM
A5485	ICD-10-CM
A5486	ICD-10-CM
A5489	ICD-10-CM
A549	ICD-10-CM

Table 2. Diagnosis Codes for Identifying Chlamydial Infections

Code	Type
A55	ICD-10-CM
A560	ICD-10-CM
A5600	ICD-10-CM
A5601	ICD-10-CM
A5602	ICD-10-CM
A5609	ICD-10-CM
A561	ICD-10-CM
A5611	ICD-10-CM
A5619	ICD-10-CM
A562	ICD-10-CM
A563	ICD-10-CM
A564	ICD-10-CM
A568	ICD-10-CM
A71	ICD-10-CM
A710	ICD-10-CM
A711	ICD-10-CM
A719	ICD-10-CM

A74	ICD-10-CM
A740	ICD-10-CM
A748	ICD-10-CM
A7481	ICD-10-CM
A7489	ICD-10-CM
A749	ICD-10-CM

Table 3. Current Procedural Terminal Codes and National Drug Codes for Identifying MenACWY Vaccination

Code	Type	Description
90734	CPT	Menactra/Menveo Vaccination
90619	CPT	Menquadfi Vaccine
49281-0589-05	NDC	Menactra Vaccine
46028-0208-01	NDC	Menveo Vaccine
58160-0955-09	NDC	Menveo Vaccine
49281-0589-58	NDC	Menactra Vaccine
49281-0590-58	NDC	Menquadfi Vaccine
46028-0218-11	NDC	Menveo Vaccine
58160-0958-01	NDC	Menveo Vaccine
58160-0959-01	NDC	Menveo Vaccine
46028-0219-11	NDC	Menveo Vaccine
54569-5687-01	NDC	Menactra Vaccine
50090-1890-01	NDC	Menactra Vaccine
49281-0590-05	NDC	Menquadfi Vaccine

Table 4. Current Procedural Terminal Codes and National Drug Codes for Identifying Trumemba (fHbp) Vaccination

Code	Type	Description
90621	CPT	Trumenba Vaccination
00005-0100-01	NDC	Trumenba Vaccine
00005-0100-02	NDC	Trumemba Vaccine
00005-0100-05	NDC	Trumenba Vaccine
00005-0100-10	NDC	Trumenba Vaccine

Table 5. Current Procedural Terminal Codes and National Drug Codes for Identifying Bexsero 4CMenB Vaccination

Code	Type	Description
90620	-CPT	Meningococcal recombinant protein and outer membrane vesicle (OMV) vaccine, serogroup B (MenB-4C), 2 dose schedule, for intramuscular use
46028011401	NDC	Bexsero vaccine
46028011402	NDC	Bexsero vaccine
46028011411	NDC	Bexsero vaccine
58160097602	NDC	Bexsero vaccine
58160097606	NDC	Bexsero vaccine
58160097620	NDC	Bexsero vaccine