

7 Ottobre 2024

LE INFEZIONI E LE VACCINAZIONI NELL'OSPITE IMMUNOCOMPROMESSO

VIRTUAL EVENT

# Le vaccinazioni nell'ospite immunocompromesso

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DIBIC

Sistema Socio Sanitario
Regione Lombardia
ASST Fatebenefratelli Sacco

UNIVERSITÀ DEGLI STUDI DI MILANO

# Conflict of Interest Disclosure

I have the following conflicts of interest to declare:

I received speaker's honorarium from the following companies:

- Gilead
- VIIV
- MERCK
- MSD
- Sanofi
- Glaxo
- Novartis
- Roche

# Medical specialties utilizing FDA-approved biologics

- cardiovascular disease
- neurology
- rheumatology
- nephrology
- gastroenterology
- dermatology
- ophtalmology
- oncology
- metabolic conditions
- infections
- transplant
- hematology
- pneumology

# Biological and Small Molecule Targeted Immunomodulatory Therapies

- TNF- INHIBITORS
- ANTI-T LYMPHOCYTE THERAPIES
- ANTI-B LYMPHOCYTE ANTIBODIES
- COMBINATION LYMPHOCYTE-DEPLETING AGENTS
- IL-1 PATHWAY INHIBITORS
- DRUGS TARGETING IL-4
- AGENTS TARGETING IL-5 AND IgE
- IL-6-TARGETED AGENTS
- IL-12/IL-23 PATHWAY INHIBITORS IL-17-TARGETED AGENTS
- TYROSINE KINASE INHIBITOR
- JAK INHIBITORS
- BTK INHIBITORS
- PI3K INHIBITORS
- BCR-ABL INHIBITORS
- Syk INHIBITORS
- ALK INHIBITORS
- INTEGRIN INHIBITORS
- IMMUNE CHECKPOINT INHIBITORS
- COMPLEMENT PATHWAY INHIBITORS

# Piano Nazionale della Prevenzione Vaccinale 2023-2025



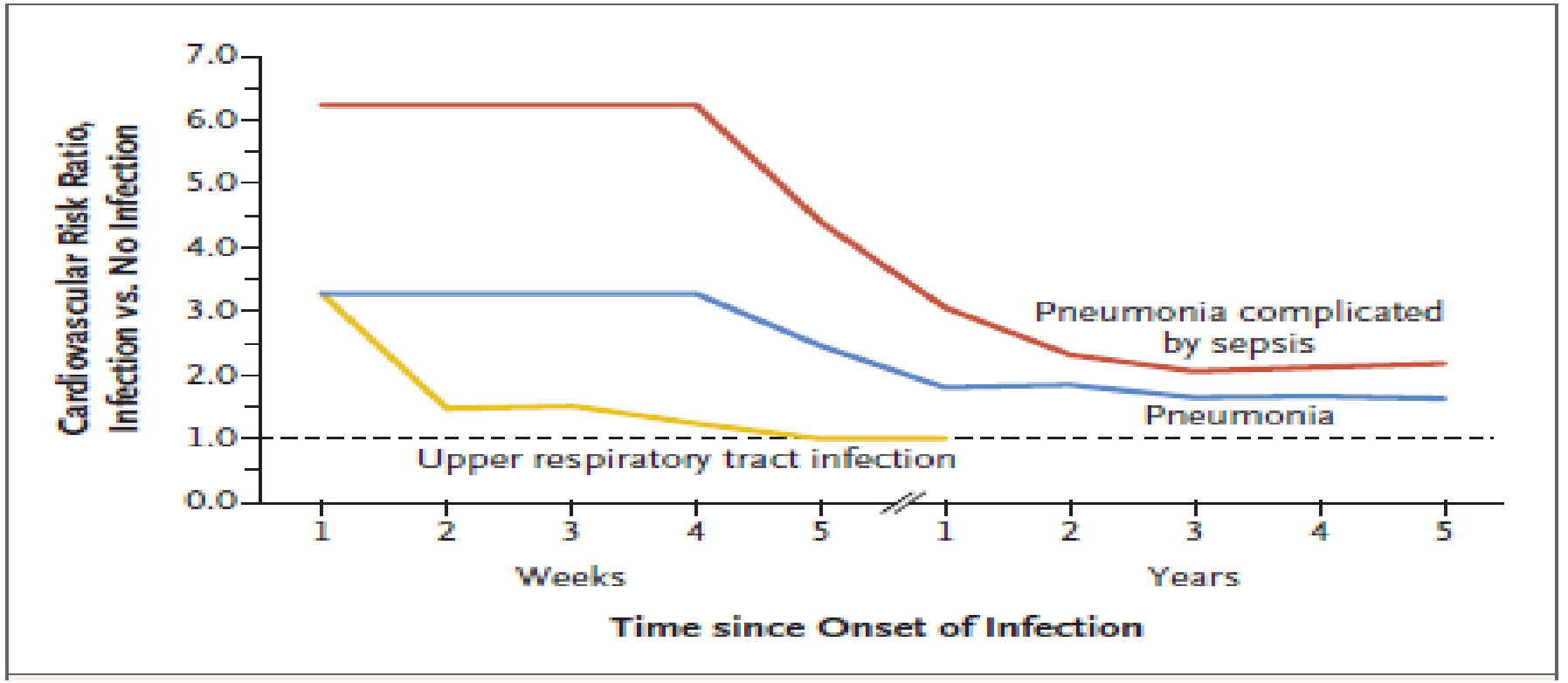



Dan L. Longo, M.D., *Editor*

# Acute Infection and Myocardial Infarction

The NEW ENGLAND JOURNAL of MEDICINE

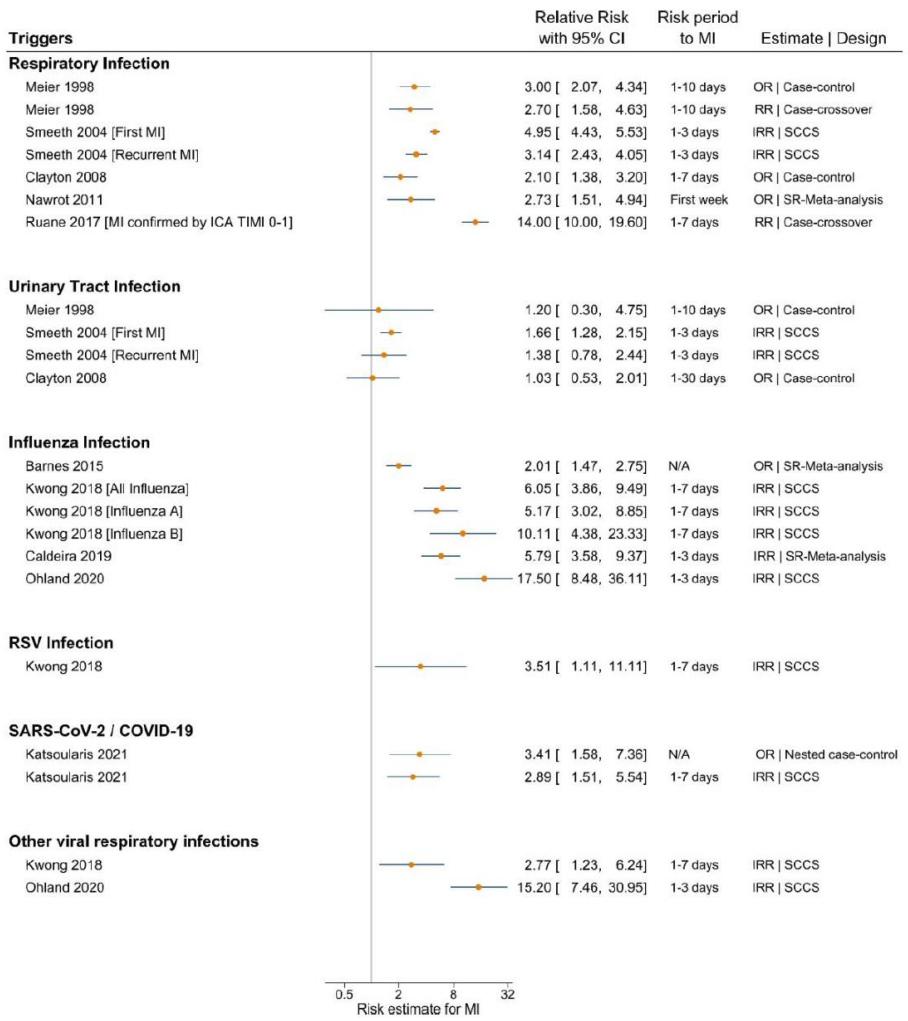
Daniel M. Musher, M.D., Michael S. Abers, M.D.,
and Vicente F. Corrales-Medina, M.D.



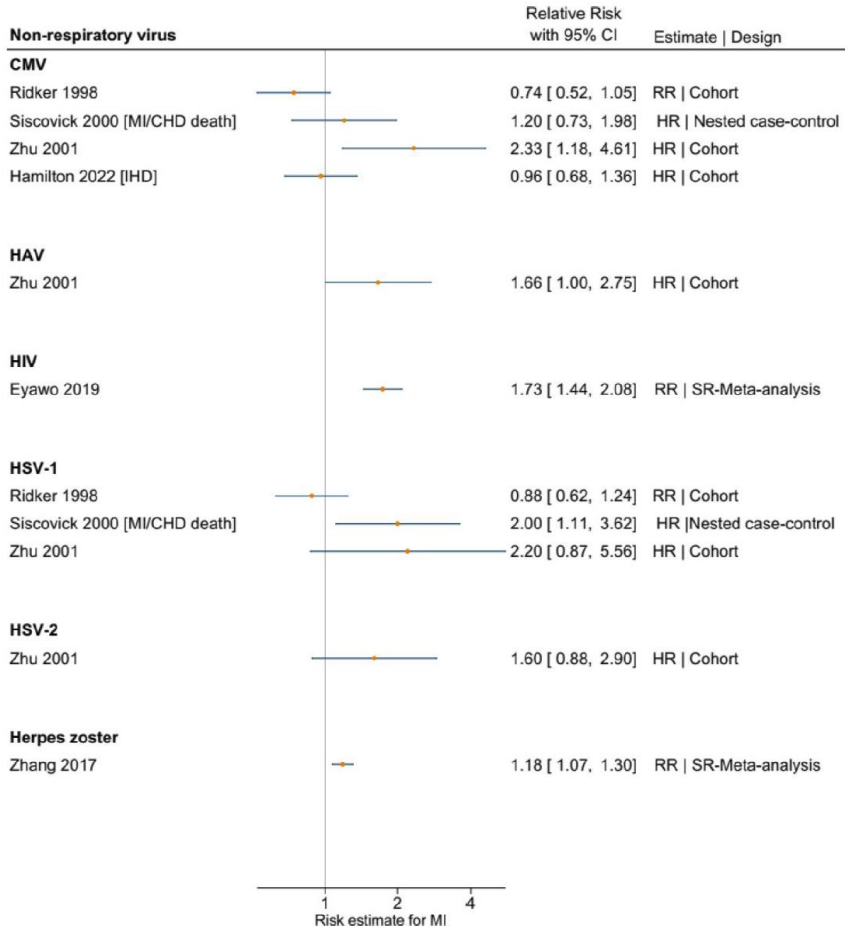

Temporal Pattern of Cardiovascular Risk after the Onset of Acute Infection

Daniel Caldeira and Beatriz Nogueira-Garcia European Heart Journal 2023

# Myocardial infarction and viral triggers




Summary of estimates of the main studies evaluating viral infection and myocardial infarction risk




Summary of estimates of the selected studies evaluating non-respiratory viral infection and myocardial infarction risk, not necessarily as a trigger.

# Influenza Infection and Acute Myocardial Infarction

Relative Incidence of Acute Myocardial Infarction and Influenza Infection: Primary Analysis and Subgroup Analysis

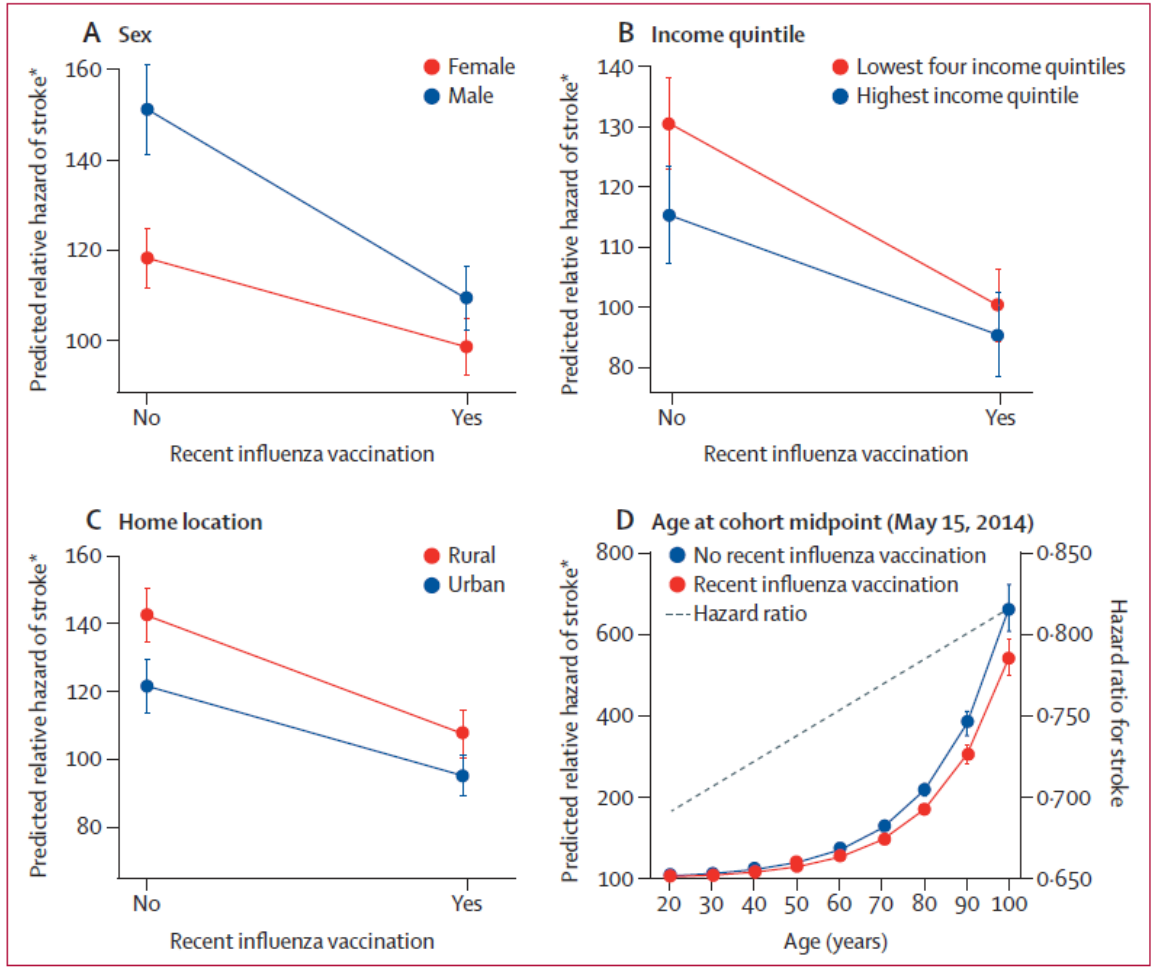
| Analysis | Relative Incidence (95% CI) |
|---|---|
| **Primary analysis: risk period, days 1–7** | 6.16 (4.11–9.24) |
| Days 1–3 | 6.68 (3.76–11.86) |
| Days 4–7 | 5.48 (3.15–9.53) |
| Days 8–14 | 1.96 (0.97–3.95) |
| Days 15–28 | 1.90 (1.13–3.18) |
| Days 1–28 | 3.18 (2.35–4.30) |
| **Subgroup analysis** | |
| History of AMI | |
| Yes | 3.82 (1.21–12.13) |
| No | 6.73 (4.36–10.37) |
| History of CAD | |
| Yes | 1.43 (0.53–3.84) |
| No | 16.60 (10.45–26.37) |
| **Post hoc exploratory analyses** | |
| Antithrombotic medication use | |
| Yes | 4.10 (2.35–7.14) |
| No | 13.50 (7.39–24.70) |
| Preventive cardiovascular medication use | |
| Yes | 4.99 (3.11–8.03) |
| No | 16.13 (7.25–35.91) |
| Age | |
| ≤65 yr | 6.56 (2.87–15.01) |
| >65 yr | 6.05 (3.80-9.62) |
| Sex | |
| Male | 6.03 (3.64–10.00) |
| Female | 6.41 (3.26–12.59) |
| Influenza type | |
| Influenza A | 6.45 (3.75–11.09) |
| Influenza B | 3.72 (1.52–9.09) |
| Time period | |
| 2017 or earlier | 7.81 (4.76–12.81) |
| 2018–2019 | 4.26 (2.10–8.65) |

## Conclusions

Influenza infection was associated with increased risk of acute myocardial infarction, especially in individuals without a prior admission for coronary artery disease

Annemarijn R. de Boer et al. NEJM Evid 2024

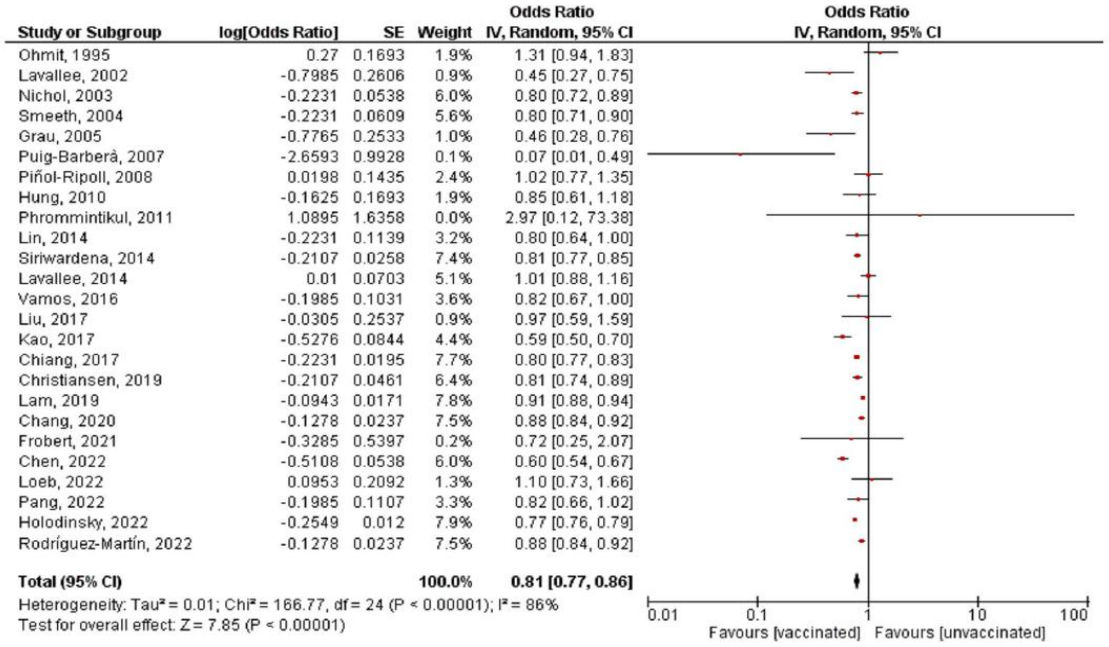
# Association between influenza vaccination and risk of stroke in Alberta, Canada: a population-based study




Interaction plots of the effects of demographic covariates and influenza vaccination on stroke risk

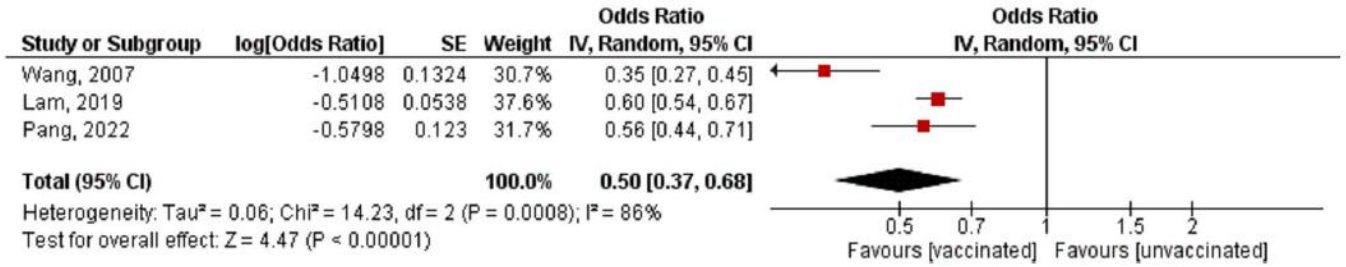
Jessalyn K Holodinsky et al, Lancet Public Health 2022

# Influenza vaccine effect on risk of stroke occurrence: a systematic review and meta-analysis



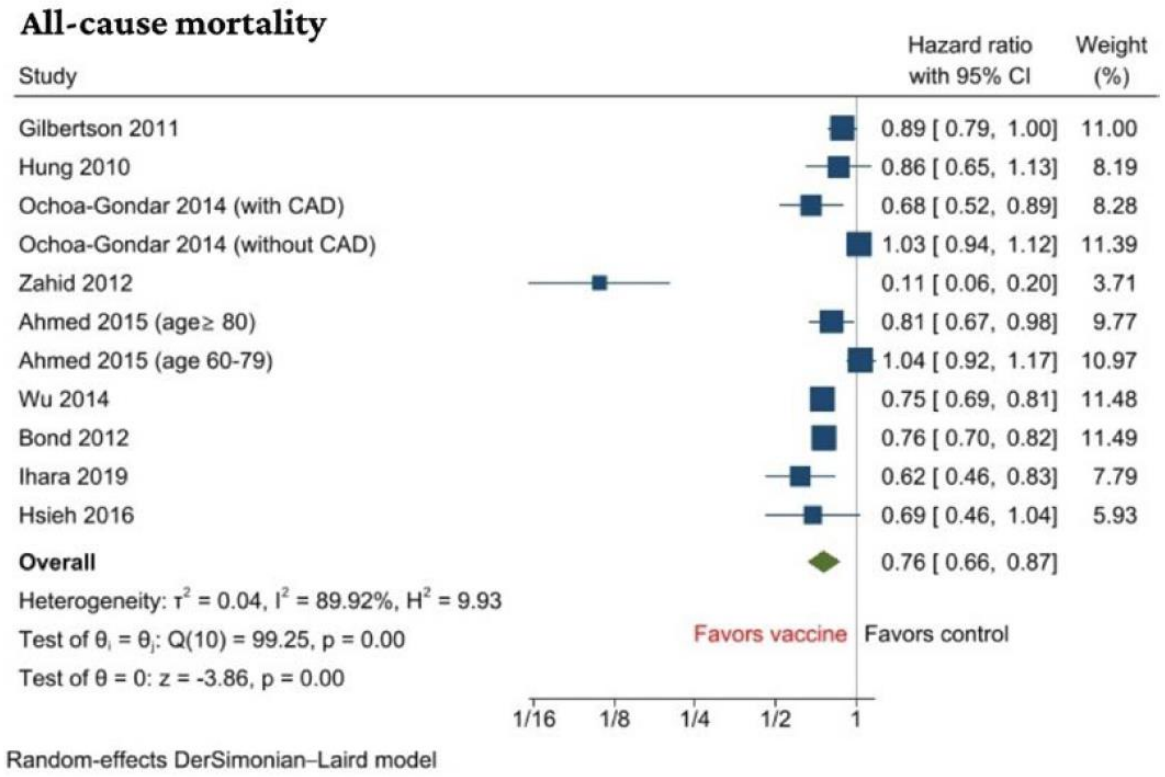

Forest plot showing the effectiveness of influenza vaccine on stroke incidence/hospitalization

Forest plot showing the effectiveness of influenza vaccine on mortality in stroke patients

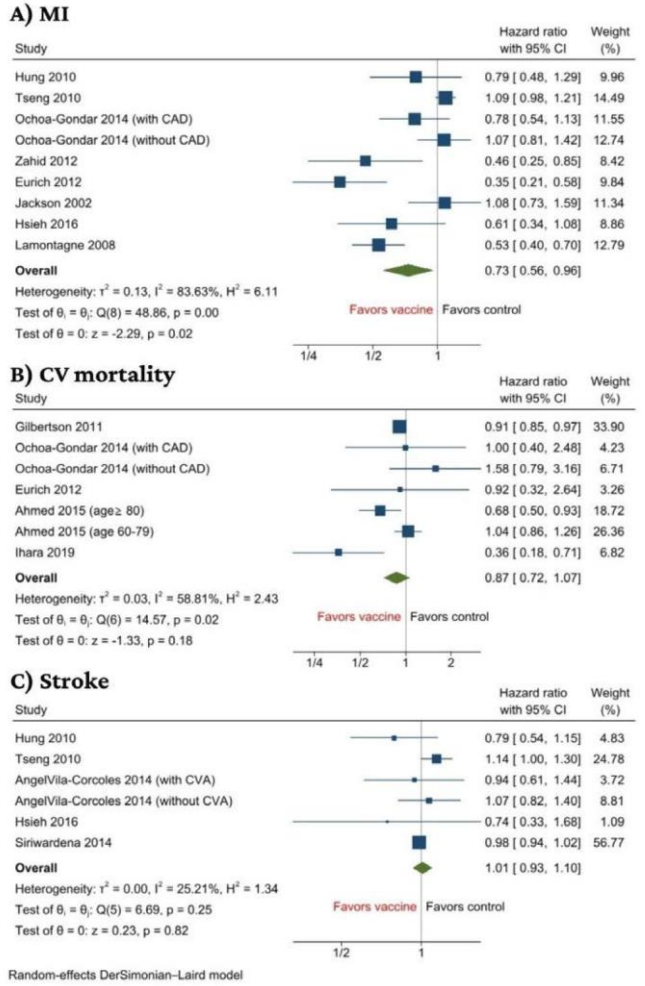



Zahhar JA, et al. 2024. *Front. Neurol.*

# Effect of Pneumococcal Vaccine on Mortality and Cardiovascular Outcomes: A Systematic Review and Meta-Analysis




Forest plot of primary outcome: all-cause mortality




Forest plot of secondary outcomes including MI, CV mortality, and stroke

# Increased Stroke Risk Following Herpes Zoster Infection and Protection With Zoster Vaccine

| Variable | PCP (2 093 594) | Zoster (71 911) | *P* Value |
|---|---|---|---|
| Age, mean ± SD | 68.8 ± 13.2 | 71.1 ± 12.4 | <.0001 |
| Male sex | 1 929 083 (92.14) | 65 645 (91.29) | <.0001 |
| Recombinant zoster vaccine | 126 111 (6.02) | 1592 (2.21) | <.0001 |
| Live zoster vaccine | 190 378 (9.09) | 6839 (9.51) | .0001 |
| COPD | 175 533 (8.38) | 5156 (7.17) | <.0001 |
| CVA (history of) | 81 822 (3.91) | 2255 (3.14) | <.0001 |
| Dementia | 37 323 (1.78) | 1049 (1.46) | <.0001 |
| Diabetes without complications | 329 458 (15.74) | 8000 (11.12) | <.0001 |
| Diabetes with complications | 124 641 (5.95) | 3154 (4.39) | <.0001 |
| Heart failure | 93 194 (4.45) | 2654 (3.69) | <.0001 |
| HIV | 4920 (0.24) | 253 (0.35) | <.0001 |
| Liver disease (mild) | 68 042 (3.25) | 1459 (2.03) | <.0001 |
| Liver disease (severe) | 4354 (0.21) | 111 (0.15) | .0018 |
| Metastatic cancer | 18 201 (0.87) | 505 (0.70) | <.0001 |
| MI | 14 572 (0.70) | 413 (0.57) | .0001 |
| PVD | 89 163 (4.26) | 2371 (3.3) | <.0001 |
| Paralysis | 7475 (0.36) | 186 (0.26) | <.0001 |
| Renal disease | 132 973 (6.35) | 3783 (5.26) | <.0001 |
| Rheumatoid arthritis | 16 607 (0.79) | 703 (0.98) | <.0001 |
| Solid tumor | 139 680 (6.67) | 4073 (5.66) | <.0001 |

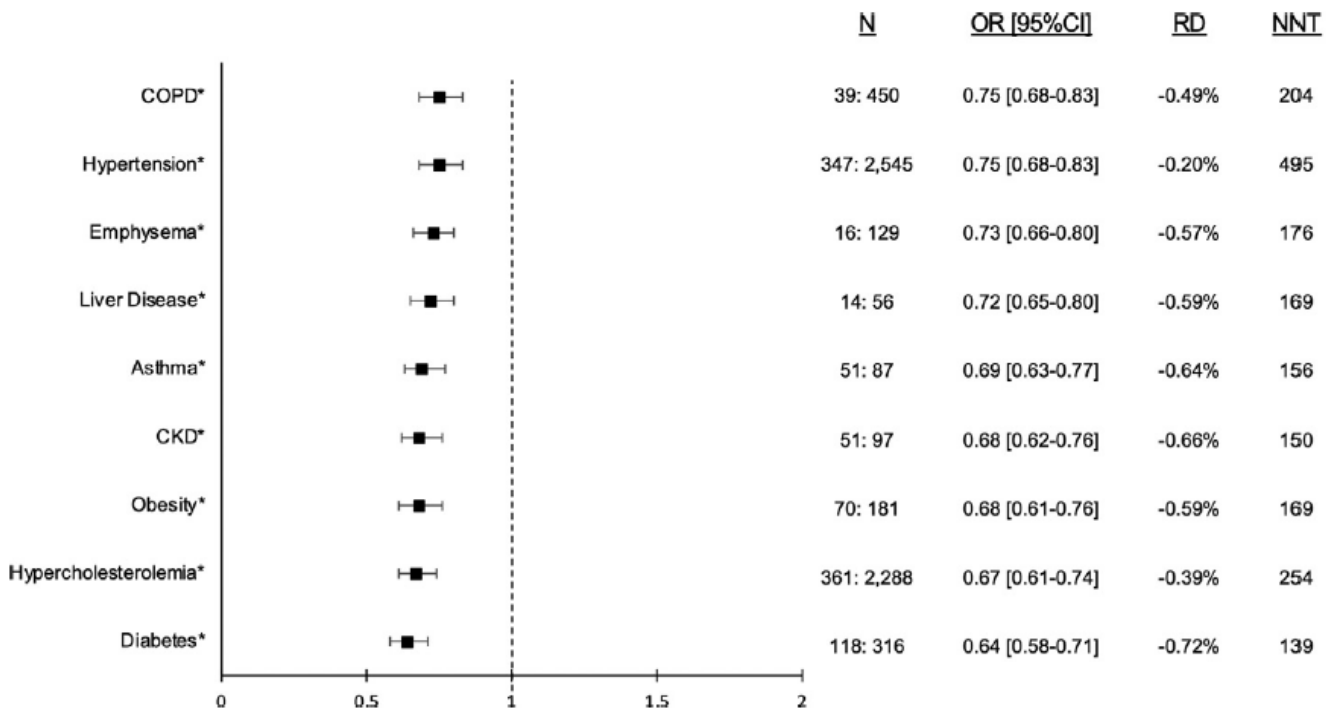
| Variable | OR | (95% CI) | *P* Value |
|---|---|---|---|
| Age | 1.008 | (1.004–1.01) | .0001 |
| Male sex | 1.34 | (1.05–1.7) | .0165 |
| Recombinant zoster vaccine | 0.57 | (.46–.72) | <.0001 |
| Live zoster vaccine | 0.77 | (.65–.91) | .0020 |
| PVD | 0.79 | (.66–.94) | .0092 |
| CVA | 35.3 | (32.0–38.9) | <.0001 |
| Dementia | 1.29 | (1.05–1.59) | .0148 |
| Solid tumor | 0.81 | (.68–.98) | .0313 |
| Zoster | 1.93 | (1.57–2.4) | <.0001 |

Abbreviations: CI, confidence interval; CVA, cerebrovascular accident; OR, odds ratio; PVD, peripheral vascular disease.

Multivariable Analysis for Odds of Stroke 30 Days Postevent

Ganapathi Iyer Parameswaran et al. 2023, Clinical Infectious Diseases

# Zoster Vaccine Lowers Stroke and Myocardial Infarction Risk in Chronic Disease




Risk of stroke for vaccinated persons by comorbid indications

| Predictor | OR [95% CI] | *p*-Value |
|---|---|---|
| Model: Stroke (n=3,420) | | |
| Vaccination | 0.67 [0.60-0.75] | **<0.001** |
| Hypertension | 3.10 [2.82-3.42] | **<0.001** |
| DM | 1.42 [1.27-1.60] | **<0.001** |
| Obesity | 0.94 [0.81-1.09] | 0.41 |
| Hypercholesterolemia | 1.70 [1.56-1.85] | **<0.001** |
| CKD | 2.05 [1.71-2.47] | **<0.001** |
| COPD | 1.93 [1.73-2.15] | **<0.001** |
| Emphysema | 1.66 [1.38-2.00] | **<0.001** |
| Asthma | 1.12 [0.94-1.35] | 0.21 |
| Chronic Liver Disease | 1.57 [1.23-2.01] | **<0.001** |
| Model: MI (n=2,815) | | |
| Vaccination | 0.66 [0.58-0.74] | **<0.001** |
| Hypertension | 4.11 [3.63-4.66] | **<0.001** |
| DM | 1.07 [0.94-1.22] | 0.33 |
| Obesity | 1.14 [0.98-1.33] | 0.10 |
| Hypercholesterolemia | 2.89 [2.58-3.22] | **<0.001** |
| CKD | 2.20 [1.81-2.67] | **<0.001** |
| COPD | 2.61 [2.34-2.91] | **<0.001** |
| Emphysema | 1.49 [1.22-1.81] | **<0.001** |
| Asthma | 0.86 [0.68-1.07] | 0.17 |
| Chronic Liver Disease | 1.66 [1.28-2.15] | **<0.001** |

Multiariable Logistic Regression Models Predicting Stroke and MI

Helm et al / Am J Prev Med 2024

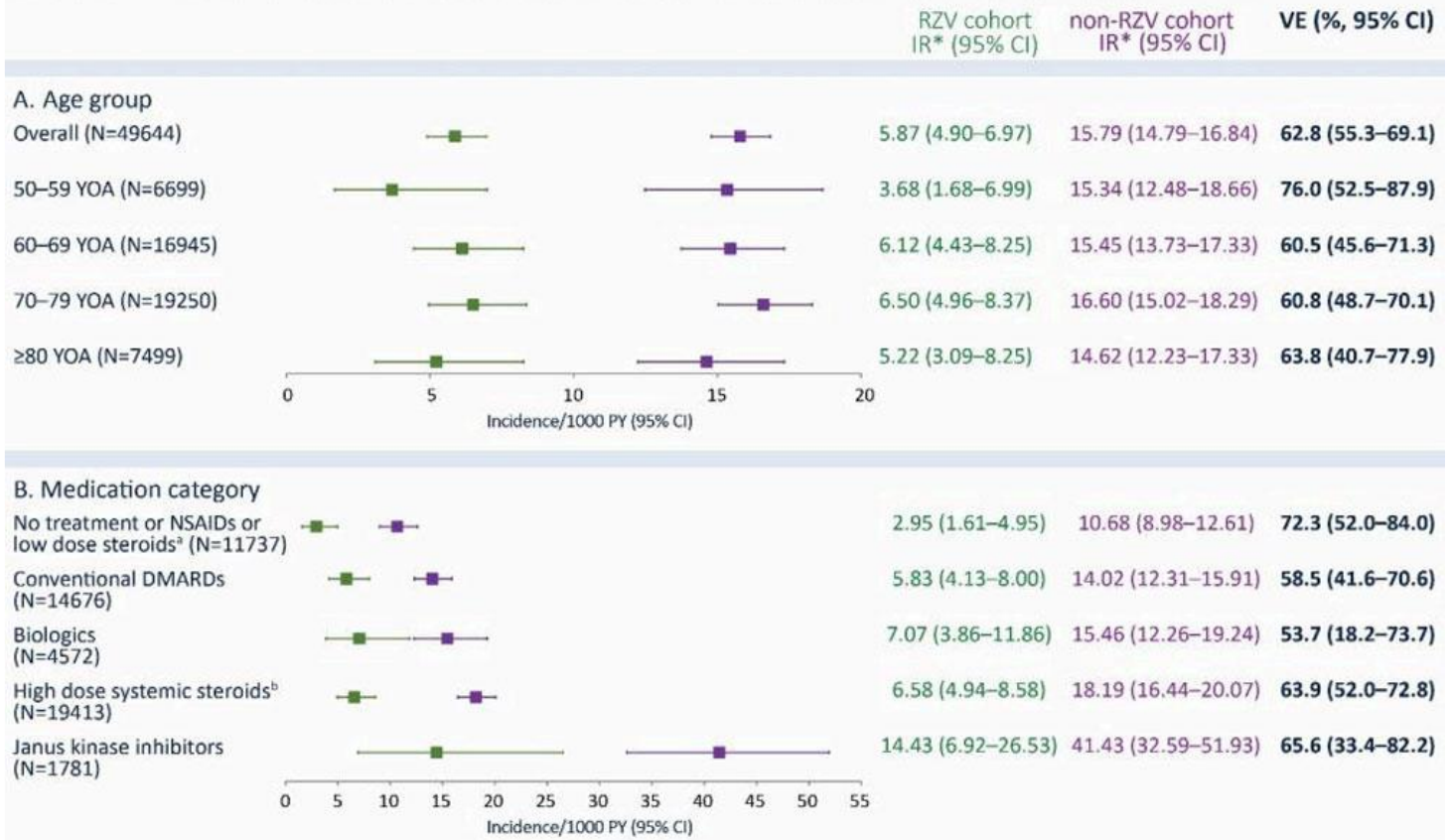
# Disease activities before and after RZV administration

| | 0 month | 3 months | 6 months | P value |
|---|---|---|---|---|
| DAS28-CRP, median (IQR) | | | | |
| csDMARDs (n=20) | 1.3 (1.2–2.3) | 1.5 (1.2–2.0) | 1.3 (1.2–2.1) | 0.947 |
| bDMARDs (n=23) | 1.5 (1.1–1.9) | 1.5 (1.2–2.2) | 1.3 (1.1–2.0) | 0.546 |
| tsDMARDs (n=10) | 1.3 (1.1–2.7) | 1.7 (1.4–2.6) | 1.4 (1.2–2.8) | 0.187 |
| CDAI, median (IQR) | | | | |
| csDMARDs (n=20) | 1.9 (0.3–4.9) | 1.6 (0.9–3.9) | 1.6 (0.6–5.7) | 0.899 |
| bDMARDs (n=23) | 2.4 (1.0–5.5) | 2.2 (0.8–5.3) | 2.0 (0.6–5.4) | 0.858 |
| tsDMARDs (n=10) | 2.0 (1.1–5.6) | 3.9 (1.9–7.3) | 3.2 (0.9–8.7) | 0.329 |

Kojima S, *et al*. *RMD Open* 2024

# RZV effectiveness data in RA patients above 50 YOA

**Figure.** IRs of HZ and VE overall and stratified by age and medication category (2-dose cohort)




**IR**, incidence rate; **HZ**, herpes zoster; **VE**, vaccine effectiveness; **YOA**, years of age; **RZV**, adjuvanted recombinant zoster vaccine; **CI**, confidence interval; **PY**, person-years; **NSAID**, nonsteroidal anti-inflammatory drug; **DMARD**, disease-modifying anti-rheumatic drug.

[a]all <5 mg or equivalent; [b]any ≥5 mg prednisone or equivalent.

*IR was defined as the incidence/1000 PY.

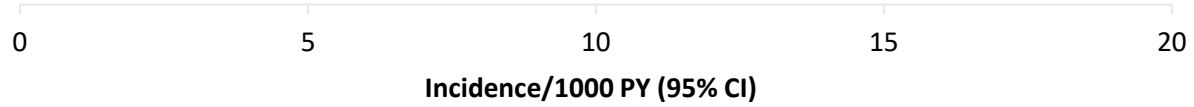
# RZV effectiveness data in RA patients above 50 YOA

EPI-ZOSTER- 097

Patients aged ≥50 years with RA who received 2 doses of RZV, ≥28 days apart, were matched 1:3 to unvaccinated counterparts by age, medication category, and other confounders

IRs of HZ and overall VE stratified by age (2-dose cohort)

| Age Group | RZV Cohort IR (95% CI) | Non-RZV Cohort IR* (95% CI) | VE (%, 95% CI) |
|---|---|---|---|
| **Overall (N=49,644)** | 5.87 (4.90–6.97) | 15.79 (14.79–16.84) | 62.8 (55.3–69.1) |
| **50–59 years (N=6699)** | 3.68 (1.68–6.99) | 15.34 (12.48–18.66) | 76.0 (52.5–87.9) |
| **60–69 years (N=16,945)** | 6.12 (4.43–8.25) | 15.45 (13.73–17.33) | 60.5 (45.6–71.3) |
| **70–79 years (N=19,250)** | 6.50 (4.96–8.37) | 16.60 (15.02–18.29) | 60.8 (48.7–70.1) |
| **≥80 years (N=7499)** | 5.22 (3.09–8.25) | 14.62 (12.23–17.33) | 63.8 (40.7–77.9) |




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IR was defined as incidence/1000PY.

HZ, herpes zoster; IR, incidence rate; N, number of patients in each cohort; PY, person-year; RA, rheumatoid arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; YOA, years of age

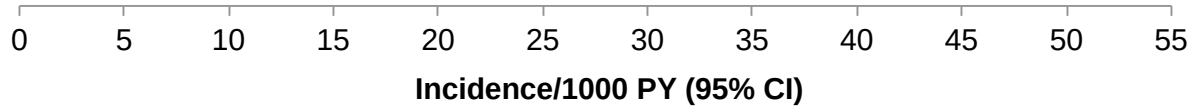
Constenla D, et al. EULAR 2024; Vienna, Austria. Abstract 2950.

# RZV effectiveness data in RA patients above 50 YOA

EPI-ZOSTER- 097

## IRs of HZ and overall VE stratified by medication category (2-dose cohort)

| Medication Category | RZV Cohort IR* (95% CI) | Non-RZV Cohort IR* (95% CI) | VE (%, 95% CI) |
|---|---|---|---|
| No treatment or NSAIDs or low-dose steroids† (N=11,737) | 2.95 (1.61–4.95) | 10.68 (8.98–12.61) | 72.3 (52.0–84.0) |
| Conventional DMARDs (N=14,676) | 5.83 (4.13–8.00) | 14.02 (12.31–15.91) | 58.5 (41.6–70.6) |
| Biologics (N=4572) | 7.07 (3.86–11.86) | 15.46 (12.26–19.24) | 53.7 (18.2–73.7) |
| High-dose systemic steroids‡ (N=19,413) | 6.58 (4.94–8.58) | 18.19 (16.44–20.07) | 63.9 (52.0–72.8) |
| Janus kinase inhibitors (N=1781) | 14.43 (6.92–26.53) | 41.43 (32.59–51.93) | 65.6 (33.4–82.2) |




**RZV vaccination was found to be effective in preventing HZ in this population having an increased risk of HZ with associated complications due to age and immunosuppressive therapy**

The table has been reproduced from Constenla D, et al, with permission from the author.

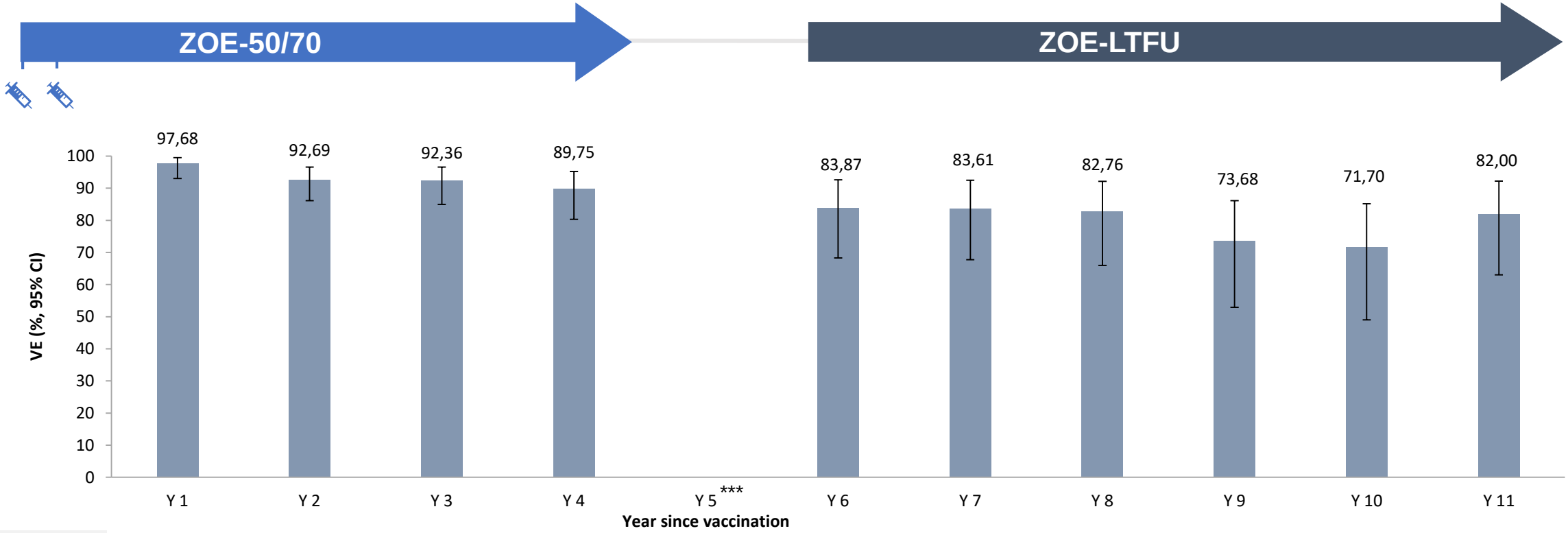
IR was defined as incidence/1000PY; †All <5 mg prednisone or equivalent; ‡Any ≥5 mg prednisone or equivalent.

DMARD, disease-modifying anti-rheumatic drug; HZ, herpes zoster; IR, incidence rate; N, number of patients in each cohort; NSAID, nonsteroidal anti-inflammatory drug; PY, person-year; RA, rheumatoid arthritis; RZV, recombinant zoster vaccine; VE, vaccine effectiveness; YOA, years of age

Constenla D, et al. EULAR 2024; Vienna, Austria. Abstract 2950.

# Annual VE of RZV against HZ in participants ≥50 YOA at vaccination pooled ZOE-50/70 and mTVC-LTFU and Control group)

(mTVC




| | Y 1 | Y 2 | Y 3 | Y 4 | Y 5 | Y 6 | Y 7 | Y 8 | Y 9 | Y 10 | Y 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **n/N (RZV*)** | 3/13,881 | 10/13,569 | 9/13,185 | 10/12,757 | | 10/7258 | 10/7083 | 10/6857 | 15/6627 | 15/6239 | 9/5849 |
| **n/N† (Placebo or HC**)** | 130/14,035 | 136/13,564 | 116/13,074 | 95/12,517 | | 62/7258 | 61/7083 | 58/6857 | 57/6627 | 53/6239 | 50/5849 |

- This graph has been independently created by GSK.

CI, confidence intervals; HC, historical controls; HZ, herpes zoster; mTVC, modified total vaccinated cohort (participants receiving 2 doses without confirmed HZ within 30 days post-dose 2); N, number of individuals included in each group; n, number of individuals having at least 1 confirmed HZ episode; LTFU, long-term follow-up; RZV, recombinant zoster vaccine; VE, vaccine efficacy; Y, year; YOA, years of age. $ ; Randomized Control group in ZOE-LTFU for revaccination with 1 or 2 additional doses of RZV and does NOT refer to historical controls used for VE assessment. ^ In ZOE-LTFU, VE analysis against first or only HZ episode was descriptive and conducted in mTVC using Poisson regression. * Participants from RZV group in ZOE-50/70 were used for year 1–4 and participants from ZOE-LTFU follow-up and the Control group in ZOE-LTFU were used for Year 6 onwards. ** Participants from the Placebo groups in ZOE-50/70 were used for year 1–4 and participants in Placebo groups in ZOE-50/70 were used to form the historical control data for Year 6 onwards in ZOE-LTFU. VE estimates were adjusted for region. *** Gap between ZOE-50/70 and ZOE-LTFU, VE was not estimated in Y5. † N and years of follow-up assumed to be the same as for RZV group over ZOE-LTFU study (Y6 onwards).



Strezova A, et al. ECCMID 2024; Barcelona, Spain. Abstract number: 09154.

# Safety of the Zoster Vaccine Recombinant Adjuvanted in Rheumatoid Arthritis and Other Systemic Rheumatic Disease Patients

| Baseline Patient Characteristics | Results |
|---|---|
| Age, mean (SD), y | 67.3 (10.6) |
| Females, n (%) | 302 (74.9) |
| White, n (%) | 345 (85.6) |
| Received second vaccine, n (%) | 222 (55.1) |
| Time between first and second vaccine, mean (SD), wk | 18.3 (8.5) |
| Patients with RA, n (%) | 239 (59.3) |
| Patients with SRD,a n (%) | 164 (40.7) |
| Medications | |
| On any immunosuppressant medication, n (%) | 316 (78.4) |
| MTX, n (%) | 143 (35.5) |
| Mean MTX dose, mg/wk | 17.1 |
| MTX dose, median (IQR), mg/wk | 20 (15-25) |
| Prednisone, n (%) | 106 (26.3) |
| Mean prednisone dose, mg/d | 4.7 |
| Prednisone dose, median (IQR), mg/d | 5 (4–8) |
| Tofacitinib, n (%) | 52 (12.9) |
| TNF inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), n (%) | 105 (26.1) |
| Other biologic therapy (abatacept, belimumab, tocilizumab, rituximab, sarilumab), n (%) | 49 (12.2) |
| Other immunosuppressants (azathioprine, cyclophosphamide, mycophenolic acid, leflunomide), n (%) | 49 (12.2) |

Baseline characteristics of 403 study subjects

| Patients Who Experienced Flares | Flare Rate |
|---|---|
| After first dose, n (%) | 23 (5.7) |
| After second dose, n (%) | 5 (2.3) |
| After both, n (%) | 1 (0.2) |
| Patients with RA, n (%) | 19 (5.0) |
| Patients with SRD, n (%) | 9 (3.6) |
| First 110 patients called by nurse, n (%) | 3 (2.7) |

Flare rate of 403 study subjects at a single-center investigation of the safety of the zoster vaccine recombinant

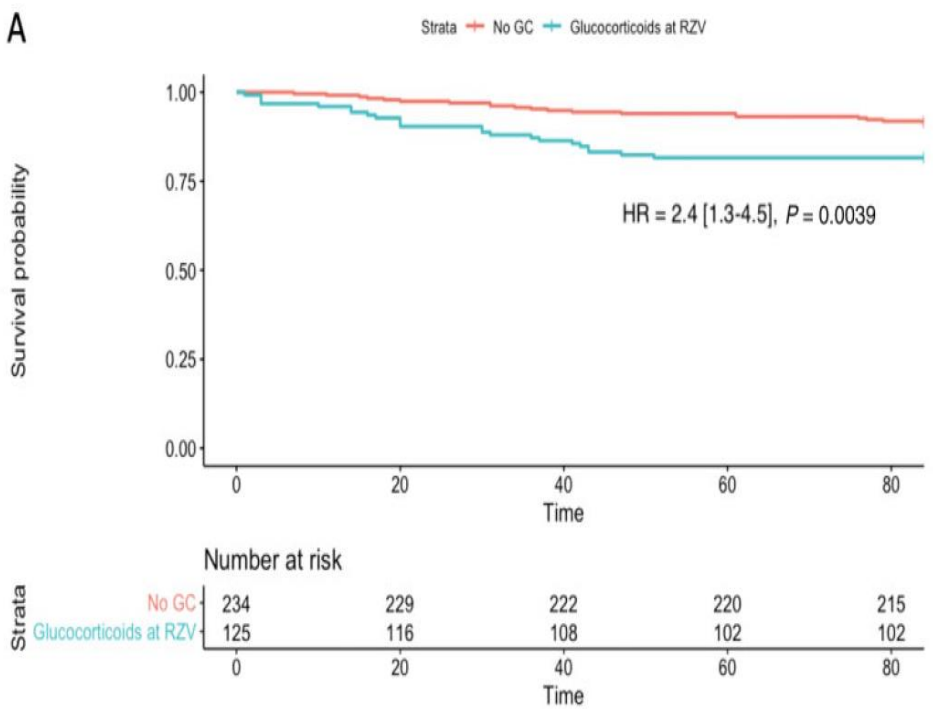
Emma Stevens et al. ACR Open Rheumatology 2020

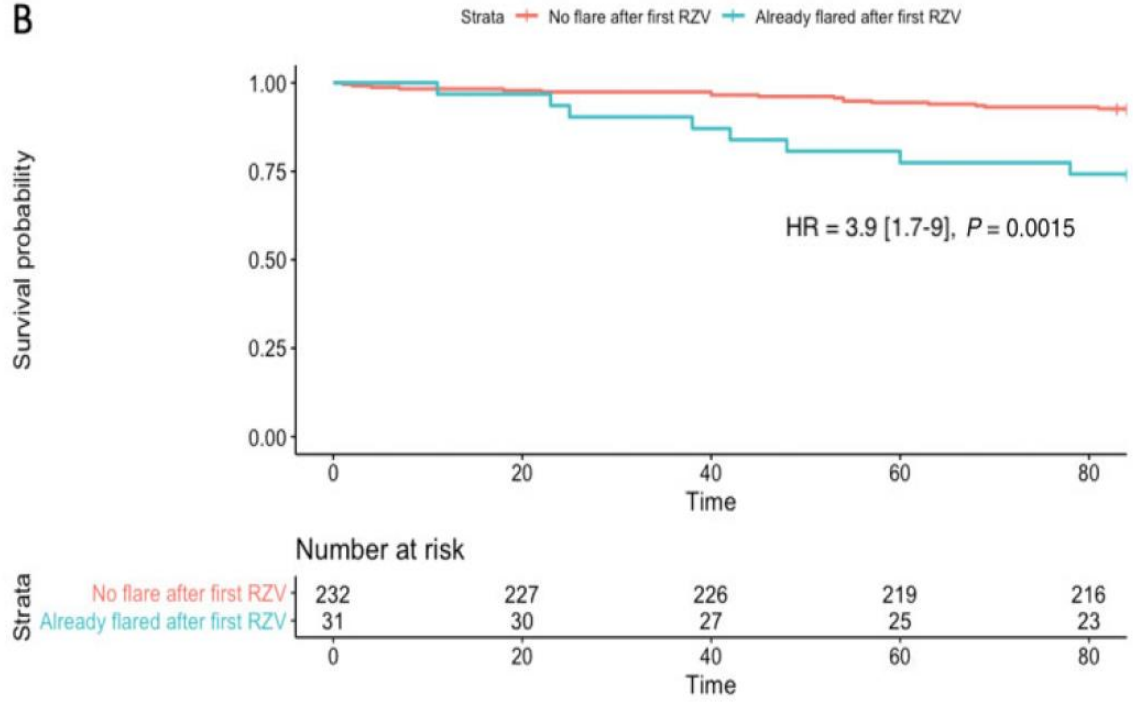
# Safety of recombinant zoster vaccine: a retrospective study of 622 rheumatology patients

| | No flare ($n = 300$) | Flare ($n = 59$) | Univariate analysis | Multivariate analysis adjusted for significant factors | |
|---|---|---|---|---|---|
| | | | *P*-value | Adjusted OR [IC95%] | *P*-value |
| Median age (years) | 67 | 67 | 0.962 | | |
| Gender (female) | 66% | 63% | 0.592 | | |
| Ethnicity (white) | 84% | 86% | 0.445 | | |
| RA (*vs* others) | $n = 67$ 22% | $n = 21$ 36% | **0.030** | 1.57 [0.8, 2.98] | 0.173 |
| Treatment at RZV | | | | | |
| Glucocorticoids | 31% | 53% | **0.002** | **2.31 [1.3, 4.1]** | **0.004** |
| Jak-inhibitors | 4% | 10% | **0.032** | 2.09 [0.64, 6.34 | 0.203 |
| HCQ | 21% | 25% | 0.416 | | |
| MTX | 22% | 25% | 0.565 | | |
| TNF inhibitors | 14% | 17% | 0.509 | | |
| Other biologic | 12% | 15% | 0.539 | | |
| Other immunosuppressant | 14% | 19% | 0.358 | | |
| Baseline laboratory findings | | | | | |
| Elevated CRP ($n = 270$) | 14% | 11% | 0.631 | | |
| Median CRP (mg/dl) | 0.3 | 0.4 | 0.597 | | |
| Elevated ESR ($n = 227$) | 31% | 28% | 0.710 | | |
| Median ESR (mm) | 9 | 10 | 0.842 | | |
| Positive RF | 19% | 24% | 0.405 | | |
| Positive CCP | 14% | 20% | 0.213 | | |
| Positive ANA | 27% | 25% | 0.803 | | |
| Positive ANCA | 6% | 2% | 0.177 | | |

Statistical analysis of risk factors for IMID flare after RZV

# Survival analysis of the time to flare in the 12-week time period following the first and the second dose of RZV  dose




Tiphaine Lenfant et al. Rheumatology 2021

# Safety and Healthcare Use Following COVID-19 Vaccination Among Adults With Rheumatoid Arthritis: A Population-Based Self-Controlled Case Series Analysis

| Outcome | Exposure/Risk Period | RA | | | | General Population Comparators | | | | RIR[a] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Events | Cumulative PY | Crude Rate/PY | RIR (95% CI) | No. of Events | Cumulative PY | Crude Rate/PY | RIR (95% CI) | Between RA and Comparators (95% CI) |
| AESI (within 21 days of dose) | 0 - Control period | 3753 | 133,722.0 | 0.03 | Ref | 10,644 | 535,418.1 | 0.02 | Ref | Ref |
| | 1 - Risk period after 1st dose | 223 | 7431.6 | 0.03 | 1.05 (0.90-1.22) | 589 | 29,731.4 | 0.02 | 0.98 (0.90-1.08) | 1.07 (0.90-1.28) |
| | 2 - Risk period after 2nd dose | 183 | 7347.4 | 0.02 | 0.89 (0.75-1.04) | 530 | 29,400.4 | 0.02 | 0.91 (0.82-1.00) | 0.98 (0.81-1.18) |
| | 3 - Risk period after 3rd dose | 181 | 5905.3 | 0.03 | 1.12 (0.95-1.31) | 385 | 22,925.7 | 0.02 | 0.87 (0.78-0.97) | 1.28 (1.05-1.56) |
| | 4 - Risk period after 4th dose | 14 | 460.8 | 0.03 | 1.06 (0.60-1.87) | 19 | 431.3 | 0.04 | 1.75 (0.97-3.18) | 0.61 (0.27-1.39) |
| All-cause hospitalization + ED visits (within 21 days of dose) | 0 - Control period | 94,279 | 133,722.0 | 0.71 | Ref | 247,129 | 535,418.1 | 0.46 | Ref | Ref |
| | 1 - Risk period after 1st dose | 5148 | 7431.6 | 0.69 | 0.95 (0.92-0.99) | 13,478 | 29,731.4 | 0.45 | 0.96 (0.94-0.98) | 1.00 (0.96-1.04) |
| | 2 - Risk period after 2nd dose | 5424 | 7347.4 | 0.74 | 1.04 (1.00-1.07) | 14,712 | 29,400.4 | 0.50 | 1.08 (1.06-1.10) | 0.96 (0.93-1.00) |
| | 3 - Risk period after 3rd dose | 3640 | 5905.3 | 0.62 | 0.90 (0.87-0.94) | 8863 | 22,925.7 | 0.39 | 0.86 (0.84-0.88) | 1.04 (0.99-1.09) |
| | 4 - Risk period after 4th dose | 314 | 460.8 | 0.68 | 0.95 (0.84-1.08) | 425 | 431.3 | 0.99 | 1.36 (1.14-1.61) | 0.72 (0.58-0.89) |
| All-cause hospitalization (within 21 days of dose) | 0 - Control period | 24,607 | 133,722.0 | 0.18 | Ref | 58,595 | 535,418.1 | 0.11 | Ref | Ref |
| | 1 - Risk period after 1st dose | 1165 | 7431.6 | 0.16 | 0.83 (0.78-0.88) | 2756 | 29,731.4 | 0.09 | 0.83 (0.80-0.86) | 1.01 (0.93-1.08) |
| | 2 - Risk period after 2nd dose | 1171 | 7347.4 | 0.16 | 0.86 (0.81-0.92) | 2799 | 29,400.4 | 0.10 | 0.87 (0.84-0.90) | 0.99 (0.92-1.07) |
| | 3 - Risk period after 3rd dose | 924 | 5905.3 | 0.16 | 0.89 (0.83-0.95) | 2036 | 22,925.7 | 0.09 | 0.84 (0.81-0.88) | 1.04 (0.96-1.13) |
| | 4 - Risk period after 4th dose | 85 | 460.8 | 0.18 | 0.92 (0.72-1.18) | 141 | 431.3 | 0.33 | 1.81 (1.37-2.38) | 0.52 (0.36-0.75) |
| All-cause ED visit (within 21 days of dose) | 0 - Control period | 86,187 | 133,722.0 | 0.64 | Ref | 226,930 | 535,418.1 | 0.42 | Ref | Ref |
| | 1 - Risk period after 1st dose | 4818 | 7431.6 | 0.65 | 0.97 (0.94-1.01) | 12,722 | 29,731.4 | 0.43 | 0.99 (0.97-1.01) | 1.00 (0.96-1.04) |
| | 2 - Risk period after 2nd dose | 5082 | 7347.4 | 0.69 | 1.06 (1.03-1.10) | 13,878 | 29,400.4 | 0.47 | 1.11 (1.08-1.13) | 0.96 (0.93-1.00) |
| | 3 - Risk period after 3rd dose | 3409 | 5905.3 | 0.58 | 0.93 (0.89-0.96) | 8312 | 22,925.7 | 0.36 | 0.88 (0.86-0.90) | 1.04 (1.00-1.09) |
| | 4 - Risk period after 4th dose | 295 | 460.8 | 0.64 | 0.99 (0.87-1.12) | 401 | 431.3 | 0.93 | 1.39 (1.17-1.65) | 0.73 (0.58-0.91) |
| Rheumatologist visit (within 30 days) | 0 - Control period | 205,032 | 125,552.8 | 1.63 | Ref | – | – | – | – | – |
| | 1 - Risk period after 1st dose | 18,110 | 10,327.6 | 1.75 | 1.08 (1.07-1.10) | – | – | – | – | – |
| | 2 - Risk period after 2nd dose | 15,900 | 10,350.3 | 1.54 | 0.95 (0.93-0.96) | – | – | – | – | – |
| | 3 - Risk period after 3rd dose | 12,673 | 8305.6 | 1.53 | 0.92 (0.91-0.94) | – | – | – | – | – |
| | 4 - Risk period after 4th dose | 1396 | 612.9 | 2.28 | 1.01 (0.94-1.08) | – | – | – | – | – |

Jennifer J.Y. Lee et al. The Journal of Rheumatology 2024

Risk of AESIs and health services use in the postvaccination periods in adults with RA and non-RA matched comparators

# Real-World Coverage With Influenza, Pneumococcal, and Herpes Zoster Vaccines Among Patients With Rheumatic Diseases in a Nationwide Healthcare Plan

| Diagnosis[a] | Vaccine Coverage (Time Window)[b] | Age Group, Years | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 18-24 n = 261 | 25-34 n = 809 | 35-44 n = 1660 | 45-54[c] n = 3001 | 55-64 n = 3359 | 65-74 n = 3278 | 75-84 n = 1594 | 85+ n = 566 |
| RA (n = 6932) | Influenza (1 yr) | 28.6 | 16.2 | 19.7 | 25.3 | 35.3 | 59.3 | 68.9 | 64.9 |
| | PPSV23 (5 yrs or since age 65) | 4.2 | 2.9 | 4.6 | 6.4 | 9.5 | 81.8 | 86.1 | 92.7 |
| | PPSV23 (5 yrs) | 4.2 | 2.9 | 4.6 | 6.4 | 9.5 | 53.6 | 8.2 | 7.7 |
| | PCV13 (5 yrs) | 1.7 | 3.2 | 4.8 | 5.9 | 6.2 | 5.5 | 4.1 | 3 |
| | HZ (5 yrs) | – | – | – | 2.7 | 3 | 5.7 | 4.5 | 1.8 |
| PsA (n = 4395) | Influenza (1 yr) | 16.4 | 21.2 | 19 | 23.3 | 33.6 | 60 | 67.8 | 60 |
| | PPSV23 (5 yrs or since age 65) | 9.8 | 4.5 | 4.9 | 6.1 | 6.6 | 80.2 | 88.6 | 87.1 |
| | PPSV23 (5 yrs) | 9.8 | 4.5 | 4.9 | 6.1 | 6.7 | 54.8 | 10.4 | 8.6 |
| | PCV13 (5 yrs) | 9.8 | 4.1 | 4.4 | 4.1 | 4.6 | 2.8 | 4 | 1.4 |
| | HZ (5 yrs) | – | – | – | 1 | 2.3 | 6.9 | 4 | 1.4 |
| SLE (n = 1951) | Influenza (1 yr) | 22.2 | 25.6 | 23.9 | 23.5 | 35.9 | 60.8 | 75.9 | 59.1 |
| | PPSV23 (5 yrs or since age 65) | 11.1 | 3.6 | 5 | 4.7 | 7.1 | 78.1 | 85.5 | 100 |
| | PPSV23 (5 yrs) | 11.1 | 3.6 | 5 | 4.7 | 7.1 | 57.3 | 8.4 | 9.1 |
| | PCV13 (5 yrs) | 5.6 | 5.4 | 3.8 | 3.2 | 4.7 | 4.6 | 2.4 | 0 |
| | HZ (5 yrs) | – | – | – | 0 | 0.5 | 5.4 | 2.4 | 4.5 |
| > 1 condition (n = 1250) | Influenza (1 yr) | 33.3 | 22.5 | 32.9 | 32.5 | 38.4 | 60.9 | 76.9 | 77.1 |
| | PPSV23 (5 yrs or since age 65) | 0 | 7.5 | 5.9 | 8 | 8.1 | 80.1 | 87.6 | 100 |
| | PPSV23 (5 yrs) | 0 | 7.5 | 5.9 | 8 | 8.1 | 51.2 | 5.8 | 5.7 |
| | PCV13 (5 yrs) | 11.1 | 12.5 | 7.9 | 5.9 | 4.8 | 8.4 | 5.8 | 2.9 |
| | HZ (5 yrs) | – | – | – | 2 | 2.3 | 4.4 | 4.1 | 0 |

Age-specific vaccine coverage among patients with RA, PsA, and/or SLE

Tvictoria Furer et al. he Journal of Rheumatology 2024

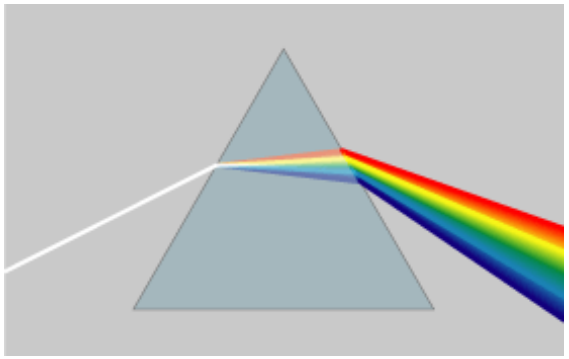
# COVID-19 Vaccination Perceptions in Patients With Rheumatic Disease: A Cross-Sectional Online Survey

| | Patients With RD Who Responded, n (%) | | | Rank[a] |
|---|---|---|---|---|
| | Yes | No | Not Sure | |
| COVID-19 infection concerns | | | | |
| COVID-19 infection and rheumatic condition | | | | |
| Are you concerned about worse outcome after infection due to rheumatic condition? (n = 215) | 127 (59.1) | 52 (24.2) | 36 (16.7) | 1 |
| Rheumatic condition increases risk of infection (n = 217) | 124 (57.1) | 61 (28.1) | 32 (14.8) | 2 |
| Rheumatic medications increase risk of infection (n = 218) | 102 (46.8) | 86 (39.5) | 30 (13.8) | 3 |
| Previous COVID-19 infection | | | | |
| [illegible] | [illegible] | [illegible] | [illegible] | |
| COVID-19 vaccine concerns | | | | |
| Possible impact on rheumatic condition (n = 219) | 99 (45.2) | 105 (48) | 15 (6.9) | 1 |
| Reduced effectiveness (n = 215) | 97 (45.1) | 103 (47.9) | 15 (7) | 2 |
| Risk of blood clots (n = 214) | 85 (39.7) | 114 (53.3) | 15 (7) | 3 |
| Safety (n = 216) | 85 (39.4) | 116 (53.7) | 15 (6.9) | 4 |
| Severe adverse reactions (n = 215) | 76 (35.4) | 128 (59.5) | 11 (5.1) | 5 |
| Speed of vaccine development (n = 215) | 71 (33) | 124 (57.7) | 20 (9.3) | 6 |
| Side effects (n = 212) | 69 (32.6) | 135 (63.7) | 8 (3.8) | 7 |
| Impact on rheumatic medications (n = 219) | 58 (27.2) | 133 (62.4) | 22 (10.3) | 8 |
| Components (ie, vaccine ingredients) (n = 211) | 53 (25.1) | 128 (60.7) | 30 (14.2) | 9 |
| [illegible] | [illegible] | [illegible] | [illegible] | |
| COVID-19 vaccination and rheumatology medications | | | | |
| Know what to do with medications when getting vaccine (n = 217) | 81 (37.3) | 101 (46.5) | 35 (16.1) | – |
| HCP communication, information, and influence | | | | |
| Perception of interaction with HCP | | | | |
| Spoke to HCP about getting COVID-19 vaccine (n = 228) | 173 (75.9) | 54 (23.7) | 1 (0.4) | 1 |
| Feel that providers can answer questions regarding COVID-19 vaccine (n = 226) | 171 (75.6) | 29 (12.8) | 26 (11.5) | 2 |
| Spoke to HCP about risks and benefits of COVID-19 vaccine (n = 227) | 150 (66.1) | 71 (31.3) | 6 (2.6) | 3 |
| HCP encouraged getting COVID-19 vaccine (n = 225) | 144 (64) | 51 (22.7) | 30 (13.3) | 4 |
| Confidence in the information given by HCPs (n = 225) | | | | |
| Completely confident | 103 (45.8) | – | – | – |
| Mostly confident | 85 (37.8) | – | – | – |
| Somewhat confident | 25 (11.1) | – | – | – |
| Not very confident | 9 (4) | – | – | – |
| Not very confident at all | 3 (1.3) | – | – | – |
| Individuals who influence COVID-19 vaccine decision making | | | | |
| HCP | 144 (62.3) | 87 (37.7) | – | 1 |
| No one—I make my own decisions | 101 (43.7) | 130 (56.3) | – | 2 |
| Family/friends | 44 (19.1) | 187 (81) | – | 3 |
| Other | 6 (2.6) | 225 (97.4) | – | 4 |
| Not applicable | 5 (2.2) | 226 (97.8) | – | 5 |
| HCP role in COVID-19 vaccine decision making | | | | |
| Major role | 60 (42) | – | – | – |
| Minor role | 50 (35) | – | – | – |
| No role | 30 (21) | – | – | – |
| Other | 3 (2.1) | – | – | – |

Concerns of patients with rheumatic disease related to COVID-19 infection and vaccines, and perceptions regarding communication, information, and influence of their HCPs

Imana N, Burr et al. The Journal of Rheumatology 2023

# Vaccination coverage and attitude in AIIRD patients



PRISMA

| Parients 210 | DTP | Men B | Men ACWY | Pneumo | Flu | Zoster | MPR |
|---|---|---|---|---|---|---|---|
| Vaccinated | 20 (9.5%) 10 aa | 2 (0.95%) | 19 9.0% | 29 (13.8%) | 31 (14.7%) | 2 (0.95%) | ND |
| Not vaccinated | 190 (90.5%) | 208 (99.05%) | 191 (91%) | 181 (86.2%) | 179 (86.3%) | 208 (99.05%) | ND |
| Subsequent Adhesion to vaccination | 180 (94.7%) | 23 | 24 | 169 (93.4%) | 210 (100%) | 208 (99.05%) | NA |
| Subsequent refusal of vaccination | 10 (5.3%) | 3 | 2 | 12 (6.6%) | 0 (0%) | NA | NA |

F. Atzeni,
A. Mutti,
B. P Sarzi Puttini

# Vaccine implementation

- Involvement of general practitioners
- Scientific formation of the specialists
- Identification of susceptible subjects needing vaccination
- Grant proactive vaccine offer
- Free vaccinations
- Easy access to vaccination
- Infectivologist consultation

# Immunogenicity and safety of high-dose versus standard-dose inactivated influenza vaccine in rheumatoid arthritis patients: a randomised, double-blind, active-comparator trial

Inés Colmegna, Mariana L Useche, Katherine Rodriguez, Deirdre McCormack, Giuliana Alfonso, Aakash Patel, Agnihotram V Ramanakumar, Elham Rahme, Sasha Bernatsky, Marie Hudson, and Brian J Ward

Baseline characteristics of study participants included in the intention-to-treat analysis




| | HD-TIV (n=138) | SD-QIV (n=136) |
|---|---|---|
| Sex | | |
| Female | 109 (79%) | 109 (80%) |
| Male | 29 (21%) | 27 (20%) |
| Age*, years | 59·7 (13·9) | 61·9 (11·8) |
| Ethnic origin | | |
| White | 110 (80%) | 106 (78%) |
| African American | 6 (4%) | 7 (5%) |
| Asian | 13 (9%) | 14 (10%) |
| Hispanic | 1 (1%) | 4 (3%) |
| Other | 8 (6%) | 5 (4%) |
| Comorbidities | | |
| Diabetes | 16 (12%) | 9 (7%) |
| Cancer | 11 (8%) | 24 (18%) |
| Angina or myocardial infarction | 5 (4%) | 5 (4%) |
| Congestive heart failure | 2 (1%) | 0 |
| Asthma, COPD, or emphysema | 16 (12%) | 22 (16%) |
| RAPID3 score | 2·2 (2) | 2·3 (2·1) |
| RADAI-5 score | 2·9 (2·2) | 3·3 (2·2) |
| Current rheumatoid arthritis treatment | | |
| Steroids | 30 (22%) | 28 (21%) |
| Dose, mg/day | 8·2 (9·0) | 8·6 (6·0) |
| Methotrexate | 70 (51%) | 69 (51%) |
| Dose, mg/week | 18·1 (5·5) | 18·0 (4·6) |
| Biologics | 59 (43%) | 65 (48%) |
| Etanercept | 22 (16%) | 18 (13%) |
| Adalimumab | 8 (6%) | 20 (15%) |
| Certolizumab pegol | 5 (4%) | 1 (1%) |
| Golimumab | 3 (2%) | 2 (1%) |
| Infliximab | 1 (1%) | 2 (1%) |
| Tocilizumab | 4 (3%) | 6 (4%) |
| Sarilumab | 1 (1%) | 0 |
| Abatacept | 9 (7%) | 9 (7%) |
| Rituximab | 6 (4%) | 7 (5%) |
| JAK inhibitors | 10 (7%) | 7 (5%) |

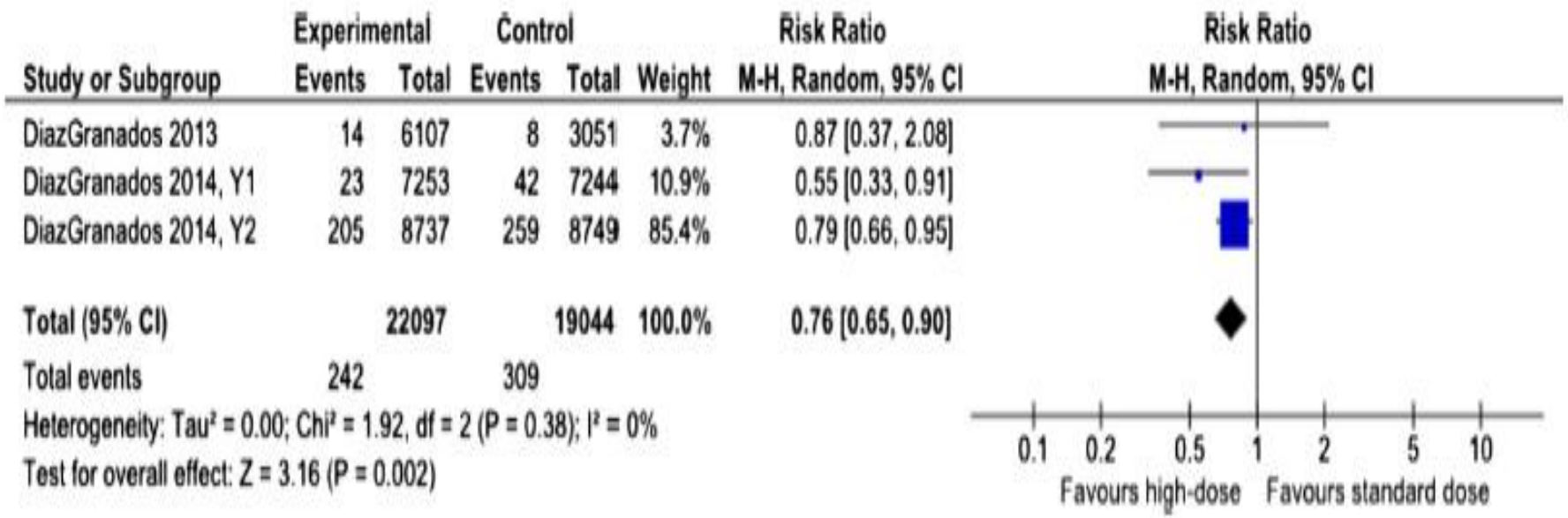
# Seroconversion in the modified intention-to-treat population at day 28

| | Seroconversion, HD-TIV group | Seroconversion, SD-QIV group | Unadjusted odds ratio (95% CI), HD-TIV *vs* SD-QIV |
|---|---|---|---|
| **Haemagglutination-inhibition antibodies** | | | |
| A/Hong Kong/4801/2014* | 31/138 (22%) | 12/136 (9%) | 2·99 (1·46–6·11) |
| B/Brisbane/60/2008† | 62/138 (45%) | 40/136 (29%) | 1·95 (1·19–3·22) |
| A/California/7/2009‡ (year 1) | 36/69 (52%) | 18/71 (25%) | 3·21 (1·57–6·56) |
| A/Michigan/45/2015‡ (year2) | 32/69 (46%) | 17/65 (26%) | 2·44 (1·18–5·06) |
| **Microneutralisation antibodies** | | | |
| A/Hong Kong/4801/2014 | 61/138 (44%) | 45/136 (33%) | 1·60 (0·98–2·62) |
| B/Brisbane/60/2008† | 58/138 (42%) | 26/136 (19%) | 3·07 (1·78–5·28) |
| A/California/7/2009‡ (year 1) | 37/69 (54%) | 20/71 (28%) | 2·95 (1·46–5·94) |
| A/Michigan/45/2015‡ (year2) | 42/69 (61%) | 26/65 (40%) | 2·33 (1·17–4·66) |

## 2022 American College of Rheumatology Guideline for Vaccinations

For patients with RMD age ≥65 years and patients with RMD age >18 and <65 years who are taking immunosuppressive medication, giving high-dose or adjuvanted influenza vaccination is conditionally recommended over giving regular-dose influenza vaccination.

# Laboratory-confirmed influenza infection in patients randomized to high-dose influenza vaccine versus standard-dose influenza vaccine



# Herpes Zoster Recurrence

Following an initial HZ episode, individuals remain at risk of HZ recurrence.

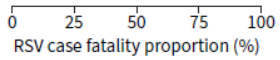
- General population studies estimate that approximately 10% of individuals may experience an HZ recurrence in the first decade after an initial HZ episode
- Multiple recurrences are observed in up to 25% of this group
- The risk of recurrence increases in women, immunocompromised populations, and populations with comorbidities. Other factors that may predispose individuals to recurrence include longlasting pain after the initial HZ episode and the presence of HZO

# Respiratory syncytial virus

- RSV is a leading cause of acute respiratory tract infection, including URTI and LRTI
- RSV infection is transmitted by direct or indirect contact, with infection rates typically peaking in colder months in temperate climates.
- Globally, prior to the COVID-19 pandemic, LRTIs represented the fourth cause of overall disability-adjusted life-years at all ages, and RSV was the second most common aetiology
- The burden of RSV infection is highest in children aged <5 years (global incidence 17.0 per 1000 people), older adults (global incidence 6.3 per 1000 people aged >70 years) and adults with underlying comorbidities (such as the immunocompromised and those with an underlying chronic cardiopulmonary disease), who are at risk of severe outcomes of infection

# Based on 29 studies, the estimated RSV infection CFP was 9.88%, with substantial heterogeneity observed between studies

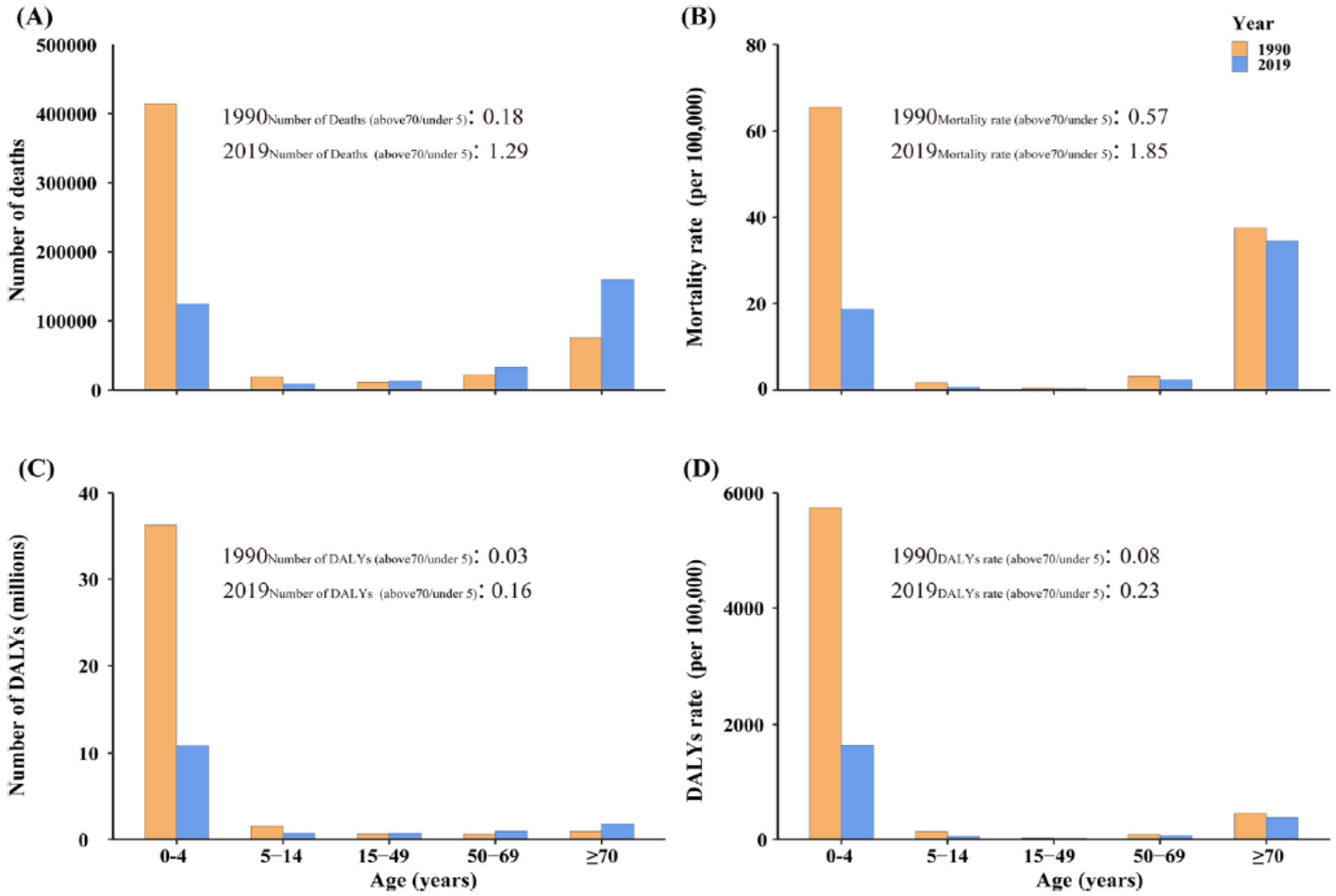
| Study | Country | Age group (years) | Study setting | Population type | Sample and infection | ROB | Deaths (n) | RSV cases (n) | Total (n) | RSV case fatality proportion % (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Cardiopulmonary** | | | | | | | | | | |
| Falsey, 2005 | US | ≥21 | comm | | SS ARI | 2/9 | 2 | 56 | 540 | 3.57 (0.98–12.12) |
| Ong, 2014 | NL | ≥18 | meda | ICU | SS RF | 3/9 | 0 | 1 | 57 | 0.00 (0.00–79.35) |
| Yousaf, 2017 | US | ≥18 | meda | RSV+ IP | CI | 3/9 | 3 | 23 | 23 | 13.04 (4.54–32.13) |
| Loubet, 2017 | FR | ≥18 | meda | IP | SS ILI | 2/9 | 4 | 29 | 659 | 13.79 (5.50–30.56) |
| Jeannoel, 2019 | FR | ≥18 | meda | RSV+ ARI | CI | 4/9 | 10 | 55 | 55 | 18.18 (10.19–30.33) |
| Falsey, 2005 | US | ≥65 | meda | IP | SS ARI | 2/9 | 10 | 142 | 1388 | 7.04 (3.87–12.48) |
| REM for subgroup (Q=8.54, p=0.13; $I^2$=42.3%) | | | | | | | | | | 10.08 (6.45–17.55) |
| **Immunodeficiency** | | | | | | | | | | |
| Lopez-Medrano, 2017 | ES | ≥18 | comm | | SS RVI | 2/9 | 0 | 6 | 152 | 0.00 (0.00–39.03) |
| Weinberg, 2010 | US | ≥18 | comm | | SS ARI | 0/9 | 0 | 13 | 112 | 0.00 (0.00–22.81) |
| Milstone, 2006 | US | ≥18 | comm | | SS ARI | 1/9 | 0 | 8 | 50 | 0.00 (0.00–32.44) |
| Peghin, 2017 | ES | ≥18 | comm | | SS ARI | 0/9 | 1 | 7 | 162 | 14.29 (2.57–51.31) |
| Teh, 2015 | AU | ≥18 | meda | | CI RVI | 3/9 | 0 | 15 | 100 | 0.00 (0.00–20.39) |
| Mikulsa, 2014 | IT | ≥18 | meda | OP | SS ARI | 1/9 | 0 | 18 | 193 | 0.00 (0.00–17.59) |
| Ong, 2014 | NL | ≥18 | meda | ICU | SS RF | 3/9 | 0 | 3 | 32 | 0.00 (0.00–56.15) |
| Li, 2012# | US | ≥18 | meda | RSV+ | CI | 2/9 | 0 | 21 | 21 | 0.00 (0.00–15.46) |
| Schmidt, 2019 | US | ≥18 | meda | RSV+ IP | CI | 3/9 | 2 | 216 | 216 | 0.93 (0.25–3.31) |
| Spahr, 2018 | CH | ≥18 | meda | RSV+ | CI ARI | 4/9 | 2 | 33 | 33 | 6.06 (1.68–19.61) |
| Garcia-Noblejas, 2015 | ES | ≥18 | meda | | CI ARI | 5/9 | 2 | 32 | 570 | 6.25 (1.73–20.15) |
| Chatzis, 2018 | CH | ≥18 | meda | RSV+ | CI ARI | 2/9 | 11 | 175 | 175 | 6.29 (3.55–10.90) |
| Pilie, 2015 | US | ≥18 | meda | RSV+ IP | CI | 3/9 | 5 | 69 | 69 | 7.25 (3.13–15.87) |
| Damlaj, 2016 | US | ≥18 | meda | RSV+ | CI | 3/9 | 4 | 45 | 45 | 8.89 (3.51–20.73) |
| Khanna, 2018 | CH | ≥18 | meda | RSV+ | SS ARI | 4/9 | 6 | 34 | 34 | 17.65 (8.35–33.51) |
| Jeannoel, 2019 | FR | ≥18 | meda | RSV+ ARI | CI | 4/9 | 8 | 37 | 37 | 21.62 (11.39–37.20) |
| Renaud, 2013 | US | ≥18 | meda | RSV+ | CI | 3/9 | 8 | 23 | 23 | 34.78 (18.81–55.11) |
| REM for ≥18 age group (Q=40.52, p<0.01; $I^2$=63.0%) | | | | | | | | | | 8.32 (4.94-13.68) |
| D'Angelo, 2016¶ | US | ≥50 | meda | | SS ARI | 3/9 | 3 | 6 | 118 | 50.00 (18.76-81.24) |
| REM for subgroup (Q=47.48, p<0.01; $I^2$=67.1%) | | | | | | | | | | 9.27 (5.42–15.39) |
| REM for all studies (Q=56.02, p<0.01; $I^2$=62.7%) | | | | | | | | | | 9.88 (6.66–14.43) |




Case fatality proportion among RSV-positive high-risk groups

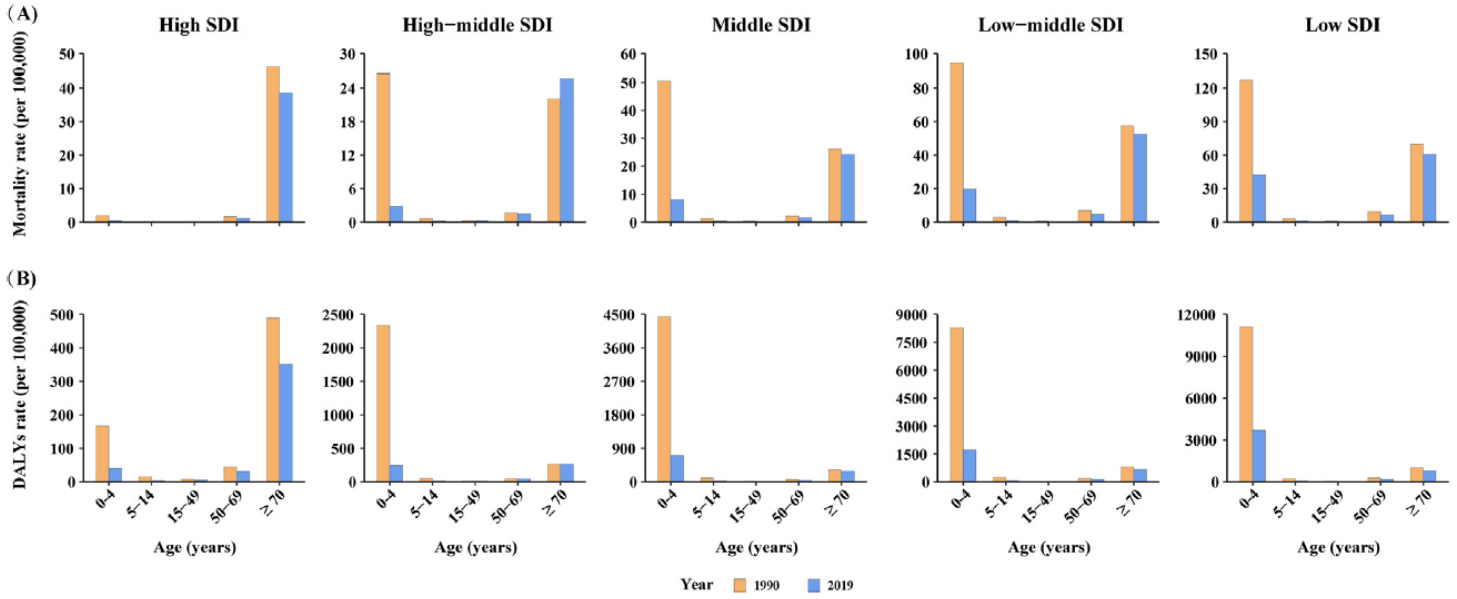
Nguyen-Van-Tam JS, et al. Eur Respir Rev 2022

# Global burden and trends of respiratory syncytial virus infection across different age groups from 1990 to 2019: A systematic analysis of the Global Burden of Disease 2019 Study

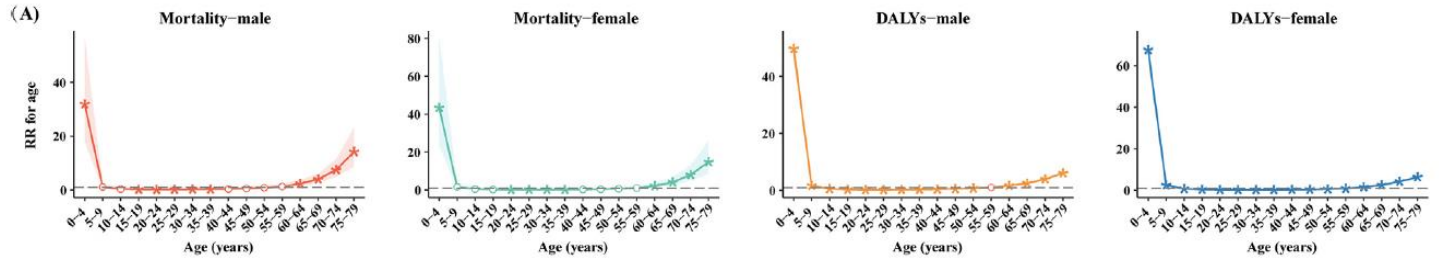



Global mortality and DALYs counts and rates due to respiratory syncytial virus infection in 1990 and 2019, by age group. (A) Number of deaths; (B) Mortality rate; (C) Number of DALYs; (D) DALYs rate. DALYs, disability-adjusted life years.

# Global burden and trends of respiratory syncytial virus infection across different age groups from 1990 to 2019




Mortality and DALYs rates due to respiratory syncytial virus infection in different SDI regions in 1990 and 2019, by age group




**Age effect**

Age-period-cohort model analysis of the mortality and DALYs rates of respiratory syncytial virus infection globally between 1990 and 2019

Y. Du, et al. International Journal of Infectious Diseases 2023

# The disease burden of respiratory syncytial virus in older adults

| Settings | Population | Regions | RSV proportion positive | RSV incidence rate | Proportion hospitalized among RSV positive |
|---|---|---|---|---|---|
| Community | ≥60 years | | 3.4% to 8.8% [1–7] | | |
| | ≥65 years | Industrialized countries | | 600.7 cases per 100 000 (95% CI: 100.4–3100.5) person-years [8▪▪] | |
| | ≥60 years, RSV-positive | | | | 0% to 19.5% [2–4] |
| Outpatients | ≥60 years | | 5.2% to 14.9% [7, 9–16] | 500.9 to 2300.2 per 100 000 person-years [17,18▪] | |
| | ≥60 years, RSV-positive | | | | 11.9% [10] |
| Emergency department | ≥65 years | | | 300.3 (95% CI: 1100.7–9000.8) per 100 000 person-years [19] | |

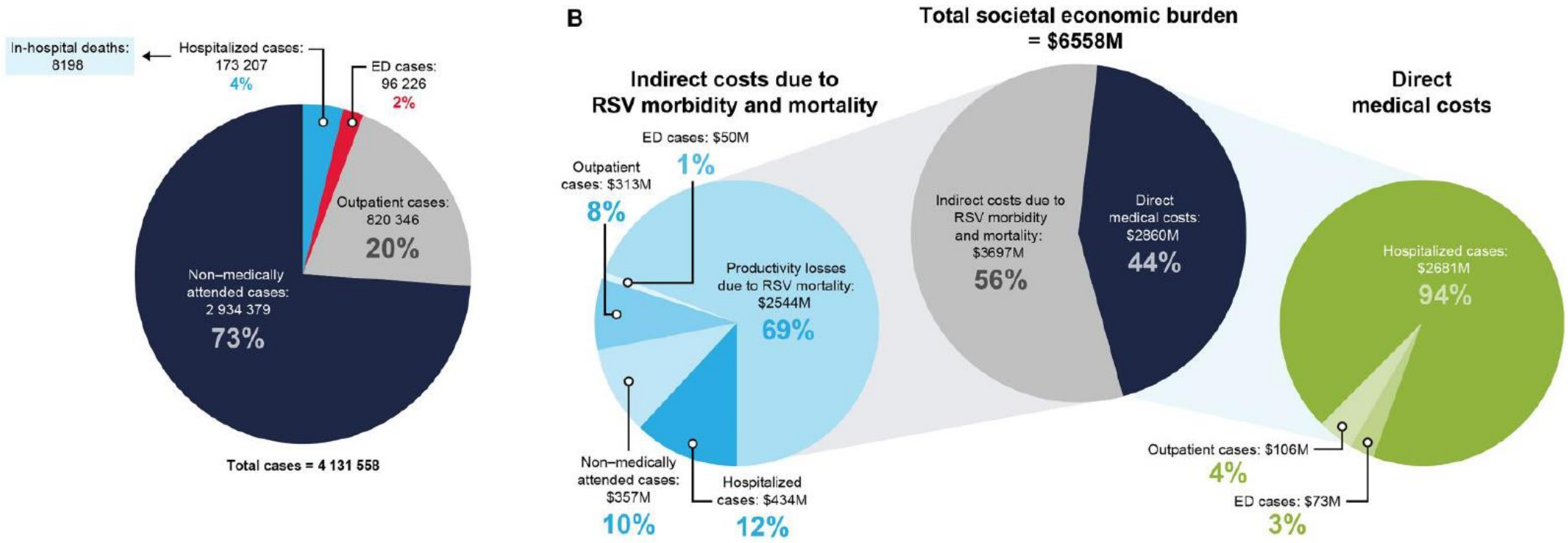
RSV burden among older adults in community studies

| Settings | Population | Regions | RSV hospitalization rate | RSV in hospital case fatality rate |
|---|---|---|---|---|
| Inpatients | ≥65 years | Industrialized countries | 157 (95% CI: 98–252) RSV infections per 100 000 person-years [20] | 6.1% (95% CI: 3.3–11.0) [20] |
| | ≥65 years | Industrialized countries | 100 (95% CI: 50–210) RSV infections per 100 000 person-years [8▪▪] | 1.6% (95% CI: 0.7–3.8%) [8▪▪] |
| | ≥65 years | Developing countries | 30 (95% CI: 10–70) RSV infections per 100 000 person-years [8▪▪] | 9.1% (95% CI: 2.6–31.8%) [8▪▪] |
| | ≥60 years | Industrialized countries | | 7.1% (95% CI: 5.4–9.3) [21] |

RSV burden among older adults in inpatient studies

Sebastien Kenmoea and Harish Nair, Curr Opin Infect Dis 2024

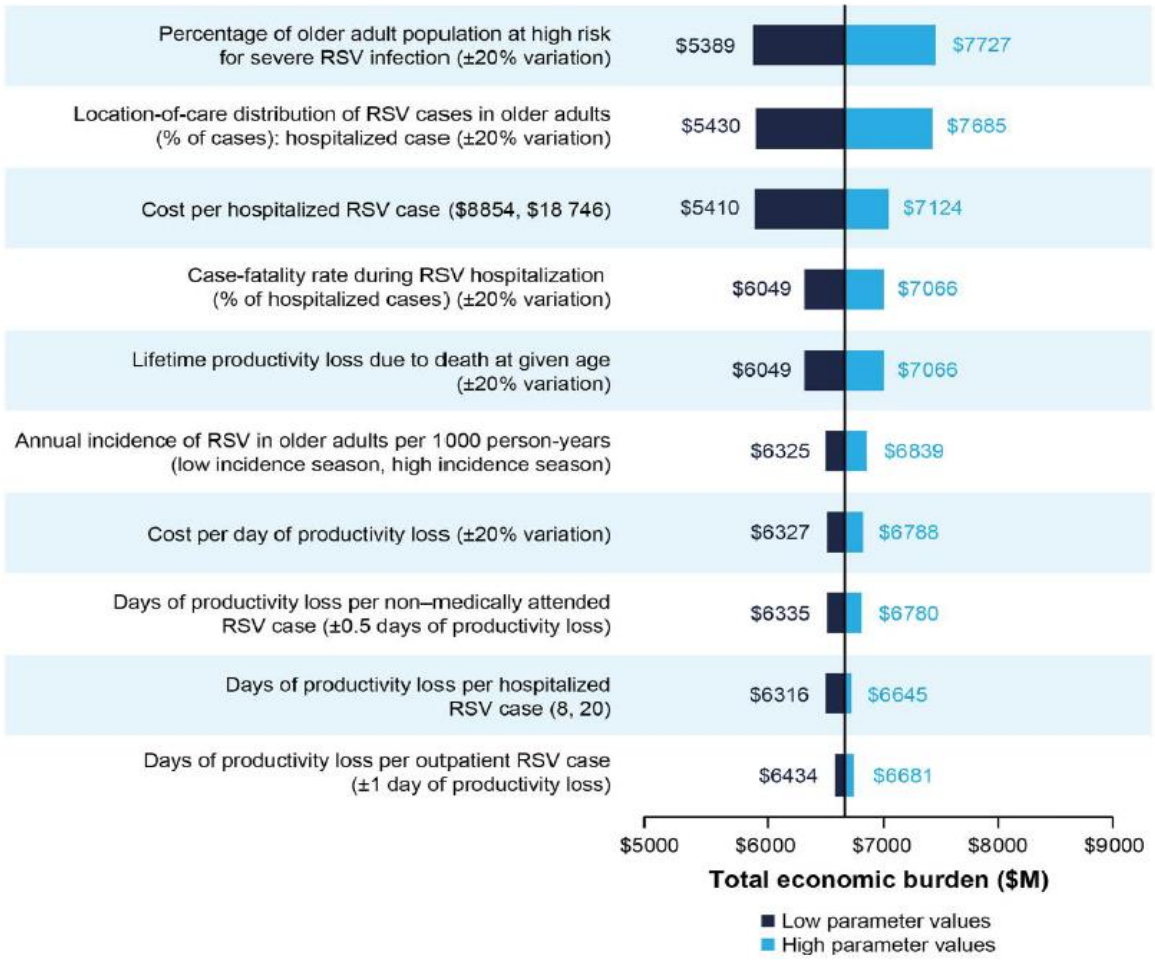
# The Annual Economic Burden of Respiratory Syncytial Virus in Adults in the United States




Estimates of health and economic burden of RSV in US adults aged ≥60 years. *A*, morbidity and mortality. *B*, Societal economic burden, inclusive of direct medical costs and indirect medical costs.

Justin Carrico et al. The Journal of Infectious Diseases 2024

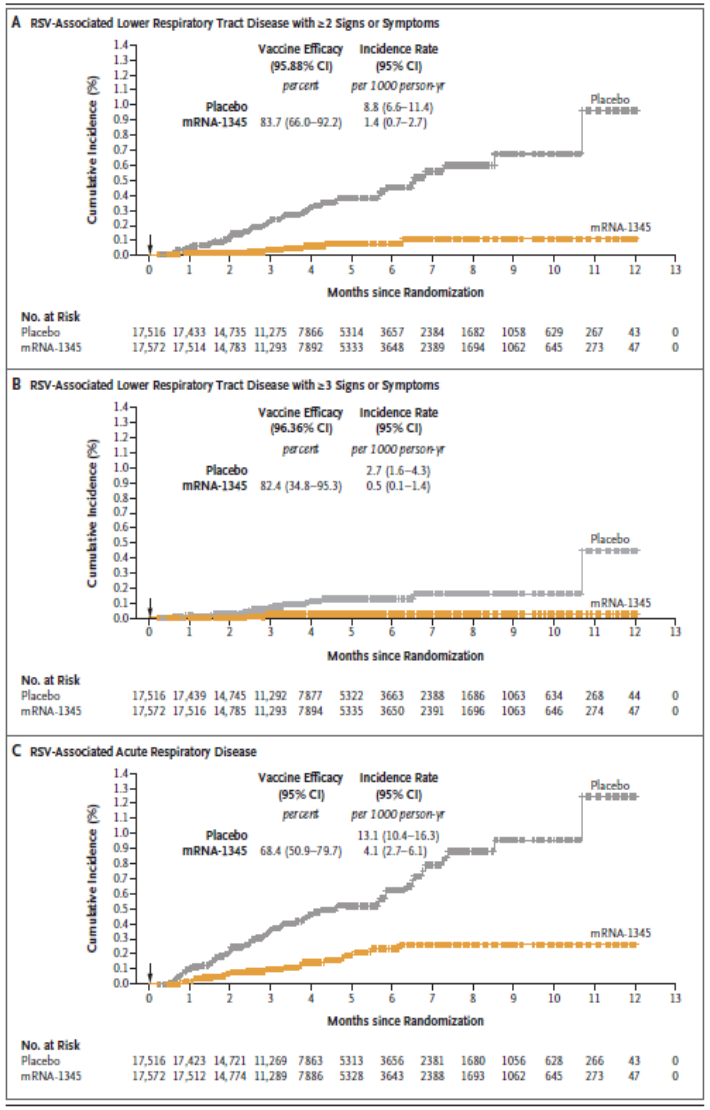
# One-way sensitivity analysis results for RSV economic burden in adults aged ≥60 years

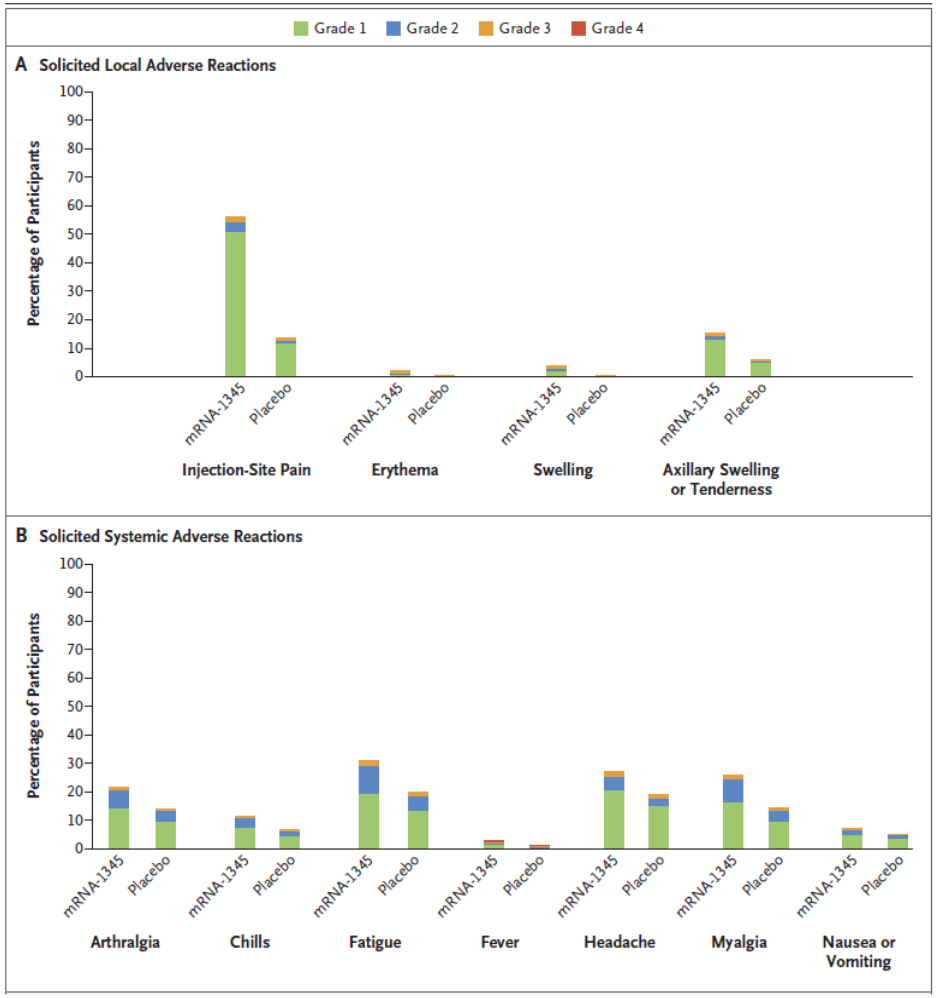



Justin Carrico et al. The Journal of Infectious Diseases 2024

# Efficacy and Safety of an mRNA-Based RSV PreF Vaccine in Older Adults

Cumulative Incidence of RSV-Associated Lower Respiratory Tract Disease and RSV-Associated Acute Respiratory Disease




Solicited Local and Systemic Adverse Reactions

E. Wilson, et al. N Engl J Med 2023

# mRNA-Based RSV PreF Vaccine

- Indicazioni terapeutiche

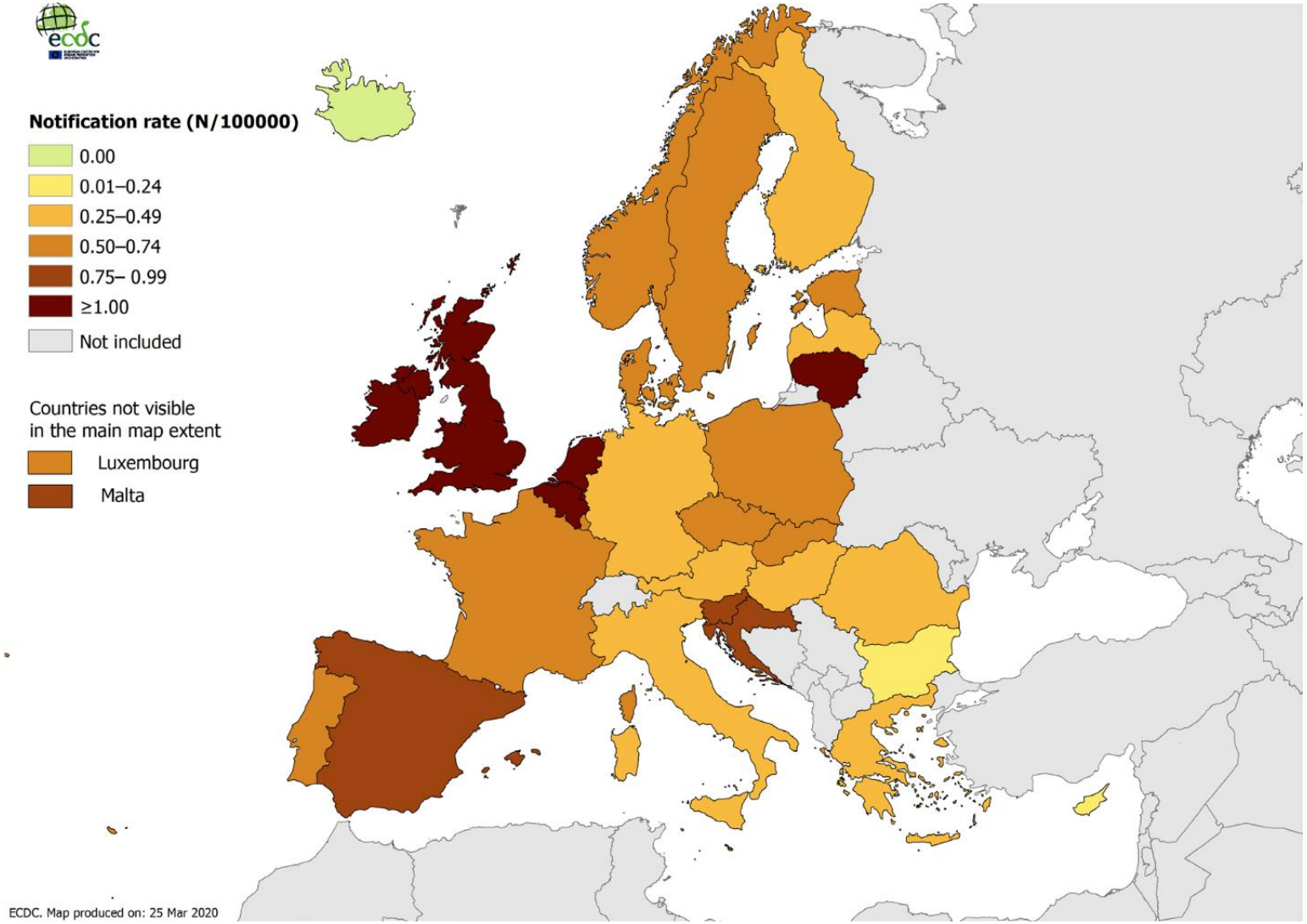
Arexvy è indicato per l'immunizzazione attiva per la prevenzione della malattia del tratto respiratorio inferiore (LRTD) provocata dal virus respiratorio sinciziale in:

  - adulti di età pari o superiore a 60 anni;
  - adulti di età compresa tra 50 e 59 anni che sono a maggior rischio di malattia da RSV.

# Meningococcal disease: key facts

- In 2018, 3 233 confirmed cases of invasive meningococcal disease (IMD), including 324 deaths, were reported in 30 European Union/European Economic Area (EU/EEA) Member States.
- France, Germany, Spain, and the United Kingdom accounted for 59% of all confirmed cases in 2018.
- The notification rate of IMD was 0.6 cases per 100 000 population, similar to the 2015-2017 period.
- Age-specific rates were highest in infants, followed by 1-4-year-olds, with a second peak in 15-24-year-olds.
- Serogroup B remains the major cause of IMD. It caused 51% of cases overall and was the dominating serogroup in all age groups below 65 years. Incidence remained stable between 2014 and 2018.
- The incidence of serogroups W and Y has been increasing. Serogroup W is now the second cause of IMD reported in 18% of cases.
- The continued strengthening of disease surveillance for IMD is essential to evaluate the impact of ongoing immunisation programmes and support decision-makers concerning vaccination strategies.

# Distribution of confirmed invasive meningococcal disease cases and rates per 100.000 population by country, EU/EEA, 2014–2018



# IMD in Italia

**Istituto Superiore di Sanità**
EpiCentro - L'epidemiologia per la sanità pubblica

- Nel 2021 sono stati segnalati 26 casi di malattia invasiva da meningococco; nel 2020 e 2019 ne sono stati segnalati 74 e 190, rispettivamente.
- Nel periodo di riferimento, l'incidenza delle malattie invasive da meningococco in Italia è stata di 0,32 casi/100.000 abitanti nel 2019 e 0,12 casi/100.000 abitanti nel 2020; nel 2021 il valore è sceso a 0,04 casi/100.000 abitanti.
- Nel 2021 l'incidenza (x 100.000 abitanti) della malattia invasiva da meningococco è risultata maggiore nei neonati <1 anno (1,48) e, a seguire, nella fascia degli adolescenti/giovani adulti di 15-24 anni (0,07) e nei bambini di 1-4 anni (0,06).
- I meningococchi di sierogruppo C e quello B sono i più frequenti in Italia. Il sierogruppo B è stato il più frequentemente riscontrato, circa il 51% nel 2019 ed in crescita rispetto al biennio precedente (41% nel 2017 e 45% nel 2018).
- Nella classe di età 0-4 anni il sierogruppo B rappresenta l'81% dei casi (65% nel 2017 e 69% nel 2018), seguito dal sierogruppo C 15% (16% nel 2017 e 15% nel 2018) e dal sierogruppo Y 4% (13% nel 2017 e 8% nel 2018).
- Anche nella fascia di età dei giovani adulti 15-24 anni, il sierogruppo B è il più frequente, 45% (56% nel 2017 e 52% nel 2018), seguito dal sierogruppo C 31% (16% nel 2017 e 34% nel 2018).

# Eculizumab for treating AQP4-antibody-positive NMOSD

Safety data are available from a small pilot study, the placebo-controlled pivotal trial PREVENT, and its open-label extension (OLE) study

Most common AEs were

- Headache
- Nasopharyngitis (27.6 in 100 PY)
- Upper respiratory tract and urinary tract infection (25.7 each in 100 PY)
- Back pain and diarrhoea (12.4 each in 100 PY),
- Nausea (13.2 in 100 PY), and arthralgia (8.8 in 100 PY).
- The rate of treatment-related SAEs was 8.0 in 100 PY.

SAEs included severe infections, which occurred in 25/137 patients, corresponding to 10.2 events in 100 PY. Among these, five patients suffered from pneumonia,  four patients each from urinary tract infection or cholecystitis, and two patients each from cellulitis or sepsis

Giglhuber K, et al. Immunotherapy. 2020
Pittock, S.J. et al. Lancet Neurol. 2013
Pittock SJ, et al. N Engl J Med. 2019;381(7):614-625.
Wingerchuk, D.M. et al.  Ann. Neurol. 2021

# Eculizumab is known to especially increase the risk of infections with encapsulated bacteria

- The risk has been estimated to be 2000-fold higher than in the untreated population.
- There have been reports of meningococcal infections despite proper vaccination.
- One NMOSD patient in the pilot study with eculizumab.
- Neither the PREVENT study nor the OLE observed meningococcal infections.
- However, one patient in the OLE developed an infection due to Neisseria gonorrhoeae.

Pittock, S.J. et al. Lancet Neurol. 2013
Wingerchuk, D.M. et al. Ann. Neurol. 2021
Food and Drug Administration, US SOLIRIS Product Information.
McNamara, L.A.et al. MMWR Morb. Mortal. Wkly. Rep. 2017

*J Infect.* 2020 March ; 80(3): 350–371. doi:10.1016/j.jinf.2019.11.015.

# Antibiotic prophylaxis in vaccinated eculizumab recipients who developed meningococcal disease

Page E. Crew, PharmD, MPH[1], Lucy McNamara, PhD, MS[2], Peter E. Waldron, MD[1], Lynda McCulley, PharmD[1], S. Christopher Jones, PharmD, MS, MPH[1], Susan J. Bersoff-Matcha, MD[1,3]

Search for meningococcal disease cases in eculizumab recipients in the FDA Adverse Event Reporting System (FAERS) and the literature (PubMed, Embase) between March 2007 (U.S. approval date) and May 2017

- The series included 47 patients, of whom 15 were taking antibiotic prophylaxis at the time of meningococcal disease onset and 32 were not.
- There were four fatalities due to meningococcal disease (all among patients not taking prophylaxis).
- All 47 patients reportedly received ≥1 dose of a meningococcal vaccine.
- Three of 47 patients had ≥1 episode of meningococcal disease (two patients were taking prophylaxis; one was not).
- TTO of first episode of meningococcal disease was reported for 11 of 15 patients taking prophylaxis and 26 of 32 not taking prophylaxis.
- Median TTO of first episode of meningococcal disease was 835 days in prophylaxis recipients versus 333 days in patients not taking prophylaxis.
- Among patients with susceptibility results available, penicillin non-susceptibility was reported more frequently in patients taking prophylaxis (5 of 6 isolates, 83%) than in patients not taking prophylaxis (2 of 9 isolates, 22%)

# Vaccination

Patients with complement deficiency may receive all routine bacterial and viral vaccines safely and are not at increased risk for adverse reactions to live-viral vaccines.

It is important to ensure that patients are vaccinated against those diseases for which they are at increased risk:

- Meningococcus
- Pneumococcus
- Hib
- Influenza

# Vaccini antimeningococco disponibili in commercio

| Serogroup | Vaccine formulation | Vaccine type | Vaccine name | Manufacturer |
|---|---|---|---|---|
| B | MenB-fHbp | Recombinant | Trumenba | Pfizer |
| | MenB-4C | Recombinant | Bexero | GlaxoSmithKline |
| ACWY | MenACWY-DT | Conjugate | Menactra | Sanofi Pasteur |
| | MenACWY-CRM | Conjugate | Menveo | GlaxoSmithKline |
| | MenACWY-TT | Conjugate | Nimenrix | Pfizer |
| | MenACWY-TT | Conjugate | MenQuadfi | Sanofi Pasteur |

# Current ACIP recommendations for meningococcal vaccinations in adult patients receiving complement C5 inhibitors

## MenACWY

**2**

DOSES

At least 8 weeks apart

Revaccinate every

**5 years**

if risk remains

+

## MenB-4C

**2**

DOSES

At least 1 month apart

OR

## MenB-FHbp

**3**

DOSES

0, 1-2, and 6 months[a]

Booster dose 1 year following completion of primary series and every 2 to 3 years if risk remains.

MenB vaccines are not interchangeable.
You must receive the same product for all doses.

# Meningococcal vaccination

As conjugated meningococcal vaccines have been shown to reduce pharyngeal meningococcal carriage

- vaccination of close household contacts of eculizumab treatment candidates, coupled with routine surveillance aimed at identification of a Neisseria meningitidis carrier state among these contacts.
- those found to be carriers of Neisseria meningitidis should be offered a targeted, susceptibility-based antibiotic course

# Problems with vaccine efficay

Vaccine efficacy may be impaired by previous IS treatments

- Steroids
- Azathioprine
- Mycophenolate mofetil
- Tocilizumab
- Anti-CD20 moAbs

URGENT NEED FOR VACCINATION EFFICACY AND DURABILITY TRIALS


Peace
Love
Vaccines