

Vaccination in chronic respiratory diseases

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Outline

- Introduction
- Impact of infections in chronic respiratory diseases (CRD)
- Role of vaccine in CRD, efficacy and recommendations for:
 - Pneumococcal
 - Influenza
 - RSV
 - Pertussis
 - COVID
 - Varicella zoster

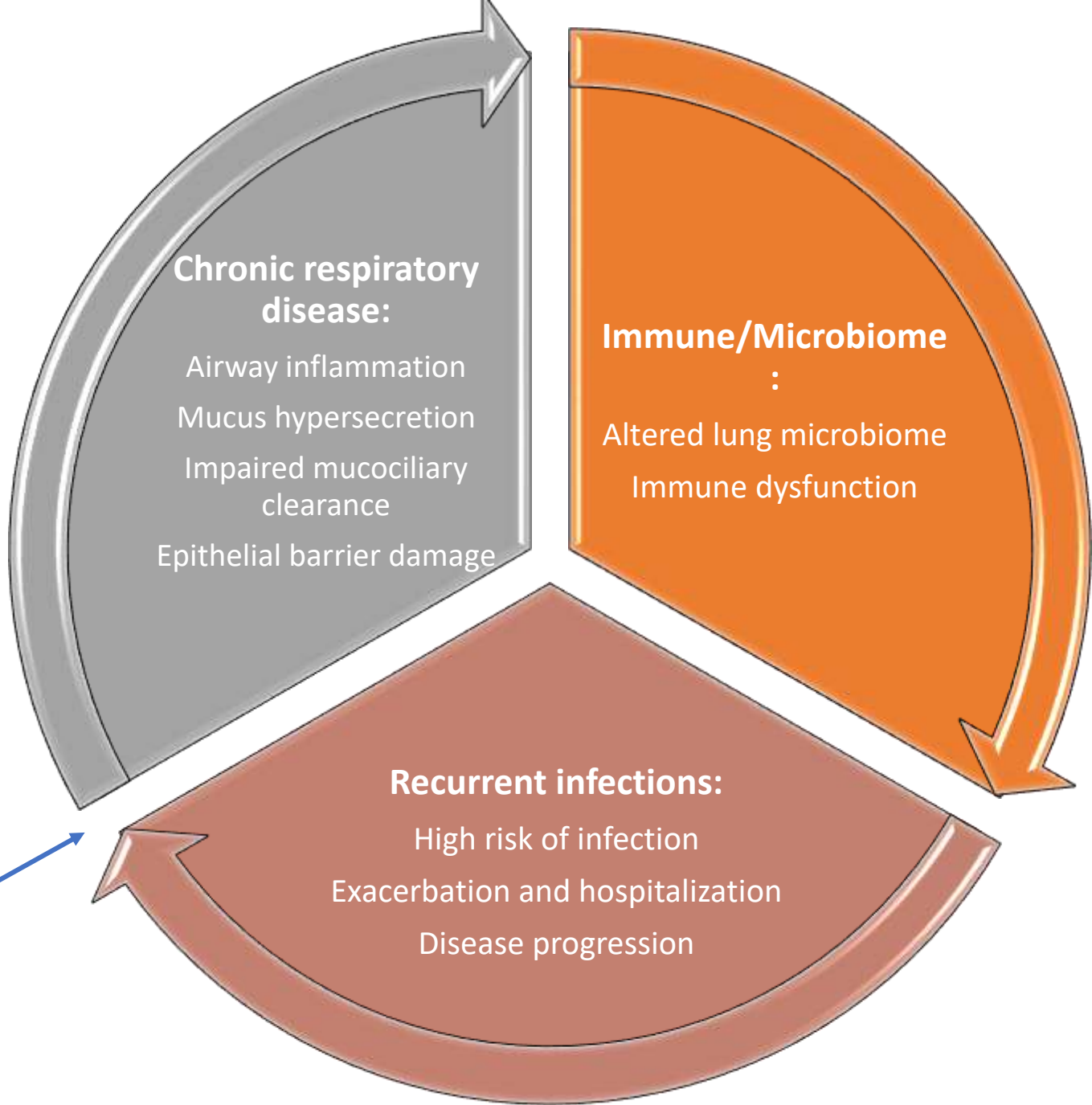
Introduction

- **Immunization:** Process by which a person becomes **protected** against a disease through the **immune response**
- Can be achieved by:
 - Active immunization – post infection or vaccination or
 - Passive immunization - administration of pre-formed antibodies (immunoglobulins)
- **Vaccination:** Act of introducing a vaccine (antigenic substance) into the body to **stimulate** the **immune system** against specific pathogens
- One of the method of achieving immunization

Chronic respiratory diseases (CRD)

- Chronic respiratory diseases are characterized by chronic inflammation and /or fibrosis of airways and interstitium of lungs
- Asthma and COPD – most prevalent CRD
- Major risk factors: Tobacco smoking, air pollution, occupational exposure, recurrent childhood respiratory infections
- Symptom control and exacerbation prevention are key in management

Vaccination



Effect of infections in CRD

| Risks | Evidence |
|----------------------|--|
| Exacerbations | <p>EXACOS-UK, 2022 study: 215234 newly diagnosed COPD, higher rates of subsequent COPD exacerbations in prior LRTI</p> <p>1 moderate LRTI: IRR - 1.81, 2+ moderate - 2.55 vs none.</p> <p>Asthma: 40% prevalence of acute infection, viruses - 38-40%</p> <p>Rhinovirus most common (20%) triggering exacerbations</p> |
| Mortality | <p>Severe LRTI at baseline than without: aHR -1.92 for all-cause mortality</p> |
| ICU admission | <p>Acute exacerbation of COPD requiring ICU admission – 61% due to respiratory infections</p> |
| Poor disease control | <p>Frequent exacerbations lead to more rapid decline in lung function, worse quality of life, increased health care use</p> |

Common infections in CRD

- Respiratory infection – common cause for exacerbation of CRD

- 36.6% caused by viral pathogens

Available vaccines

- Rhinovirus most common (13%)
- RSV (5.6%), influenza (8%)

| Bacteria | Virus |
|------------------------------|-------------------|
| Pneumococcal vaccine | Influenza vaccine |
| Hemophilus influenza vaccine | RSV vaccine |
| Pertussis vaccine | COVID 19 vaccine |

- 25% - 40% caused by bacterial pathogens

- Hemophilus influenza most common
- Streptococcus pneumoniae, Moraxella catarrhalis

- 15 – 20% by bacterial viral co-infections

Guideline recommendation of vaccine in CRD

GOLD 2025

| Vaccine | Dosing and indication |
|--|--|
| Influenza | All: Annually |
| Pneumococcal PCV 20/21 or PCV 15 → PPSV 23 | All: Once PPSV23 administered 1 year after PCV15 (or ≥8 weeks) |
| COVID 19 | All: 2 doses Immunocompromised: 3 doses |
| RSV | Age > 60 yrs: Once |
| Pertussis | All, if not vaccinated in adolescence: Once, every 10 years |
| VZV | Age > 50: 2 doses, 6 months apart |

GINA 2025

- Annual influenza vaccine for moderate and severe asthma
- Follow local guideline for pneumococcal, RSV, COVID vaccines

Pneumococcal vaccine

Burden

- 10-30 % of all bacterial pneumonia
- **Serotype 3** - leading cause (35.1%) of IPD in Europe
- Incidence of Pneumococcal pneumonia in adults with CRD: 7.7-fold high v/s no comorbidity
- 20-fold higher incidence of CAP in COPD v/s general population (22.4 v/s 1.07–1.2 per 1,000 person-years)

| Features | Polysaccharide Vaccine | Conjugate vaccine |
|--|---|--|
| Composition | Contains polysaccharide antigen | Polysaccharide antigen + carrier protein |
| Immune response | T cell independent | T cell dependent and immunological memory |
| Stimulation of antibodies in healthy | Yes | Yes |
| Stimulation of antibodies in immunocompromised | +/- | +/- |
| Antibodies are long lasting | +/- | +/- |
| Primes immunologically for enhanced responses | No | Yes |
| Nasopharyngeal carriage | No reduction in nasopharyngeal carriage | Reduces nasopharyngeal carriage |
| Herd effect | No | Yes |
| Pneumococcal disease burden | No significant impact | Decrease |
| Efficacy(IPD/NBP) | Reduction in IPD ; Unclear efficacy – NBP | Yes(IPD and NBP) |

Recommendation – ACIP 2025

Adults ≥50 years old

Complete pneumococcal vaccine schedules

| Prior vaccines | Option A | Option B |
|---|--|---------------------------|
| None* | PCV20 or PCV21 | PCV15 → ≥1 year → PPSV23† |
| PCV15 only at any age | → ≥1 year → PPSV23† | NO OPTION B |
| PCV15 & PPSV23 OR PCV20 OR PCV21 at any age | No vaccines recommended; schedule is complete. | |
| PPSV23 only at any age | → ≥1 year → PCV20 or PCV21 | → ≥1 year → PCV15 |
| PCV13 only at any age | → ≥1 year → PCV20 or PCV21 | NO OPTION B |
| PCV13 at any age & PPSV23 at <65 yrs | → ≥5 years → PCV20 or PCV21 | |

In India: PCV13 instead of 15

Immunocompromised, CSF leak, cochlear implant: 8 weeks b/w PCV and PPSV

18-49 years: same except no vaccine if full schedule completed

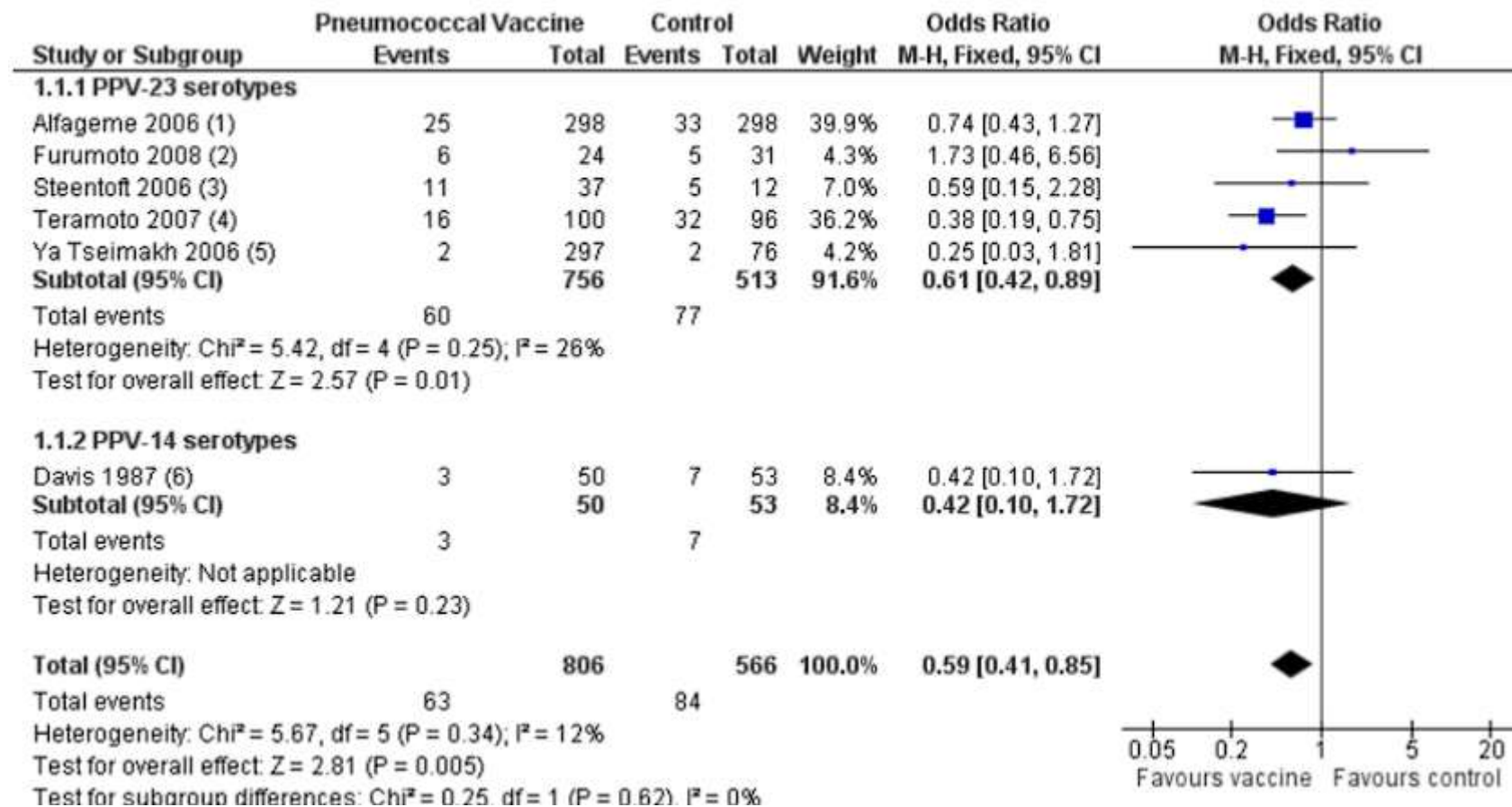
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| PCV15 & PPSV23 OR PCV20 OR PCV21 at any age | No vaccines recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 50 years old. | |
| PPSV23 only at any age | → ≥1 year → PCV20 or PCV21 | → ≥1 year → PCV15 |
| PCV13† only at any age | → ≥1 year → PCV20 or PCV21 | NO OPTION B |
| PCV13† and PPSV23 at any age | No vaccines are recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 50 years old. | |

Chronic health conditions:

- Alcoholism
- Cigarette smoking
- Chronic lung disease
- Chronic heart disease
- Chronic liver disease
- Diabetes mellitus

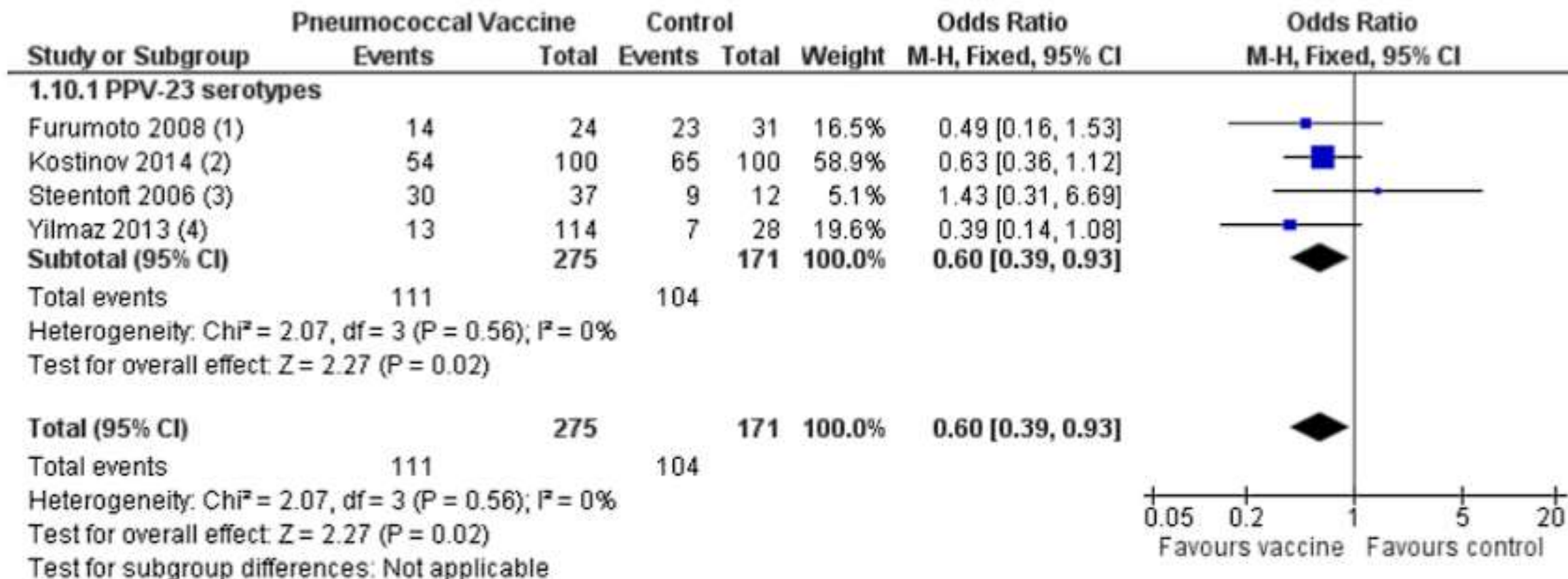
Effectiveness in COPD:

- Cochrane review: Pneumococcal vaccine in COPD
- Total RCTs: 12 trials, with 2,171 participants
- Vaccine types: PPSV23, PPSV14 (3) vs placebo 1 study PPSV14 vs PPSV23
- Follow up: 6 to 36 months
- **Primary outcome: Community-Acquired Pneumonia:** OR \approx **0.59** (95% CI: 0.41 to 0.85) in 6 studies; n = 1,372
- **Secondary: COPD exacerbations:** Vaccination reduced odds: OR \approx **0.60** (95% CI: 0.39 to 0.93); 4 studies, n = 446
- No significant difference in Pneumococcal pneumonia, all cause and cardiorespiratory mortality and hospitalization rate



Community acquired pneumonia, Pneumococcal vs control

Exacerbation of COPD, Pneumococcal vaccine vs control



Hospitalization in COPD

| | |
|---------------------------------|---|
| Study | Figueira Gonçalves et al. (2017) Impact of PCV13 on exacerbations in COPD |
| Study design | Prospective observational cohort, 3-year follow-up |
| Population | N = 121 COPD patients with FEV ₁ ≤ 65% predicted, age >40 Vaccinated proportion: 36% |
| Intervention | PCV13 vaccination vs no PCV13 |
| Baseline characteristics | <ul style="list-style-type: none"> • FEV₁ 46.6 ± 11.5 % predicted • Comorbidities: 58.7% cardiovascular disease, 53.7% respiratory comorbidity, 24% diabetes |
| Outcomes | <ul style="list-style-type: none"> • 68% ≥1 exacerbation during 18 mo follow-up • Hospitalization rate in vaccinated: 18% vs 32% • aOR for hospitalization in non-vaccinated vs vaccinated - 2.77 (p = 0.044) • No significant difference in number of exacerbations or deaths between vaccinated and unvaccinated |

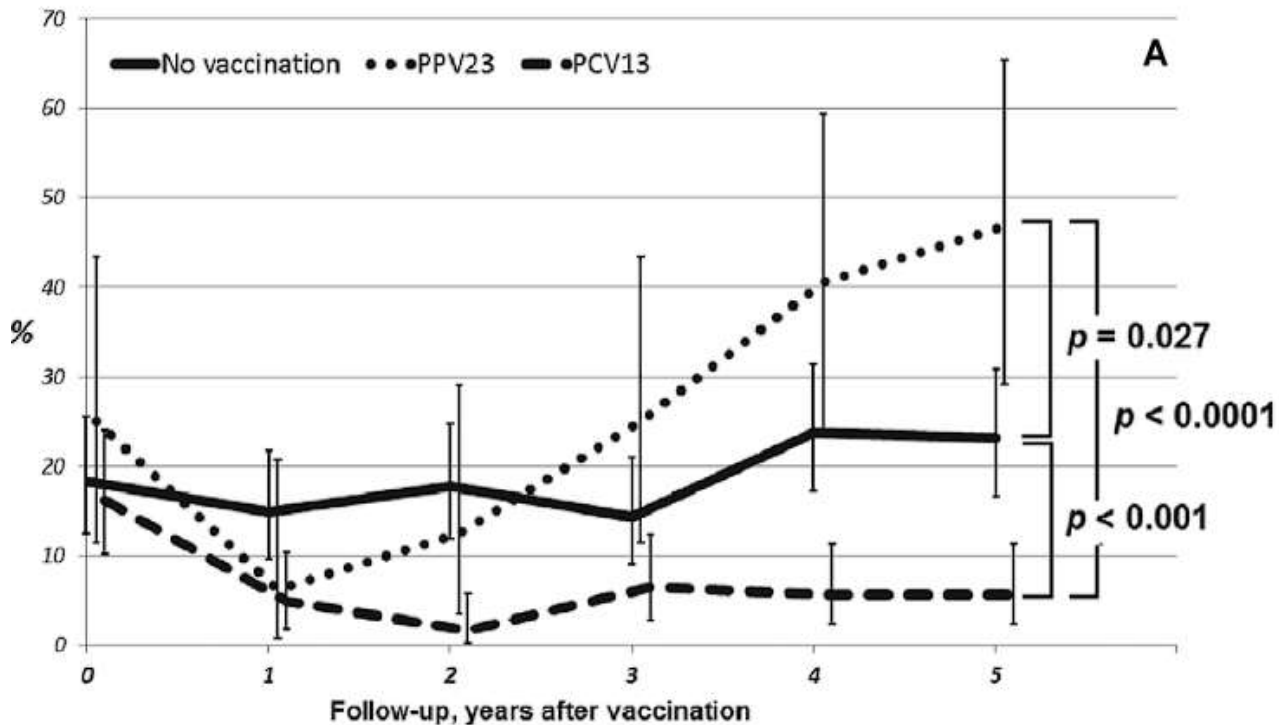
| Table 2 | | Difference between PCV13 vaccinated and non-vaccinated COPD patients during the 18-month follow up | | |
|--|-------------------|---|--------------------|--|
| | Vaccinated (n=44) | Non-vaccinated (n=77) | p | |
| No. exacerbations Median [P25-P75] | 1 [0 - 1] | 1 [0 - 2] | 0.171 ^a | |
| No. exacerbation % (n) | 61.4% (27) | 68.8% (53) | 0.404 ^b | |
| Hospital admission % (n) | 18.2% (8) | 32.2% (25) | 0.067 ^c | |
| Death % (n) | 25.0% (11) | 21.0% (16) | 0.592 ^b | |

| Table 3 | | Multivariate logistic regression analysis of the risk of hospital admission | | | |
|--------------------------------|------|--|-------|-------|--|
| | OR | CI 95% | Wald | p | |
| No. vaccinated | 2.77 | 1.03-7.50 | 4.043 | 0.044 | |
| Frequent-exacerbator phenotype | 6.30 | 2.44-16.30 | 14.42 | 0.001 | |

PCV13 vs PPSV23 in COPD

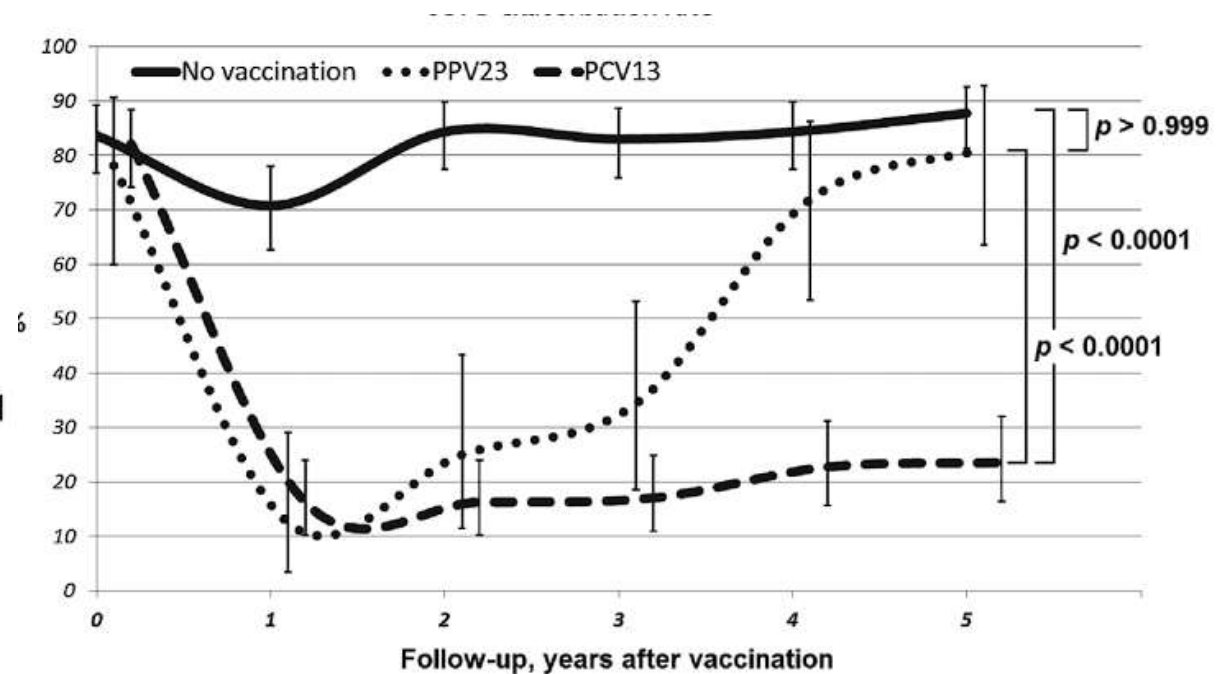
| | |
|---------------------------------|---|
| Study design | Open-label, prospective observational cohort, 5-year follow-up In Russia 2012 |
| Population | Males \geq 45 years; PCV13 group n = 150, PPSV23 group n = 32, vaccine-naïve n = 147 Other lung disease excluded, O2 therapy |
| Intervention | PCV13 (150) vs PPSV23 (32) vs no vaccination (147) |
| Baseline characteristics | <ul style="list-style-type: none">• All male; \geq45 years• Before vaccination, hospitalization due to exacerbations > 90% |

Pneumonia by 5 yr



Upto 2 yr reduced in both
 At 5 yr: 5: 47% in PPV23 group vs **3.3%** in PCV13 group
 ($p < 0.001$)
 More than control group

COPD exacerbation by 5 yr



At 1 yr both reduced
 PPSV23 declining from 2nd yr
 At 5 yr: 81.3% in PPV23 vs **23.6%** in PCV13 ($p < 0.001$)

Evidence in Asthma

| Study | Pandit S. 2023 (Systematic Review & Meta-analysis) | Lee TA et al. 2007 (Cohort Study) |
|--------------|--|--|
| Study type | 1 RCT + 2 cohort studies in asthma (children + adults) | Retrospective cohort study using VA database |
| Population | n = small (1 RCT - 100; 2 cohorts, 2890) Mixed severity, mostly mild–moderate | 2,746 asthma patients most adults (mean age -53 yrs) Controls: 1,345 patients |
| Intervention | Pneumococcal vaccination (PCV or PPSV) vs no vaccine Follow up 2-3 years | PPSV23 (23-valent polysaccharide vaccine) vs control 5 years |
| Outcomes | Hospitalization rate ↓ from 49.6 → 17.8 /100 p-yrs post-vaccination Pneumonia (all-cause) aRR = 0.79 (95% CI 0.50–1.25) Pneumococcal pneumonia aRR = 0.30 (95% CI 0.04–1.99) Asthma control: 93.2% vs 80.8% (vaccinated vs unvaccinated), p=0.08 | All pneumonia hosp. rate ↓ 1.27 → 1.11 /100 p-yrs Pneumococcal pneumonia hosp. rate ↓ 0.09 → 0.03 /100 p-yrs post-vaccination aRR: 0.76 (95% CI 0.17 to 3.53) → 0.30 (95% CI 0.04 to 1.99) |

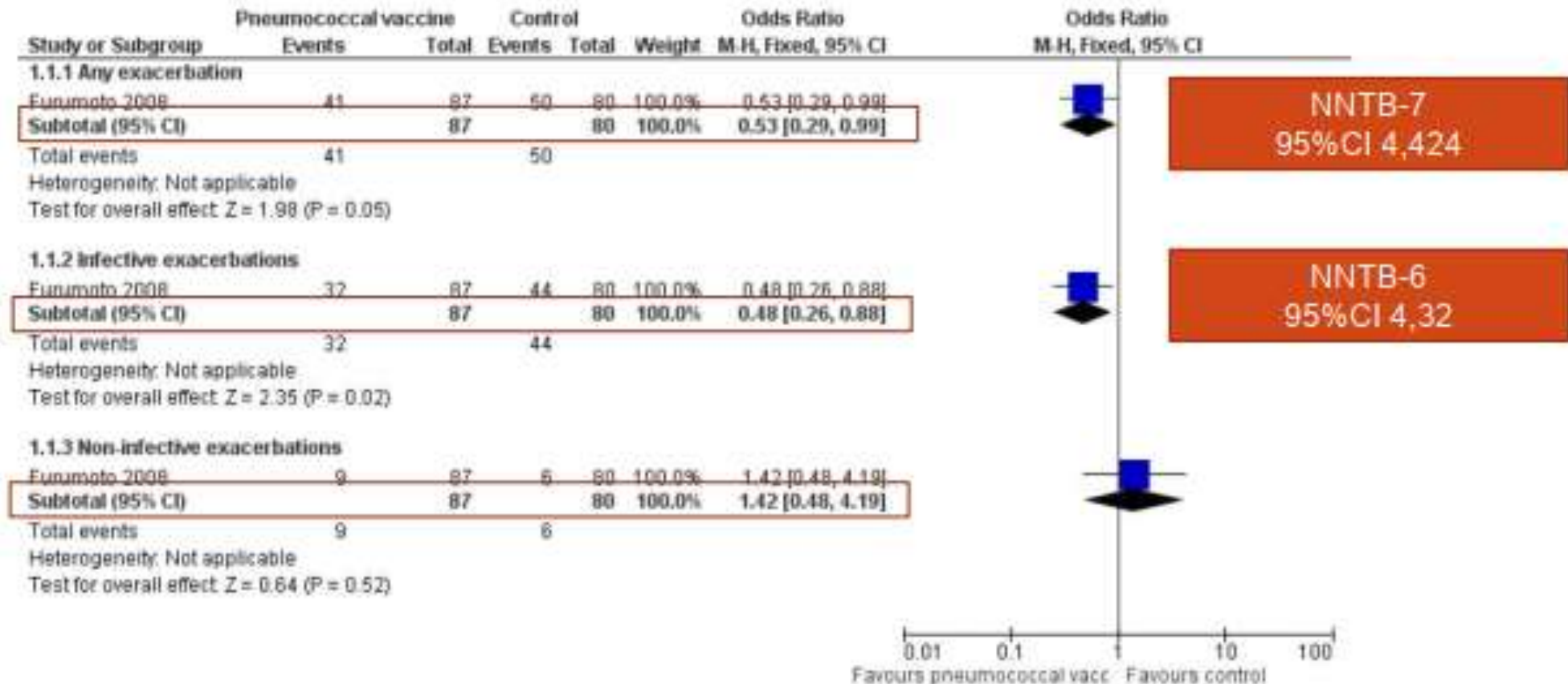
Reduced pneumonia risk and hospitalization
But wide CI

In bronchiectasis

Cochrane review: RCT-1, n=167 adults(COPD -55,Bronchiectasis -20, sequelae of pulmonary TB-50)

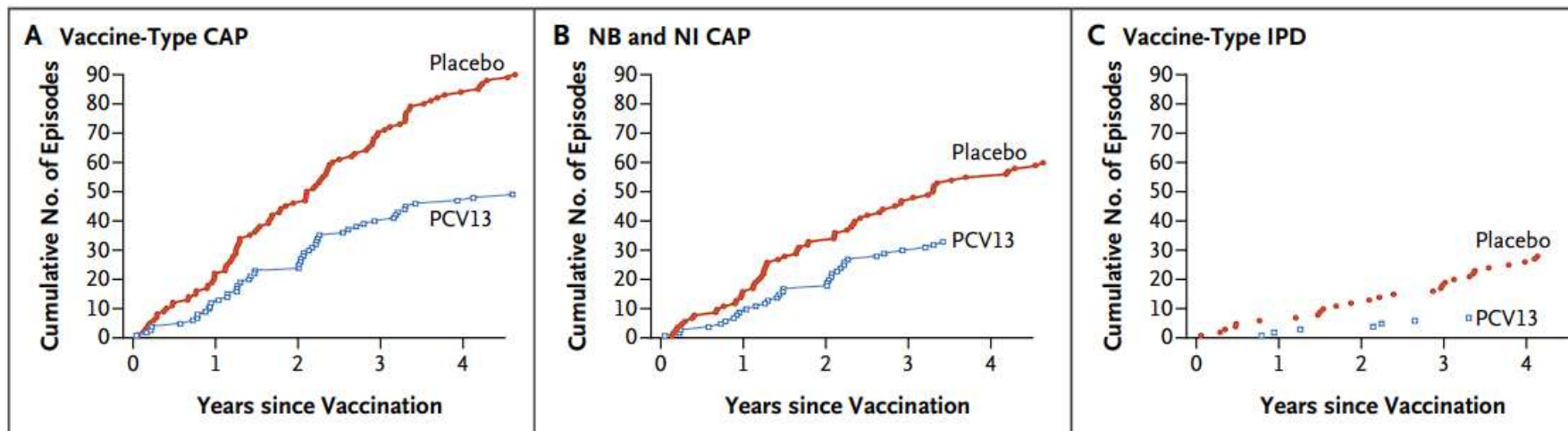
Intervention – PV23 +Influenza (80) vs IV (80)

Follow up – 2yrs



Efficacy of PCV13 in adults – CAPITA trial

| | |
|-------------------------|--|
| Feature | CAPITA (PCV13) |
| Study Design | Double-blind, placebo-controlled, randomized trial |
| Population | Adults aged ≥ 65 years 85,000 participants, 4 years follow up IC state excluded |
| Intervention | PCV13 vs placebo single dose |
| Primary Endpoint | First episode of vaccine-type (VT) nonbacteremic/noninvasive CAP |
| Outcome | - 45.6% efficacy in preventing first episode of VT nonbacteremic/noninvasive CAP - 45.0% efficacy in preventing first episode of VT bacteremic/invasive CAP - 75.0% efficacy in preventing first episode of VT invasive pneumococcal disease |



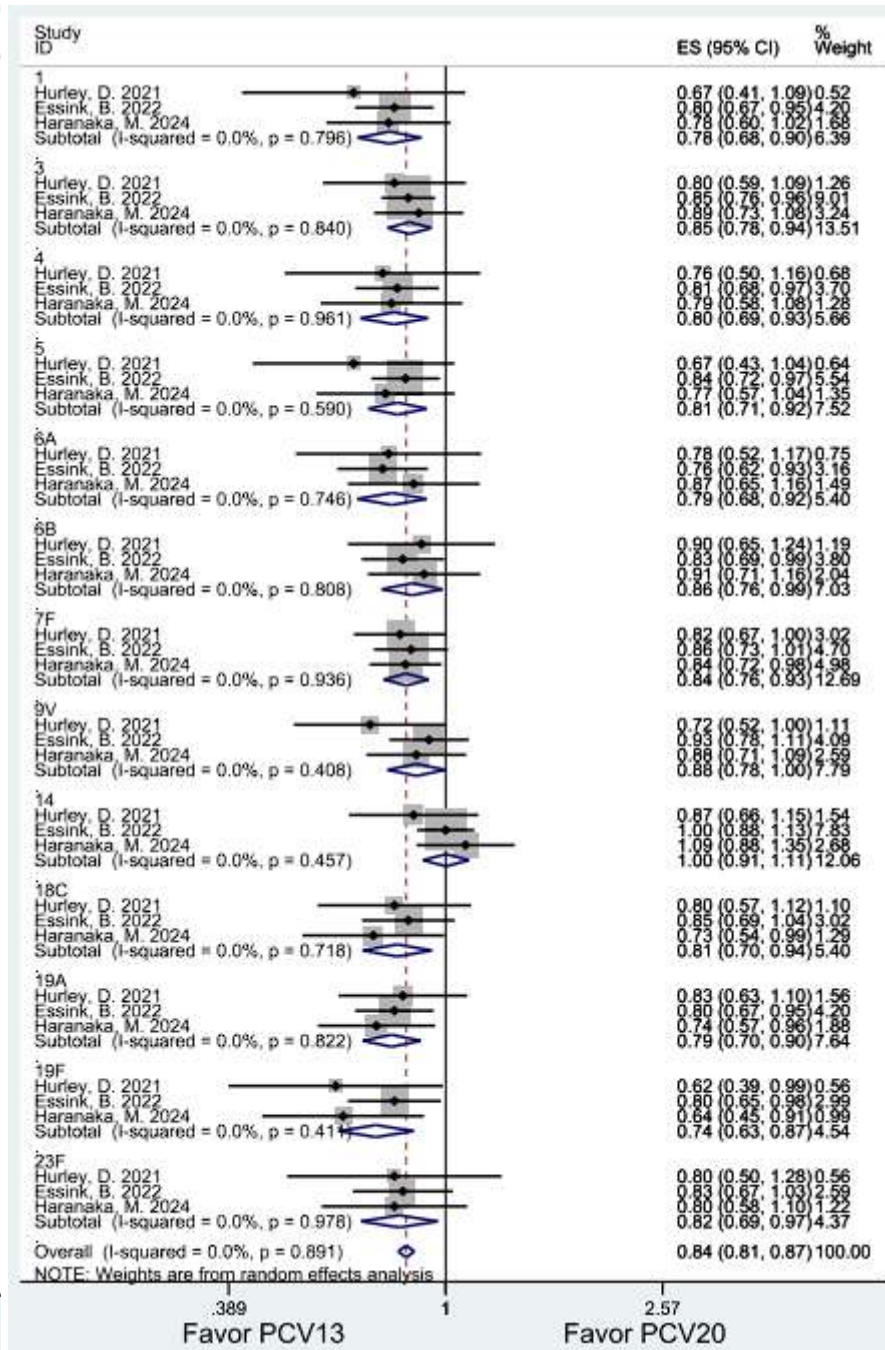
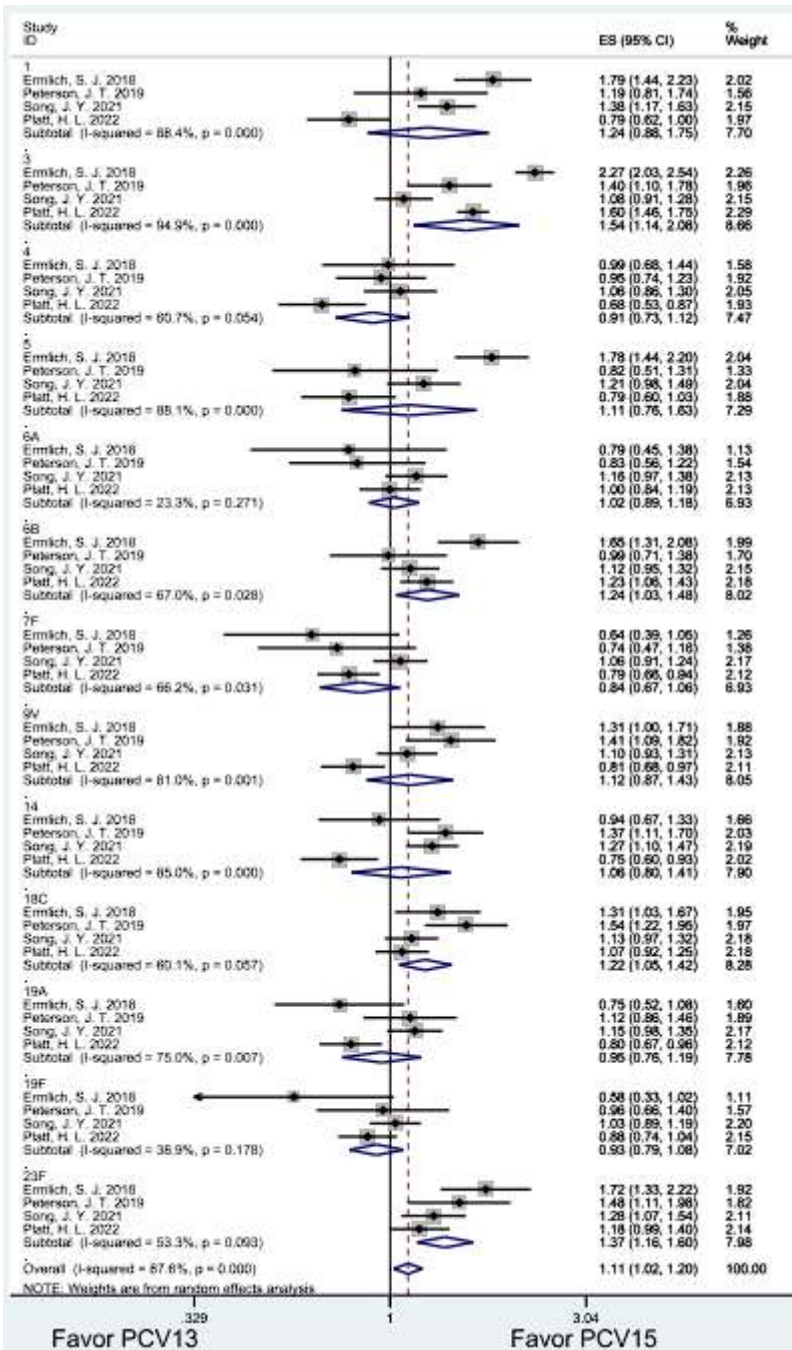
Effect starts early and persist throughout follow-up

Evidence for newer vaccines?

- Comparative immunogenicity of PCV15 and 20 with PCV13
- Meta analysis in 2025 comparing PCV 15, 20 vs PCV13
- Immunogenicity at 1 month post vaccination
- 8 RCTs, PCV15 vs PCV13 (n = 4) and PCV20 vs PCV13 (n = 3 for immunogenicity)

| Intervention: Study | Countries | Vaccine Naive | | | Preexisting Medical Conditions per Group, % | | Death, No. (%) | |
|------------------------|--------------------------|---------------|-----------------|---|--|----------------|-------------------|---------|
| | | PCV13 | PPSV23 | Age Group, y | PCV15 or PCV20 | PCV13 | PCV15 or PCV20 | PCV13 |
| PCV15 | | | | | | | | |
| Ermlich [6] | Multination ^a | Yes | Yes | ≥50 | 72/230 (31.3) | 90/230 (39.1) | 0 | 0 |
| Peterson [7] | USA | Yes | No | ≥65 | NA/127 | NA/126 | 0 | 0 |
| Song [18] | Multination ^b | Yes | Yes | ≥50 | 302/326 (92.6) | 305/325 (93.8) | 0 | 0 |
| Platt [19] | Multination ^c | Yes | Yes | ≥50 | 528/602 (87.7) | 522/600 (87.0) | 1 (0.2) | 1 (0.2) |
| PCV20 | | | | | | | | |
| Cannon [10] | USA, Sweden | Yes | No ^d | ≥65 | NA/253 | NA/122 | 0 | 0 |
| Hurley [14] | USA | Yes | Yes | 60–64 | NA/221 | NA/222 | 0 | 0 |
| Essink [8] | USA, Sweden | Yes | Yes | ≥60 ^e ; 50–59, ≥60 ^f | NA/1514 | NA/1495 | 1 | 0 |
| Haranaka [9] | Multination ^a | Yes | Yes | ≥60 | 310/711 (43.6) | 314/710 (44.2) | 0 | 0 |

- 50 yrs, immunocompetent
- Single dose PCV20/15 vs PCV13



- PCV 15: superior
- Overall GMTR: **1.11** (95% CI: 1.02–1.20)
Serotype 3, 23F larger difference
- PCV20: Although GMTRs were lower than PCV13 for many shared serotypes, the lower limit of CI stayed above the noninferiority threshold (0.5)

Why the sequence of PCV13 → PPSV23?

- Immunogenicity and safety of PCV13 compared to PPSV23 in pneumococcal vaccine-naïve adults
- Open label study, >65 yrs vaccine naïve in Japan
- Excluded: malignancy, ESRD, immunosuppression
- PCV13 → PPSV23 after 0.5 yr (n-43) vs PCV13 → PPSV23 after 1 yr(n-40) vs PPSV23 single dose (n-46)
- Higher OPA in 1 yr interval vs 0.5 yr
- More immunogenicity

GMFRs of OPA 1 month after administration of PPSV23 between the 0.5-y interval group and the 1.0-y interval.

| | The 0.5-y interval | | Pre vs Post |
|-----|---|--|-------------------|
| | Pre PPSV23 (n = 35) GMFR from baseline (95 %CI) | Post PPSV23 (n = 35) GMFR from baseline (95 %CI) | P value |
| 3 | 3.12 (1.53,6.39) | 8.17 (3.87, 17.26) | 0.001 |
| 4 | 7.23 (3.08, 16.94) | 8.22 (3.24,20.89) | 0.0484 |
| 6B | 7.47 (4.15,13.45) | 8.93 (4.97,16.05) | 0.0548 |
| 9V | 3.65 (1.71, 7.79) | 4.99 (2.42,10.30) | 0.1478 |
| 14 | 4.12 (2.28, 7.47) | 5.06 (3.00, 8.53) | 0.1965 |
| 19A | 6.54 (3.29, 12.97) | 10.85 (5.45, 21.61) | 0.011 |
| 19F | 5.15 (2.25,11.78) | 8.39 (3.71,18.99) | 0.0025 |
| 23F | 14.06 (6.74, 31.86) | 17.78 (8.44, 37.46) | 0.5888 |
| | The 1.0-y interval | | Pre vs Post |
| | Pre PPSV23 (n = 35) GMFR from baseline (95 %CI) | Post PPSV23 (n = 35) GMFR from baseline (95 %CI) | P value |
| 3 | 3.26 (1.42,7.50) | 12.30 (5.89, 25.67) | 0.001 |
| 4 | 5.87 (2.12, 16.23) | 10.13 (3.08, 33.39) | <0.0001 |
| 6B | 10.39 (4.72, 22.87) | 22.09 (10.67, 45.76) | <0.0001 |
| 9V | 1.46 (0.73, 2.92) | 2.97 (1.48, 5.81) | 0.0033 |
| 14 | 5.78 (2.70,12.38) | 10.11 (4.72, 21.67) | 0.0009 |
| 19A | 8.57 (4.50,16.35) | 14.22 (8.05,25.12) | 0.0249 |
| 19F | 5.35 (2.43, 11.75) | 11.03 (5.94, 20.50) | 0.0343 |
| 23F | 11.66 (4.77,28.46) | 24.44 (10.59,56.42) | 0.0003 |

Why interval of 8 weeks in immunocompromised?

- No direct study comparing 8 weeks vs 1 yr interval
- Evidence is from small RCTs and immunogenicity studies
- One RCT in HIV patients showed superior serotype specific OPA responses in sequential PCV13 → PPSV23 at 8 weeks compared to PPSV23 alone
- ACIP evidence statement 2014:
- No immunologic advantage in delaying PPSV23 to 1 year in immunocompromised patients
- Early administration at 8 weeks - better antibody titers and more rapid protection

Why age cutoff reduced to 50yrs?

- In 2019, IPD incidence per 100,000 population:
 - 19–49 y: 4.6
 - 50–64 y: 15.7
 - ≥ 65 y: 23.7
- All-cause pneumonia incidence per 100,000 population:
 - 19–49 y: 953
 - 50–64 y: 2,679
 - ≥ 65 y: 6,930
- Immunogenicity evidence in ≥ 50 age is favorable
- Availability of newer vaccines with broader coverage
- To simplify vaccine recommendations

Influenza vaccine

Influenza - burden

- 3–5 million cases/yr of severe illness caused by seasonal influenza in the world
- In US as per CDC (2010 to 2017): 1.4 to 7 lac hospitalizations
- In India: Influenza hospitalization – 46.8/10000 patients; CFR – 7.6%
- 30% of infective COPD exacerbation is by viruses
- Influenza virus second most common virus associated with AECOPD (prevalence 2.5 – 11.6%)
- A meta-analysis comparing HIC and LMIC: higher hospitalizations in chronic lung disease (pRR 1.96; CI: 1.73-2.23) and higher severe outcomes (pRR 1.53; CI: 1.33-1.76)

Krammer et al Nature Reviews Disease Primers 2018

Mohan Anant et al Respiriology. 2010 Apr

Chadha Mandeep et al PLoS One. 2013 May 15

Chatterjee et al American Journal of Respiratory and Critical Care Medicine 2018

Influenza outcomes risk factors PMID:29197154

TIV vs QIV

- Trivalent influenza vaccine:
 - Egg-based vaccines
 - A/Victoria/4897/2022 (H1N1)pdm09-like virus
 - A/Croatia/10136RV/2023 (H3N2)
 - B/Austria/1359417/2021 (B/Victoria lineage)-like virus
 - Cell culture, recombinant protein or nucleic acid:
 - A/Wisconsin/67/2022 (H1N1)
 - A/District of Columbia/27/2023 (H3N2)
 - B/Austria/1359417/2021 (B/Victoria lineage)-like virus
- Quadrivalent influenza vaccine:
 - B/Phuket/3073/2013 (B/Yamagata lineage)-like virus
- Southern hemisphere QIV recommended in India by NCDC (Victoria, Thailand, Austria and Phuket)

Vaccine types

| Vaccines | Standard-dose IIV | High-dose IIV | Adjuvanted IIV | Recombinant (RIV) | LAIV |
|--------------------------|---|---|---|---|--|
| Antigen Content | 15 µg HA/strain | 60 µg | 15 µg + MF59 adjuvant | 45 µg HA | LA influenza viruses (not quantified as µg) |
| Dose | ≥36 mo: 0.5 mL 6–35 mo: 0.25–0.5 mL; annually | 0.5 mL IM annually | 0.5 mL IM annually | 0.5 mL IM annually | 0.2 mL intranasal spray (0.1 mL per nostril) annually |
| Approved Age | ≥6 months | ≥65 years | ≥65 years | ≥18 years | 2–49 years (not widely used/approved in India) |
| Contraindications | Severe allergy, acute illness GBS within 6 wks Egg allergy precautions | Same as standard IIV; higher rate of local/systemic reactions | Same as IIV; caution in immunocompromised | Severe allergy to components (egg-free advantage) | Immunocompromised, pregnancy, <2 or >49 yrs, chronic respiratory conditions, concurrent antivirals |
| Co-administration | Yes | Yes | Yes | Yes | Yes (with other live vaccine simultaneously, or 4 weeks apart) |

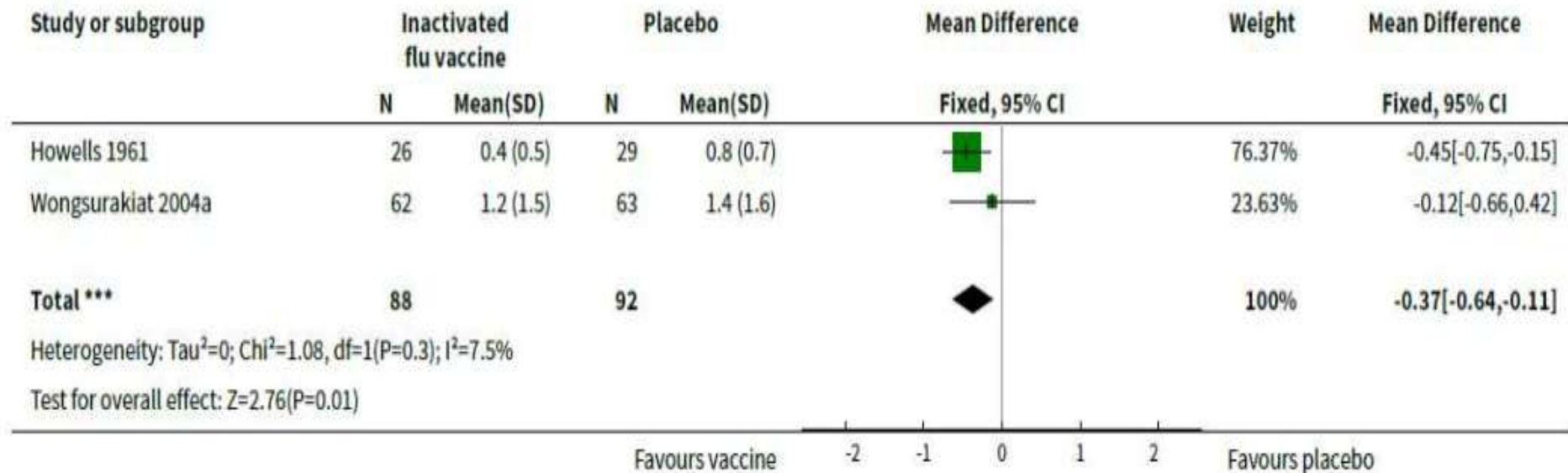
India: SD and LAIV available

Recommendation

| Guideline | Indications | Vaccine Type | Dose & Schedule | Special population |
|---|--|---|--|--|
| ACIP / CDC 2025 | All ≥ 6 months: annually Priority: COPD, asthma, chronic diseases, immunosuppression, pregnancy, HCWs | QIV (IIV4)- Recombinant (RIV4)- Adjuvanted (aIIV4)- LAIV4 Strain: Northern vs southern hemisphere | 0.5 mL IM (single annual dose) Annual revaccination ≥ 65 yrs: HD-IIV4 or RIV4 or aIIV4 preferred | Pregnancy: safe any trimester LAIV contraindicated in asthma, immunosuppression, pregnancy Annual strain update by WHO |
| Lung India / ICS-NCCP (India) 2019 | Adults > 50 yrs, 18 to 49 yrs with High-risk: COPD, asthma, diabetes, cardiac disease, immunosuppressed Pregnancy Travelers | Quadrivalent IIV preferred | 0.5 mL IM (single annual dose) Timing: Sept–Oct (temperate) Apr–May (monsoon regions) | Regional seasonality and strain updated by WHO and NCDC Southern hemisphere strains preferred |

Evidence in COPD

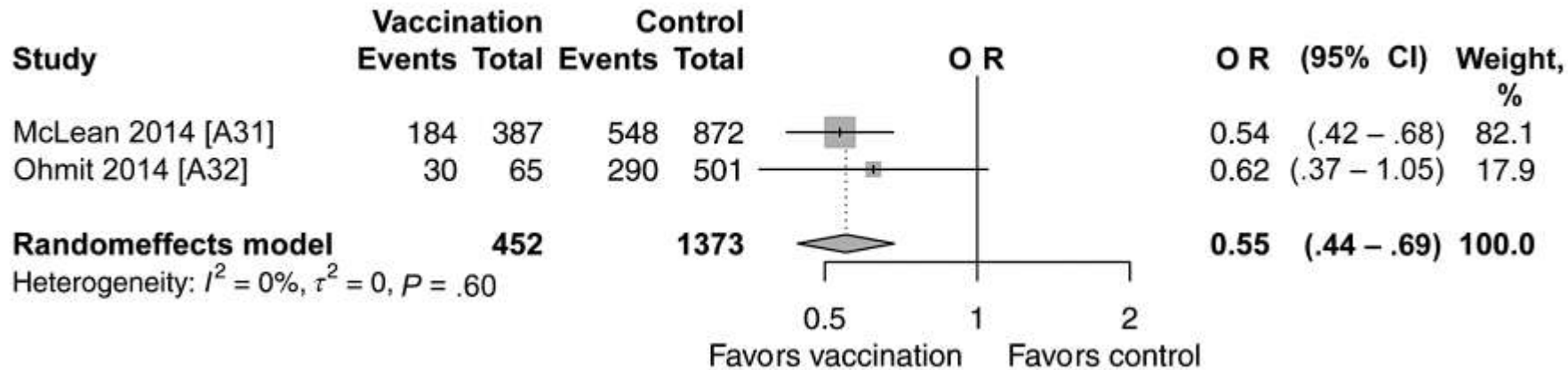
- Cochrane review and meta-analysis:
- Included study that compared live or inactivated virus vaccines with placebo, either alone or with another vaccine, in people with COPD
- 11 RCTs (6 studies people with COPD, n=2469)
- Intervention: LAIV -4; IIV -2; LAIV +IIV v/s IIV -2
- Outcome: COPD exacerbation – significant, no mortality benefit



Total exacerbations per participant (2RCT, N=180)

Asthma exacerbation

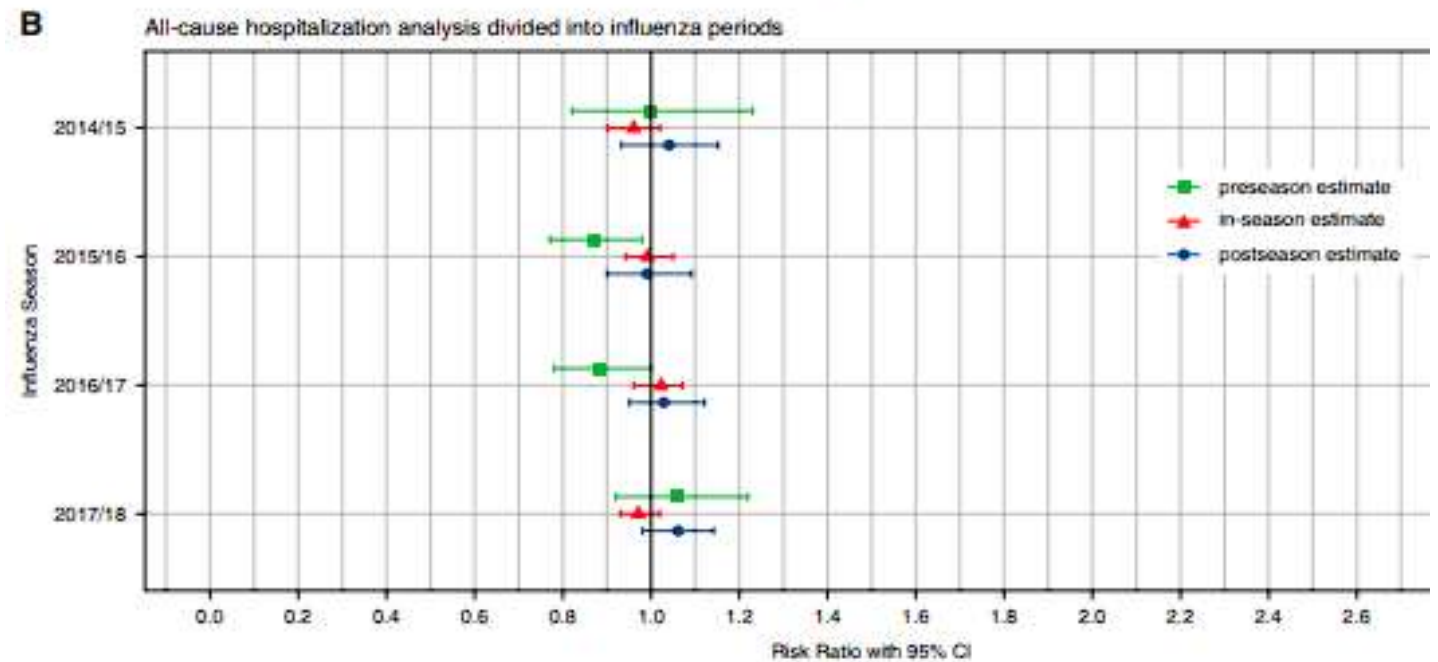
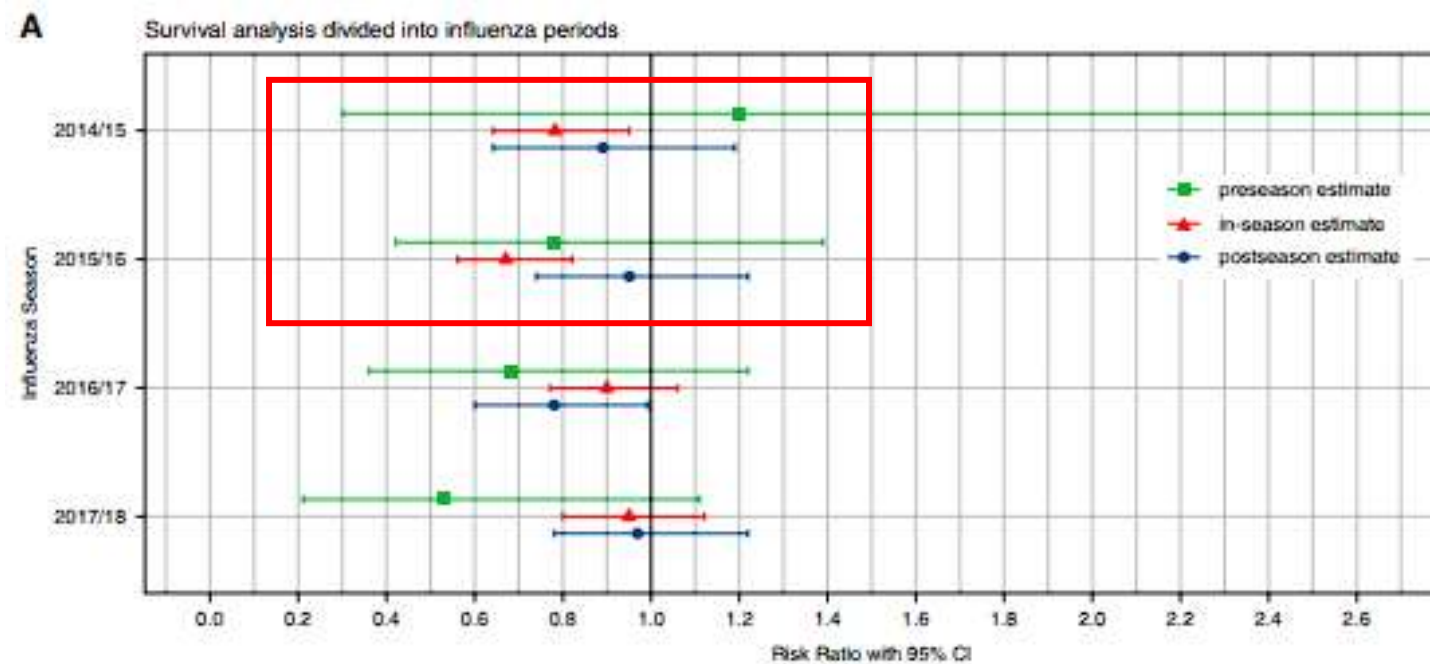
| Title & Author | Population | Intervention | Outcomes |
|--|---|---|--|
| Effectiveness of Influenza Vaccines in Asthma: A Systematic Review and Meta-Analysis Eleftheria et al 2017 | 35 studies, N = 142519 RCTs – 20, remaining analytical Asthma patients | Seasonal influenza vaccine (IIV or LAIV 1 study) | <ul style="list-style-type: none"> 1 RCT + 3 observational: Incidence of acute asthma attacks lower in vaccinated RR 0.73 (0.57–0.95) 6 studies preventing hospitalizations: RCT: duration of hospitalization for ILI alone (P < .01) and ILI accompanied by asthma (P < .05) was significantly shorter than unvaccinated Observational: No. hospitalizations was 0.2 in IIV and 1.3 in controls (P < .001) |



2 TND – pooled VE for lab confirmed influenza in 1825 asthma patients

Evidence in ILD

- Epidemiologic claims data analysis study in 2022, Germany
- 4 influenza seasons: 7,503 patients in 2014–2015, 10,318 in 2015–2016, 12,723 in 2016–2017, and 13,927 in 2017–2018 both cohorts
- Total 87477 ILD patients, vaccinated to IIV vs not and followed up through influenza season for mortality or hospitalisation



Other recommendations

- Age >65 years: HD IIV and rIIV preferred
- Travelers – 2 weeks
- Other vaccines
 - IIV3s and RIV3 - simultaneously or sequentially with other inactivated vaccines or live vaccines but at different anatomic site
 - LAIV3 - simultaneously or sequentially with other inactivated vaccines or live vaccines. If not given simultaneously then 4 weeks gap

RSV vaccine

RSV burden and CRD

- Annual RSV infection: 3%–7% in healthy adults; 4%–10 % in adults with chronic cardiopulmonary disease
- In adults >50 years, more hospitalization and mortality:
 - Hospitalization rate (per 100,000): 50–64 yrs: 20–40, 65–74 yrs: 50–100, ≥75 yrs: 150–200
 - Case fatality rate in adult with comorbidities: 11.7 % (95 % CI = 5.8%–23.4 %) vs 1.6 % (95 % CI = 0.7%–3.8 %)
- A study in UK among 377 COPD patients with 310 exacerbation events showed 8.7% of RSV associated COPD exacerbation

Current RSV vaccine recommendation

AICP/ CDC 2025:

- Single dose of any FDA approved RSV vaccine
- **All adults ≥ 75 years and**
- Adults aged 60–74 years with increased risk for **severe RSV disease**

BOX. Risk factors for severe respiratory syncytial virus disease among adults aged 60–74 years*

- Chronic cardiovascular disease (e.g., heart failure, coronary artery disease, or congenital heart disease [excluding isolated hypertension])
- **Chronic lung or respiratory disease (e.g., chronic obstructive pulmonary disease, emphysema, asthma, interstitial lung disease, or cystic fibrosis)**
- End-stage renal disease or dependence on hemodialysis or other renal replacement therapy
- Diabetes mellitus complicated by chronic kidney disease, neuropathy, retinopathy, or other end-organ damage, or requiring treatment with insulin or sodium-glucose cotransporter-2 (SGLT2) inhibitor
- Neurologic or neuromuscular conditions causing impaired airway clearance or respiratory muscle weakness (e.g., poststroke dysphagia, amyotrophic lateral sclerosis, or muscular dystrophy [excluding history of stroke without impaired airway clearance])
- Chronic liver disease (e.g., cirrhosis)
- Chronic hematologic conditions (e.g., sickle cell disease or thalassemia)
- Severe obesity (body mass index ≥ 40 kg/m²)
- Moderate or severe immune compromise[†]
- Residence in a nursing home

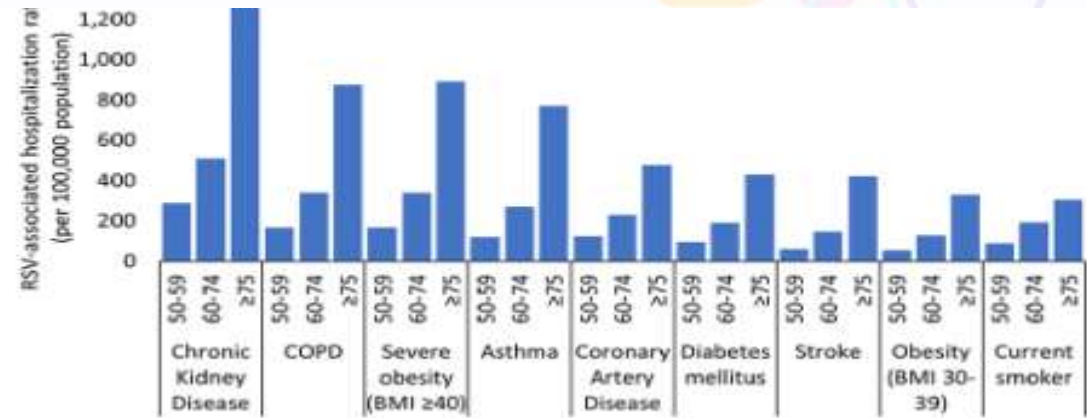
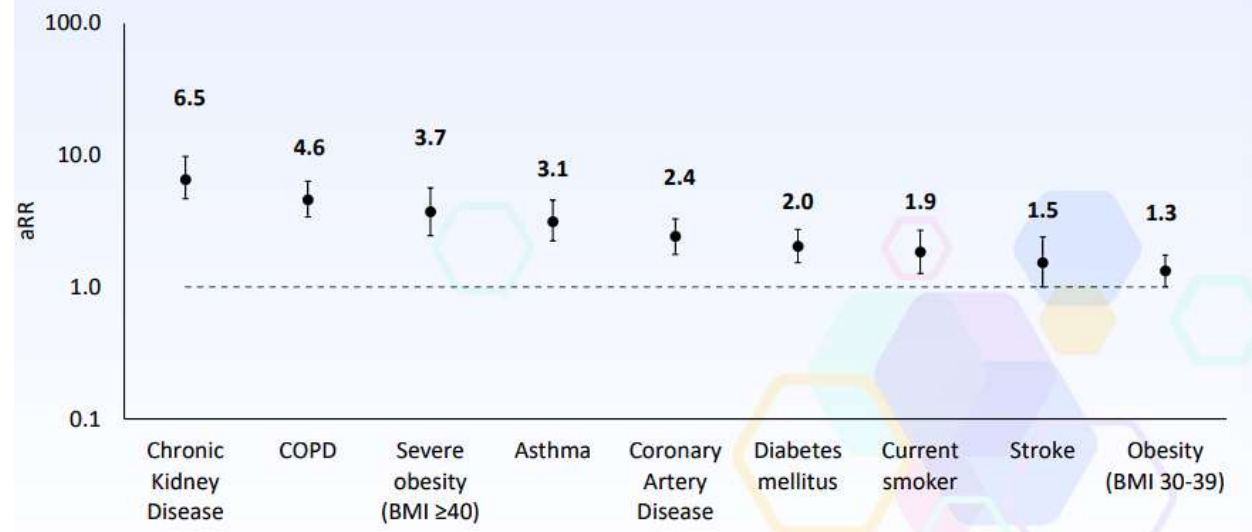
Risk factors for severe RSV disease

- Among 1,692 adults ≥ 50 hospitalized with RSV in 2017-18 season:

| | aRR (95% CI) ¹ |
|--|---------------------------|
| No. of chronic conditions² | |
| 0 | ref |
| 1 | 2.1 (1.4, 3.2) |
| ≥ 2 | 7.3 (5.0, 10.6) |
| Age group, years | |
| 50-59 | ref |
| 60-74 | 1.9 (1.3, 2.7) |
| ≥ 75 | 6.0 (4.2, 8.6) |
| Race or ethnicity group | |
| White, non-Hispanic | ref |
| Black, non-Hispanic | 1.1 (0.8, 1.5) |
| Other race or Hispanic ethnicity | 1.7 (1.3, 2.5) |
| Sex | |
| Male | Ref |
| Female | 1.3 (1.0, 1.6) |

H/o ≥ 2 chronic conditions, age ≥ 75 years - strongest independent risk factors for RSV-associated hospitalization.

Adjusted Rate Ratios for RSV-Associated Hospitalization by Chronic Condition among Community-Dwelling Adults Aged ≥ 50 Years



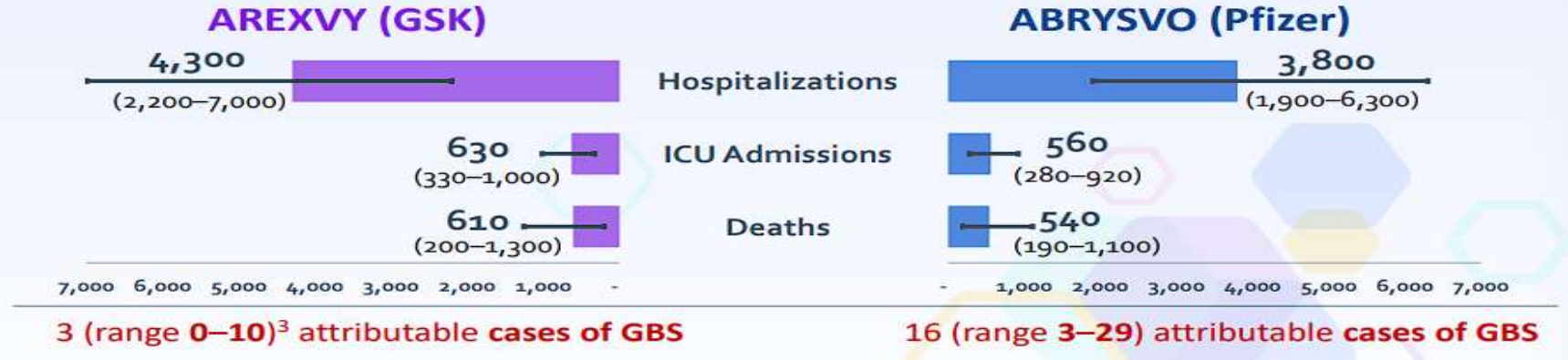
Evidence for RSV vaccines

| Vaccine | Population | Intervention | Efficacy | Durability | Safety / AEs |
|--|--|---|---|--|--|
| Arexvy (GSK) Recombinant monovalent (RSV A, adjuvanted with AS01E) | Adults ≥60 yrs I: 12,467 P: 2,499 | Phase 3, RCT Single dose vs placebo Followed for at least 2 seasons | <ul style="list-style-type: none"> • 82.6% overall LRTD • 81% (60–69 yrs) • 93.8% (70–79 yrs) • 94.6% (≥1 comorbidity) | 67.2% over 2 seasons, 62.9% over 3 seasons | Local/systemic mild–moderate; rare atrial fibrillation (10 vs 4) GBS (1) |
| Abrysvo (Pfizer) Recombinant bivalent (RSV A & B, non-adjuvanted) | Adults ≥60 yrs I: 17,215 P: 17,069 | Phase 3, RCT Single dose vs placebo Followed for at least 2 seasons | <ul style="list-style-type: none"> • 88.9% (≥3 symptoms) • 65.1% (≥2 symptoms) | Sustained across 2 seasons: 81.5% (95% CI: 63.3-91.6) | Well tolerated; rare GBS (2) |
| mResvia (Moderna) mRNA (RSV A pre-F protein) | Adults ≥60 yrs I: 17,479 P: 17,962 | Phase 3, RCT Single dose vs placebo Followed for at least 2 seasons | <ul style="list-style-type: none"> • 80.9% (≥3 symptoms) • 78.7% (≥2 symptoms) at 4 months | At 12 months: 54.9% (30.5-70.7) At 24 months: 36.0% (-12.6-64.3) | Local pain, fatigue, headache; no AF and GBS |

Role in hospitalization, ICU admission and mortality

Estimated RSV-Associated Outcomes¹ Preventable over 2 RSV Seasons vs. potential cases of GBS (*positive predictive value-adjusted* attributable risk of GBS in FDA-CMS partnership data among adults aged ≥65 years, 42-day risk interval²)

Per 1 Million Vaccine Doses Administered to **Adults Aged ≥75 Years:**



Estimated RSV-Associated Outcomes¹ Preventable over 2 RSV Seasons vs. potential cases of GBS (*positive predictive value-adjusted* attributable risk of GBS in FDA-CMS partnership data among adults aged ≥65 years, 42-day risk interval^{2,3})

Per 1 Million Vaccine Doses Administered to **Adults Aged 60–74 Years at Increased Risk of Severe RSV Disease:**



Summary

- All age >75 yrs
- 60 – 75 yrs with risk factor for severe RSV disease
- Single dose RSV vaccine 0.5 ml IM

Gaps:

- No studies in assessing prevention of COPD exacerbation
- Less VE data in < 50 yrs with risk factor for severe RSV disease
- No data about benefit of annual vaccine

Pertussis vaccine

Burden

- Pertussis underdiagnosed in adults → less severe presentation than children
- Higher risk in CRD: Retrospective study (2006-2013) from U.S.,
 - In asthma: RR - **3.96** (3.81–4.16), more in 19-64 yrs age
 - In COPD: RR - **2.53** (2.4-2.7)
 - It also showed higher hospitalization rates in CRD
- Indian study in 250 COPD patients with moderate/severe exacerbations:
 - B. pertussis in 16.1% mild, 45% moderate, 55% severe exacerbation
 - More ICU admission: 55% vs 34.7%, Lower FEV1 (p=0.04)
- Increased risk of exacerbation within 90 days of infection

1. Buck et al Epidemiol. Infect. (2017)
2. Archana et al Monaldi Arch Chest Dis 2025
3. Nager et al, CHEST 2024; 165(6):1352-1361

Efficacy and safety in OAD

- 5 RCTs, 222 adults with OAD on treatment vs 4171 general population
- Booster response rate after 1 month post vaccination:
 - 78.3% for anti-PT, 96.1% for anti-FHA and 92.2% for anti-PRN

Table 2. Immunogenicity in the OAD cohort.

| Age |
|------------------|
| Seroprot |
| Anti-D |
| ≥0.1 IU |
| ≥1.0 IU |
| Anti-T |
| ≥0.1 IU |
| ≥1.0 IU |
| Booster 1 |
| Anti-PT |
| Anti-FHA |
| Anti-PRN |

Table 3. Percentage of adults under active treatment for obstructive airway diseases with anti-PT antibody concentrations ≥5 EU/mL and antibody GMCs by timepoint (according-to-protocol cohort).

| Antibody | Timepoint | N | Seropositivity rate (≥5 EU/mL), % (95% CI) |
|----------|-----------|-----|--|
| Anti-PT | Pre | 209 | 58.4 (51.4; 65.1) |
| | Post | 209 | 95.7 (92.0; 98.0) |
| Anti-FHA | Pre | 208 | 96.6 (93.2; 98.6) |
| | Post | 206 | 100 (98.2; 100) |
| Anti-PRN | Pre | 208 | 70.7 (64.0; 76.8) |
| | Post | 208 | 98.1 (95.1; 99.5) |

- One-month post-vaccination, seropositivity rates - ≥95.7% across the pertussis antigens compared to 58.4%, 96.6% and 70.7% of anti-PT, anti-FHA and anti-PRN pre-vaccination
- Solicited local and systemic AEs were comparable. No exacerbation post vaccination

Summary

- Increased incidence of pertussis in COPD and BA patients and higher risk of exacerbation.
- No RCT comparing efficacy in reduction of exacerbation or mortality
- Immunological response was comparable
- Booster dose decennial in COPD and BA

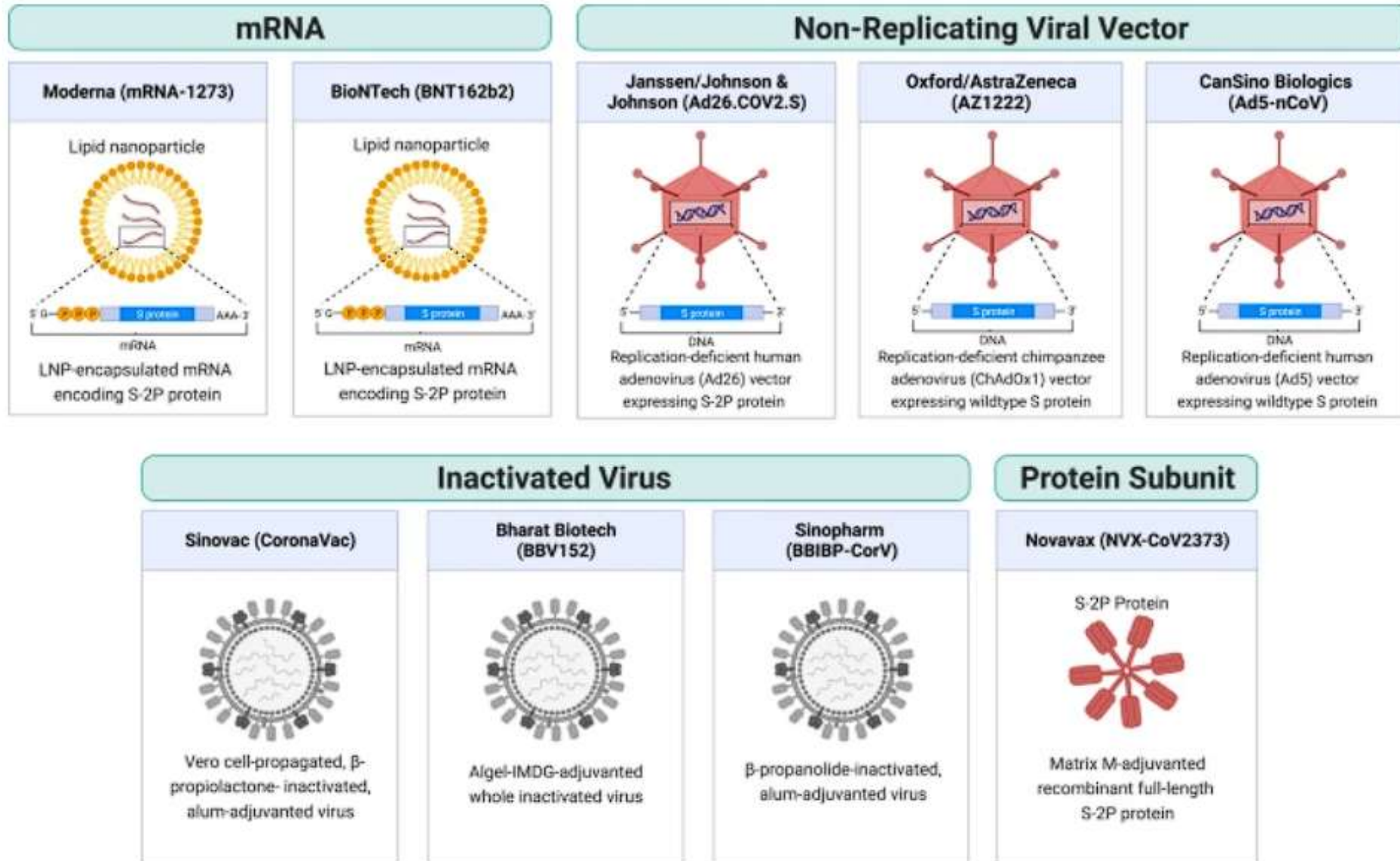
COVID 19 vaccine

Burden

- Hospitalized patients with severe COVID disease – 4 times higher risk in COPD
- Population cohort study, risk of severe COVID 19 in chronic lung disease (n= 82,56,161), followed for 4 months:

| CRD | Hospitalization (HR) | Death (HR) |
|----------------|-------------------------|-------------------------|
| COPD | 1.54 [1.45–1.63] | 1.54 [1.42–1.67] |
| Asthma | 1.18 [1.13–1.24] | 0.99 [0.91–1.07] |
| ILD | 1.66 [1.30–2.12] | 2.05 [1.49–2.81] |
| Bronchiectasis | 1.34 [1.20–1.50] | 1.12 [0.94–1.33] |

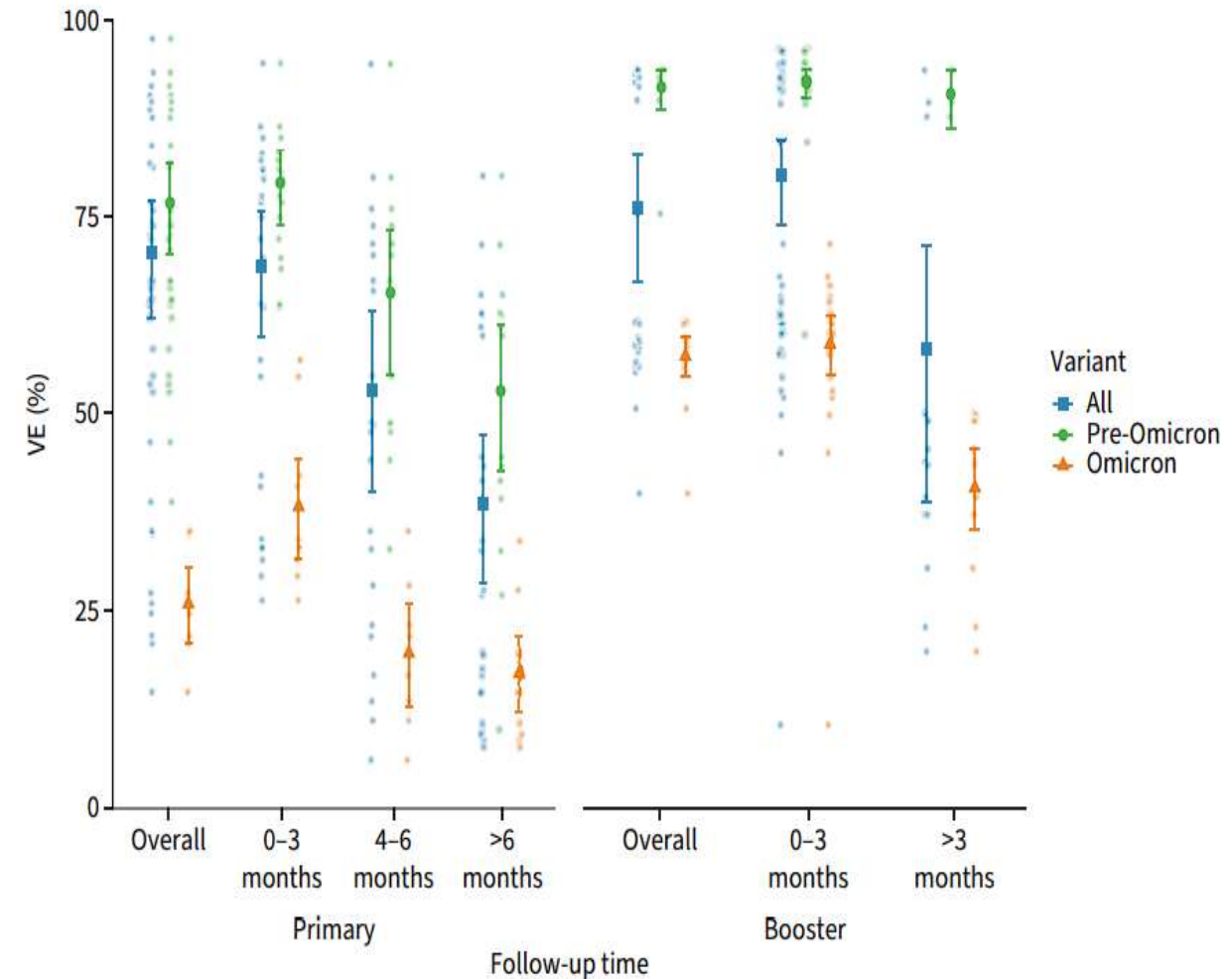
Vaccines



| Parameter | mRNA Vaccines | Viral Vector Vaccines | Inactivated Vaccines | Protein Subunit Vaccines |
|------------------------------------|--|---|---|---|
| Vaccine Name (manufacturer) | <ul style="list-style-type: none"> BNT162b2 (Comirnaty – Pfizer-BioNTech) mRNA-1273 (Moderna/Spikevax) | <ul style="list-style-type: none"> ChAdOx1-nCoV-19 (AstraZeneca/Covishield) Gam-COVID-Vac (Sputnik V) Ad26.COVS.2.S (J&J) | <ul style="list-style-type: none"> BBV152 (Covaxin – Bharat Biotech) CoronaVac (Sinovac) BBIBP-CorV (Sinopharm) | <ul style="list-style-type: none"> NVX-CoV2373 (Novavax/Nuvaxovid) |
| Type of Vaccine | mRNA (lipid nanoparticle encapsulated mRNA coding for spike protein) | Non-replicating viral vector (adenovirus) | Whole inactivated SARS-CoV-2 virus | Recombinant spike protein (nanoparticle) + Matrix-M adjuvant |
| Dose & Route | 0.3 mL IM (Pfizer), 0.5 mL IM (Moderna) | 0.5 mL IM | 0.5 mL IM | 0.5 mL IM |
| Primary Series | 2 doses: <ul style="list-style-type: none"> Pfizer (21 days apart) Moderna (28 days apart) | 2 doses: <ul style="list-style-type: none"> AstraZeneca (8–12 weeks apart) Sputnik V (21 days apart) Single dose: <ul style="list-style-type: none"> J&J | 2 doses: <ul style="list-style-type: none"> Covaxin (28 days apart) CoronaVac (14–28 days apart) Sinopharm (21 days apart) | 2 doses, 21 days apart |
| Common Adverse Events | Local pain, fatigue, headache, fever, myalgia, lymphadenopathy Rare: myocarditis/pericarditis | Injection site pain, fever, myalgia, headache Rare: Thrombosis with thrombocytopenia syndrome (VITT), GBS | Local pain, fever, fatigue, mild rash Rare: anaphylaxis | Local pain, fatigue, headache, myalgia Rare: myocarditis, anaphylaxis |
| Contraindications | Severe allergic reaction to prior dose or component (e.g., PEG) | Severe allergy to components; history of TTS (contraindication for adenovirus boosters) | Severe allergic reaction to prior dose/component | Severe allergy to vaccine component (e.g., polysorbate-80, Matrix-M) |

Effectiveness of COVID 19 vaccines

| | |
|------------------------------|---|
| Study | Effectiveness of COVID19 vaccines in adults – systematic review and meta analysis, Zhou et al. 2025 |
| Population | 33 studies (17 case control, 12 cohort, 4 both) |
| | Over 56 million participants across studies |
| Intervention | Completed primary series or booster vs unvaccinated Includes BNT-162b2, mRNA-1273 or ChAdOx1/ AZD1222, Ad26.COV2.S vaccines |
| Outcome: Vaccine efficacy | <p>Against any infection (all variants, primary series):</p> <ul style="list-style-type: none"> Overall: 70.7% VE (62.4 – 77.1) Pre-Omicron strains: 77.0% (70.4 – 82.1) Omicron: 26.1% (21.1 – 30.8) <p>Temporal waning: VE 38.9% at 6 months After booster: 76.4%, then 58.4% at 3 months</p> <p>Severe outcomes (hospitalization / ICU / death):</p> <ul style="list-style-type: none"> Overall: 87.4% (81.4 – 91.4) Pre-Omicron: 93.3% (89.1 – 95.8) Omicron: 62.8% (52.0 – 71.9) <p>Booster effect: 87.9%, then 78.5% at 3 months</p> |



Effectiveness in CRD

| Study | Population | Exposure | Outcomes |
|--|---|---|---|
| <p>Efficacy of mRNA and Inactivated Whole Virus Vaccines in Patients with Chronic Respiratory Diseases</p> <p>Case control study</p> | <p>327 with CRD from China</p> <p>109 - COVID-19</p> <p>218 - matched uninfected controls</p> | <p>Vaccination with ≥ 2 doses of either CoronaVac or BNT162b2 vs unvaccinated group</p> | <p>CoronaVac:</p> <ul style="list-style-type: none"> Symptomatic COVID-19: 31.7% Hospitalization: 81.1% (28.6-95.0) Respiratory failure: 87.2% (36.2-97.4) <p>BNT162b2:</p> <ul style="list-style-type: none"> Symptomatic COVID-19: 62.0% (23.0-81.3) Hospitalization: 79.3% (3.8-95.7) Respiratory failure: 90.7% (17.3-98.9) <p>No statistically significant difference</p> <p>Wide CI</p> |
| <p>Association between COVID-19 vaccination and first healthcare utilization for chronic obstructive pulmonary disease</p> <p>Population-based cohort study</p> | <p>N = 27,595,469 from Korea</p> <p>93.9% had received COVID-19 vaccination</p> | <p>COVID-19 vaccinated vs unvaccinated)</p> <p>Subtype (mRNA vs others) and single dose vs full vaccination</p> | <p>Risk of first healthcare utilization for COPD: HR = 0.46 (0.46-0.47)</p> <p>First ER visits or hospitalizations for COPD: HR = 0.24 (0.24-0.25)</p> <p>Vaccination subtype: mRNA HR = 0.35 (95% CI: 0.35-0.36)</p> |

Varicella Zoster vaccine

Burden

- VZV → Chickenpox → Latency in DRG → shingles
- Complication - post-herpetic neuralgia, ocular involvement, risk of hospitalization
- COPD → ↑ Risk of Herpes Zoster
 - aHR 1.68 (95% CI 1.55–1.82)
 - Due to immunosenescence, chronic inflammation, inhaled/systemic corticosteroids
- HZ triggers COPD exacerbations, ↑ hospitalization, ↑ mortality
- Post-herpetic neuralgia risk - higher in COPD

Efficacy of VZV in COPD

| Study | Population | Intervention | Outcome |
|---|---|---|---|
| Efficacy of herpes zoster subunit vaccine in adults ZOE-50 and 70 RCT | Adults >50 yrs N = 16596 No immunocompromised | Recombinant HZ vaccine (glycoprotein E) vs placebo Followed up for 3 years | <ul style="list-style-type: none"> • Overall VE: 91.3% (86.8 to 94.5) • >70 yrs: 89.8% • PHN: 88.8% (68.7 to 97.1) • COPD sub group: 90% |
| Effectiveness and safety of recombinant zoster vaccine Real world 6 cohort study | Adults >50 yrs N >2,00,000 | VZ vaccine vs placebo 3 studies prior ZVL 1 study allogenic HSCT pts | <ul style="list-style-type: none"> • Overall VE: 70 – 85% • IC: 68.2% • 2 dose > 1 dose |

Long lasting immunity > 10 yrs: 79-82%
 No increase in COPD exacerbation

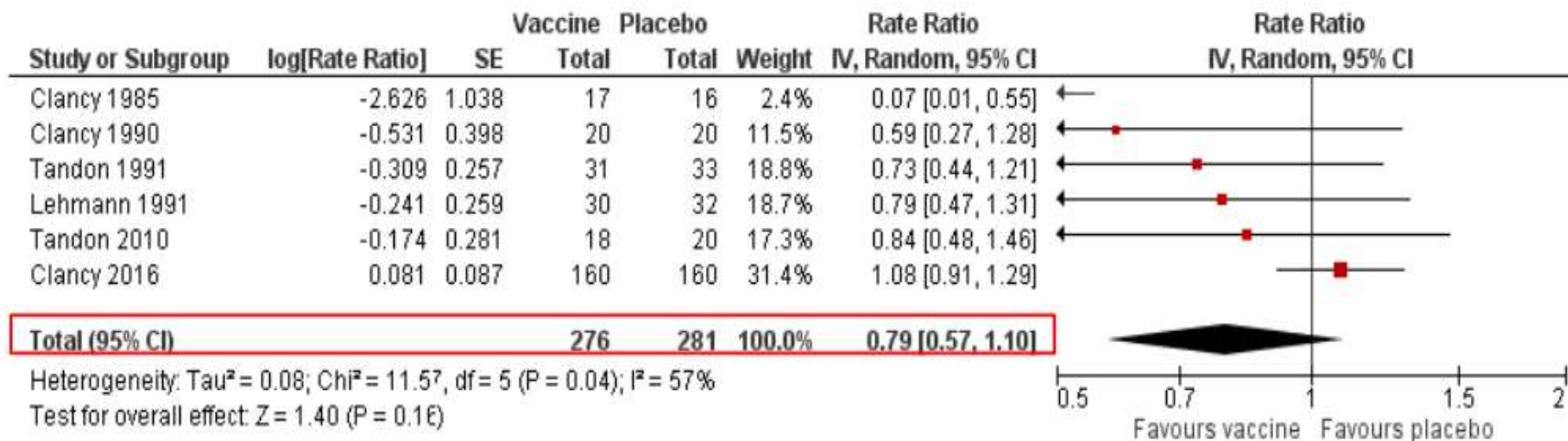
Recommendation and available vaccines

ACIP 2025 and GOLD 2025

- All adults ≥ 50 y and immunocompromised ≥ 19 y with COPD
- **RZV (Shingrix):** 2 doses (0 & 2–6 months later)
- ZVL (Zostavax): single dose (but wanes over time), not preferred

Hemophilus influenzae vaccine in COPD

- Effectiveness of oral, whole-cell NTHi vaccine in protecting against acute exacerbations of chronic bronchitis and COPD in adults – Cochrane review and meta-analysis 2018
- RCTs- 6, placebo controlled, 5 double blinded, N = 557
- Mean age: 40-80 yrs; Trial duration: 3-12 months
- Vaccine- enteric coated, killed oral preparation (two tablets for 3 consecutive days on D 0,28,56)



Exacerbations - Non significant decrease

No difference in mortality

Summary

| Vaccine | COPD | Asthma |
|---|--|---|
| Influenza IIV quadrivalent, Annually | Reduction in exacerbation No mortality benefit | Reduction in exacerbation (but low level evidence) |
| Pneumococcal: <ul style="list-style-type: none"> Age > 50 yrs: All Age 19-49 yrs: with chronic disease, immunocompromised PCV 20 – single dose PCV 15 → PPSV 23 (1 yr/8 weeks) | Reduction in exacerbation Reduction in CAP Reduction in hospitalization | Reduction in exacerbation (wide CI) Reduction in hospitalization GINA: moderate and severe asthma |
| COVID 19 All: primary series (2 doses) f/b booster dose | Only observational studies Decreased hospitalization | No evidence |
| RSV <ul style="list-style-type: none"> Age > 75 yrs: All Age 60-74 yrs: risk for severe disease | No separate evidence for COPD Reduces hospitalization and mortality overall | Same |
| Pertussis If not vaccinated in adolescent, every 10 yrs | No clinical outcomes | No clinical outcomes |
| VZV All > 50 yrs: Shingrix 2 doses | No clinical outcomes | No clinical outcomes |

Other CRDs like ILD, bronchiectasis – less evidence, to be extrapolated

Thank you