Real-World Effectiveness of RSV Vaccines Among Adults Using Target Trial Emulation in Epic Cosmos

First published: 09/11/2026

Last updated: 09/11/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000001151

Study ID

1000001151

DARWIN EU® study

No

Study countries

United States

Study status

Ongoing

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

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Primary lead investigator

Caihua Liang

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 12/12/2025

Actual: 12/12/2025

Study start date

Planned: 22/06/2026

Actual: 22/06/2026

Date of final study report
Planned: 31/01/2028

Sources of funding

- Pharmaceutical company and other private sector

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

C3671094 (Internal sponsor identifier)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Effectiveness study (incl. comparative)

Healthcare resource utilisation

Data collection methods:

Secondary use of data

Study design:

Retrospective NI study using Epic Cosmos EHR data to evaluate RSV vaccine effectiveness in adults. It compares vaccinated and eligible unvaccinated individuals using target trial emulation, matching, and time-to-event analyses.

Main study objective:

1. To evaluate the effectiveness and durability of ABRYSVO® among adults aged 60 years and older against RSV-related ARI hospitalization across RSV seasons
2. To evaluate the effectiveness and durability of ABRYSVO® among adults aged 60 years and older against RSV-related LRTD hospitalization across RSV seasons

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

This is a retrospective, non-interventional (NI) cohort study employing target trial emulation methods using de-identified, structured EHR data from Epic Cosmos. The study will implement sequential emulated trials to compare non-pregnant adult recipients of ABRYSVO® with individuals who have not yet received an RSV vaccine and are eligible at the same calendar time. The primary analysis population will include adults aged ≥60 years, with secondary analyses conducted in the broader population of adults aged ≥18 years. Eligibility criteria, baseline covariates, index dates, and follow-up windows will be aligned across vaccinated and unvaccinated groups to emulate randomization. Vaccine effectiveness will be estimated with both exact matched and propensity score matched cohorts using time-to-event models tailored to the structure of each endpoint and follow-up period. To maintain the emulation framework, matching will be performed 1:1 with replacement, allowing unvaccinated individuals to contribute to multiple sequential trials until the occurrence of an outcome of interest, death, loss to follow-up, receipt of an RSV vaccine, or the end of the study period. Covariate balance will be assessed using standardized mean differences (SMD), and adjustments will be made for any remaining imbalance.

Study drug and medical condition

Medicinal product name

ABRYSVO

Anatomical Therapeutic Chemical (ATC) code

(J07BX05) respiratory syncytial virus vaccines

respiratory syncytial virus vaccines

Population studied

Short description of the study population

The study population will include non-pregnant adults who satisfy the age criteria in the United States with care observed in Epic Cosmos–contributing healthcare systems on or after August 2023. Individuals will be required to have at least one recorded clinical encounter within 1 year prior to cohort entry. Within this population, vaccinated individuals will be identified by documented administration of an RSV vaccine in structured EHR data. Matched unvaccinated comparators will be selected from individuals who have not yet received an RSV vaccine and who meet eligibility criteria at the cohort entry of each trial, aligned to vaccinated individuals within each sequential trial period.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Study design details

Setting

This study will be conducted using de-identified EHR data from Epic Cosmos, a large U.S.-based EHR research network comprising multiple health systems across outpatient, ED, ICU, and inpatient care settings. The study period will span from August 2023 through April 2026, corresponding to the availability of RSV vaccination data within Epic Cosmos and covering the three RSV seasons (2023/2024 through 2025/2026). RSV seasons will be defined primarily using a fixed calendar-based approach, spanning from October 1 to April 30 of the following year for each study season. A sensitivity analysis may also be conducted using alternative definitions of RSV season based on RSV activity patterns, including region-specific approaches to account for geographic variation in RSV circulation, if sufficient sample size permits.

The study population will include non-pregnant adults aged ≥18 years and ≥ 60 years in the United States with care observed in Epic Cosmos, contributing healthcare systems on or after August 2023. Individuals will be required to have sufficient healthcare engagement to ensure adequate data capture and observability within the database. Within this population, vaccinated individuals will be identified by documented administration of an RSV vaccine in structured EHR data. Matched unvaccinated comparators will be selected from individuals who have not yet received an RSV vaccine and who meet all eligibility criteria and remain at risk at the start of each sequential trial, consistent with the TTE framework.

Comparators

Vaccinated individuals will be identified by documented administration of an RSV vaccine in structured EHR data. Matched unvaccinated comparators will be selected from individuals who have not yet received an RSV vaccine and who meet all eligibility criteria and remain at risk at the start of each sequential trial, consistent with the TTE framework.

Outcomes

The primary study outcomes include:

● RSV-related ARI hospitalization

● RSV-related LRTD hospitalization

Secondary outcomes include:

● RSV-related outcome: ARI/LRTD non-inpatient encounter, ARI/LRTD severe outcome, ARI/LRTD critical outcome, CV events with different care settings, thromboembolic event with different care settings, asthma exacerbation with different care settings, COPD exacerbation with different care settings, and pneumonia with different care settings.

● All-cause outcomes: all-cause ARI/LRTD encounter with different care settings, severe outcome, critical outcome, CV events with different care settings, thromboembolic event with different care settings, asthma exacerbation with different care settings, COPD exacerbation with different care settings, pneumonia with different care settings, and dementia (new onset).

Exploratory Outcomes:

● Recurrent healthcare utilization: recurrent inpatient visits, recurrent outpatient visits, recurrent medical visits of any kind

● Development of renal failure (new onset)

● Worsening frailty

● Antibiotic use

● All-cause in-hospital death

Data analysis plan

Continuous variables will be summarized using means/SDs or medians/IQRs, and categorical variables using counts and percentages. Baseline demographics, medical history, and prior vaccination will be summarized by vaccination status and age group. For primary and secondary outcomes, crude incidence rates and event counts will be reported overall and by immunocompromised status and relevant subgroups and clinical severity.

Sequential target trial emulation (TTE) will account for changes in vaccination uptake and RSV circulation. Within each trial, vaccinated and unvaccinated individuals will be matched using exact matching and propensity score matching (PSM). Propensity scores will include baseline demographics, comorbidities, prior healthcare utilization, and other relevant characteristics. Matching will be 1:1 with replacement, allowing unvaccinated individuals to contribute to multiple trials while eligible. Covariate balance will be assessed using standardized mean differences (SMD), with SMD <0.1 indicating adequate balance.

Primary vaccine effectiveness (VE) analyses will include adults aged ≥60 years, with analyses in adults aged ≥18 years considered secondary. Follow-up will be censored at the outcome of interest, death, receipt of an RSV vaccine, end of the study period, or end of the corresponding season, whichever occurs first. VE will be evaluated per season, cumulatively across seasons, and by time since vaccination to assess waning protection. Cox proportional hazards models will be applied within propensity-score-matched cohorts, with adjustment for residual covariate imbalance as needed. Hazard ratios (HRs) and 95% confidence intervals will be reported, and VE calculated as $(1 - HR) \times 100\%$.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

Epic Cosmos database

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction

Data characterisation details

After creation of study variables.