Vaccination in chronic pulmonary diseases

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04 March 2022

Introduction

Immunisation –

Process of becoming immune to a disease.

Occurs after acquiring infection or vaccine administration.

Vaccination –

Use of vaccine for protection from infectious illness

Production of specific antibodies

Memory in immune system

Need of vaccination in chronic respiratory diseases

- Chronic respiratory diseases (CRDs), associated with
  - Altered lung defenses
  - Adhesion proteins(Platelet adhesion factor receptor, ICAM 1)
  - Multiple comorbidities
  - Use of steroids in various respiratory conditions
- Vulnerable to infections with increased exacerbations, hospitalization
- Also leads to disease progression , health care burden and mortality
- Effective vaccination is a mean to solve this problem

Pneumococcal disease burden

- Responsible for 10-30 % of all bacterial pneumonia
- Most commonly identified LRTI pathogen in all age groups
- 19% of CAP in Indian patients >12years of age as per a systematic review
- Accounted for nearly 31% of CAP in a study from a tertiary care hospital in India
- 7.7-fold higher incidence of PnP in adults with CRD 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)

*CRD – Chronic respiratory diseases
PnP- Pneumococcal pneumonia

Musher et al, Clin Infect Dis. 2017 Nov 15
Troeger et al, Lancet Infect Dis. 2017
Ghia et al,Clin Med Insights Circ Respir Pulm Med. 2019
Froes etal International Journal of COPD 2017:12 3457–3468

Evolution of pneumococcal vaccine

1983 → PPV23 for >2yrs and adults

2000-1 → PCV 7 for children

2009-10 → PCV 13 for children

2011 → PCV 13 >50 yrs for IPD & pneumonia

2013 → PCV 13 immune compromised adult >19 yrs

2014 → PCV 13 for >65 yrs

CAPITA Trial

2021-22 → PCV 15/PCV 20

Sings et al Vaccine. 2017 Sep 25;35(40):5406-5417

Pneumococcal vaccine

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**
Use associated with replacement strains	No	**Yes**
Pneumococcal disease burden	No significant impact	**Decrease**
Efficacy(IPD/NBP)	Reduction in IPD ; Unclear efficacy – NBP	**Yes(IPD and NBP)**

Pneumococcal vaccine

PPSV23

1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F

PCV7

4, 6B, 9V, 14, 18C, 19F, and 23F

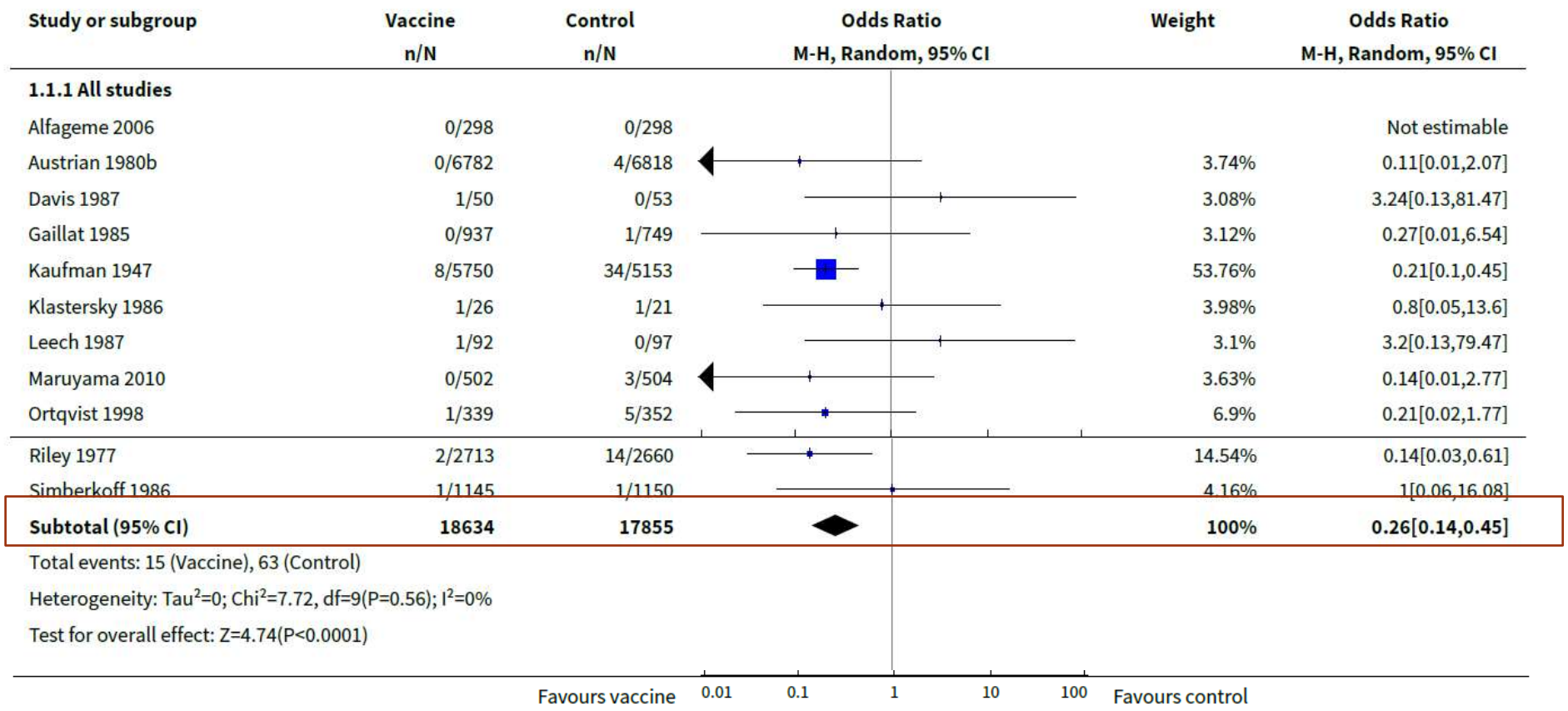
PCV13

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

PPSV 23

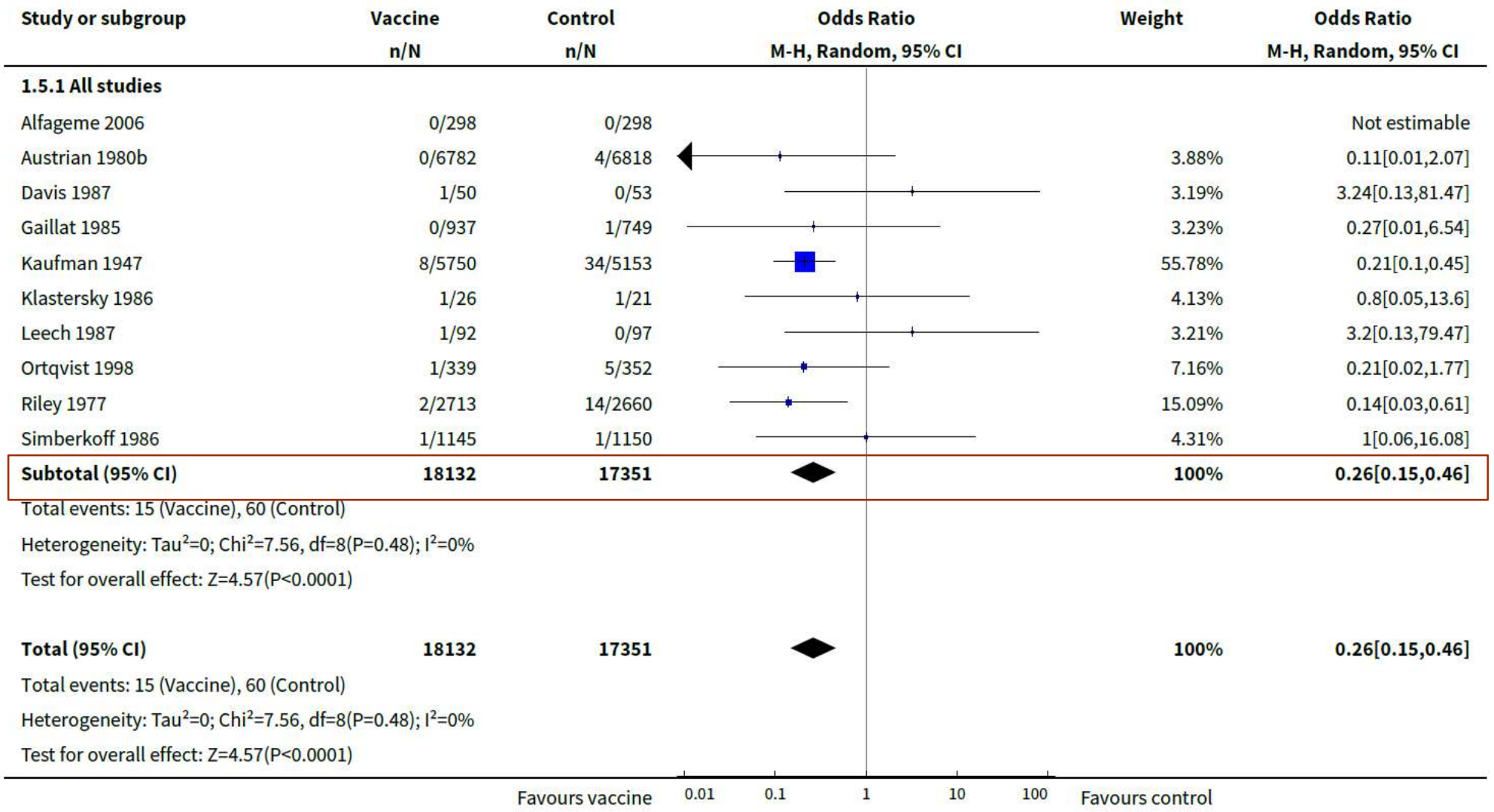
- Meta analysis of 18 RCTs (n>64500)
- Reduced risk of **IPD**(OR 0.26, 95% CI 0.14-0.45)
- Greater benefit in trials that assessed the incidence of disease caused by serotypes included in the vaccine (OR 0.18, 95% CI 0.10-0.31)
- Effective against **all cause pneumonia** with a pooled estimated OR of 0.72 (95% CI 0.56 to 0.93; statistical heterogeneity amongst the included studies)
- No evidence of protective efficacy against **all-cause mortality**, with a pooled estimated OR of 0.90 (95% CI 0.74 to 1.09)

Moberley et al Cochrane Database of Systematic Reviews 2013



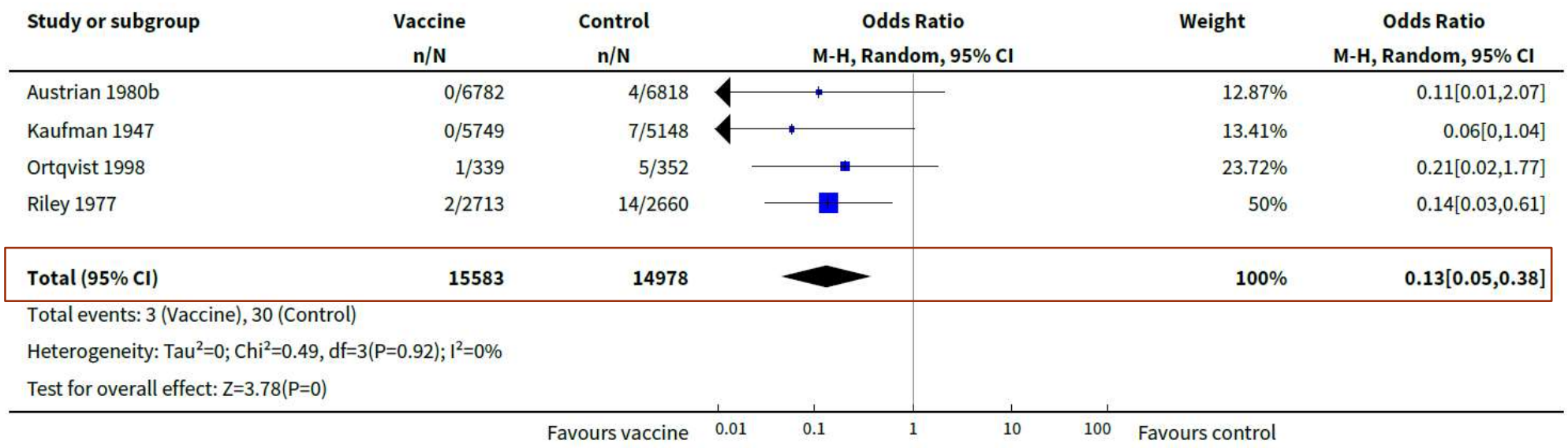
Comparison of RCTs of vaccination versus placebo, Outcome Invasive pneumococcal disease

Moberley et al Cochrane Database of Systematic Reviews 2013



Comparison of RCTs of vaccination versus placebo, Outcome Definitive pneumococcal pneumonia

Moberley et al Cochrane Database of Systematic Reviews 2013



Comparison of RCTs of vaccination versus placebo, Outcome Definitive pneumococcal pneumonia(vaccine type)

Moberley et al Cochrane Database of Systematic Reviews 2013

CAPAMIS STUDY

- Assessing the clinical effectiveness of PPV23 in >60yrs
  - CAP (pneumococcal or all-cause),
  - Death from CAP,
  - death from any cause

3 years of follow-up

.

Prospective cohort study, n= 27 204;

Vaccinated	Non Vaccinated	
n= 8981(prior 5 yrs)	n=18223	
	Never vaccinated n= 12044	Vaccinated >5 yrs prior n = 6179
	n= 2390 vaccinated later	

Gondar et al Clinical Infectious Diseases 2014;58(7):909–17

CAPAMIS study

Groups	Bacteremic CAP	Non Bacteremic CAP	All cause CAP
Whole group	I- 0.21(95% CI , 0.13-.35) HR -0.58; 95% CI, .17–2.03	I-1.45 (95% CI, 1.20–1.75) HR, 1.14; 95% CI, .76–1.72	I-7.51 (95% CI, 6.92–8.16) HR-0.98; 95% CI, .81–1.17
Vaccinated later in the study(n=2390)	HR, 0.09; 95% ;CI, .02–.48; P - .004(pneumococcal CAP)		HR, 0.53; 95% CI, .26–1.08; P = .079
N=21025 (excluding 6179 who were vaccinated >5 yrs prior)	HR, 0.38; 95% CI, .09–1.68	HR, 0.52; 95% CI, .29–.92	HR,0.75; 95% CI, .58–.98
Immunized group (vaccinated any time) – no protective effect for any analysed outcome			

Gondar et al Clinical Infectious Diseases 2014;58(7):909–17

SCIENTIFIC REPORTS

OPEN

Pneumococcal Disease and the Effectiveness of the PPV23 Vaccine in Adults: A Two-Stage Bayesian Meta-Analysis of Observational and RCT Reports

Received: 20 November 2017
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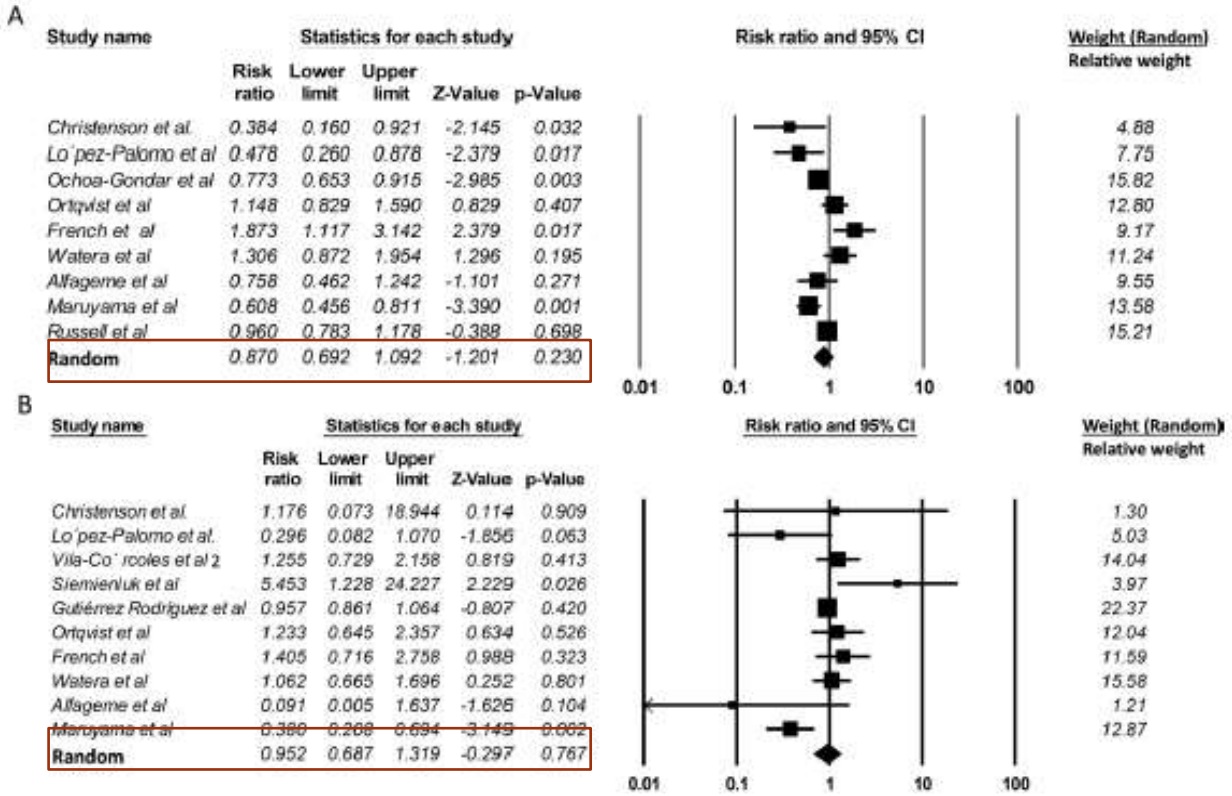
Published online: 23 July 2018

Hamid Latifi-Navid[1], Saeid Latifi-Navid[2,3], Behdad Mostafaiy[4], Sadegh Azimzadeh Jamalkandi[5] & Ali Ahmadi[1]

21 studies , n= 826109 adult participants, RCTs - 6 (28.6%), cohort studies- 10 (47.6%), Case control studies - 5 (23.8%)
RCTs - PPV-23 v/s placebo/ no intervention
Cohort studies and case-control studies – PPV-23 v/s unvaccinated



Summary plots of the random-effects meta-analyses of all studies (RCTs and observational studies) of the 23-valent pneumococcal polysaccharide vaccine for four clinical outcomes

A- All cause pneumonia
B -Pneumococcal pneumonia
C -Deaths from pneumonia
D -Invasive pneumococcal disease

Navid et al Nature,Scientific reports | (2018)8:11051

Pneumococcal Disease and the Effectiveness of the PPV23 Vaccine in Adults: A Two-Stage Bayesian Meta-Analysis of Observational and RCT Reports

Pneumococcal diseases	Overall Log OR
Invasive pulmonary diseases	**−0.1048 (−0.3920, −0.0250)**
All cause pneumonia	0.0002 (−0.0241, 0.0142)
Pneumococcal pneumonia	−0.0002 (−0.0110, 0.0122)
Death from pneumonia	$-6.3912^{\times 10^{-5}}$ (−0.0219, 0.0131)

Navid et al Nature,Scientific reports | (2018)8:11051

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault, C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij, M. Patton, A. McDonough, A. Moradoghli-Haftvani, H. Smith, T. Mellelieu, M.W. Pride, G. Crowther, B. Schmoele-Thoma, D.A. Scott, K.U. Jansen, R. Lobatto, B. Oosterman, N. Visser, E. Caspers, A. Smorenburg, E.A. Emini, W.C. Gruber, and D.E. Grobbee

The Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA)

CAPITA trial (n=84,496)

- Primary objective was to show the efficacy of PCV13 in the prevention of a first episode of confirmed vaccine-type CAP.
- Included patients with no previous pneumococcal vaccination and an absence of protocol-defined immunocompromising conditions
- significant efficacy of PCV 13 for the prevention of vaccine-type CAP and vaccine-type IPD among adults 65 years of age or older
- efficacy persisted for at least 4 years.

Bonton et al N ENGL J MED 372,March 2015

Table 2. Vaccine Efficacy.*

End Point and Analysis†	Episodes‡	PCV13 (N=42,240)	Placebo (N=42,256)	Percent Vaccine Efficacy (CI)§	P Value¶
		number			
First episode					
Infection with vaccine-type strain					
Confirmed community-acquired pneumonia					
Per-protocol analysis	139	49	90	45.6 (21.8 to 62.5)	<0.001
Modified intention-to-treat analysis	172	66	106	37.7 (14.3 to 55.1)	0.003
Confirmed nonbacteremic and noninvasive community-acquired pneumonia					
Per-protocol analysis	93	33	60	45.0 (14.2 to 65.3)	0.007
Modified intention-to-treat analysis	116	43	73	41.1 (12.7 to 60.7)	0.007
Invasive pneumococcal disease					
Per-protocol analysis	35	7	28	75.0 (41.4 to 90.8)	<0.001
Modified intention-to-treat analysis	41	8	33	75.8 (46.5 to 90.3)	<0.001
Infection with any pneumococcal strain					
Confirmed pneumococcal community-acquired pneumonia					
Per-protocol analysis	244	100	144	30.6 (9.8 to 46.7)	0.008
Modified intention-to-treat analysis	309	135	174	22.4 (2.3 to 38.5)	0.05
Confirmed nonbacteremic and noninvasive pneumococcal community-acquired pneumonia					
Per-protocol analysis	153	66	87	24.1 (−5.7 to 45.8)	0.11
Modified intention-to-treat analysis	199	90	109	17.4 (−10.2 to 38.2)	0.25
Invasive pneumococcal disease					
Per-protocol analysis	83	27	56	51.8 (22.4 to 70.7)	0.004
Modified intention-to-treat analysis	100	34	66	48.5 (20.9 to 67.0)	0.006
Community-acquired pneumonia					
Modified intention-to-treat analysis	1534	747	787	5.1 (−5.1 to 14.2)	0.32
All episodes of confirmed vaccine-type community-acquired pneumonia					
Per-protocol analysis	145	53	92	42.4 (18.4 to 59.7)	0.004
Modified intention-to-treat analysis	182	70	112	37.5 (15.0 to 54.3)	0.006
Death‖					
From confirmed vaccine-type pneumococcal community-acquired pneumonia or vaccine-type invasive pneumococcal disease	4	2	2	0 (−1279.6 to 92.8)	>0.999
From confirmed pneumococcal community-acquired pneumonia or invasive pneumococcal disease	13	6	7	14.3 (−197.9 to 76.2)	>0.999

Bonton et al N ENGL J MED 372,March 2015

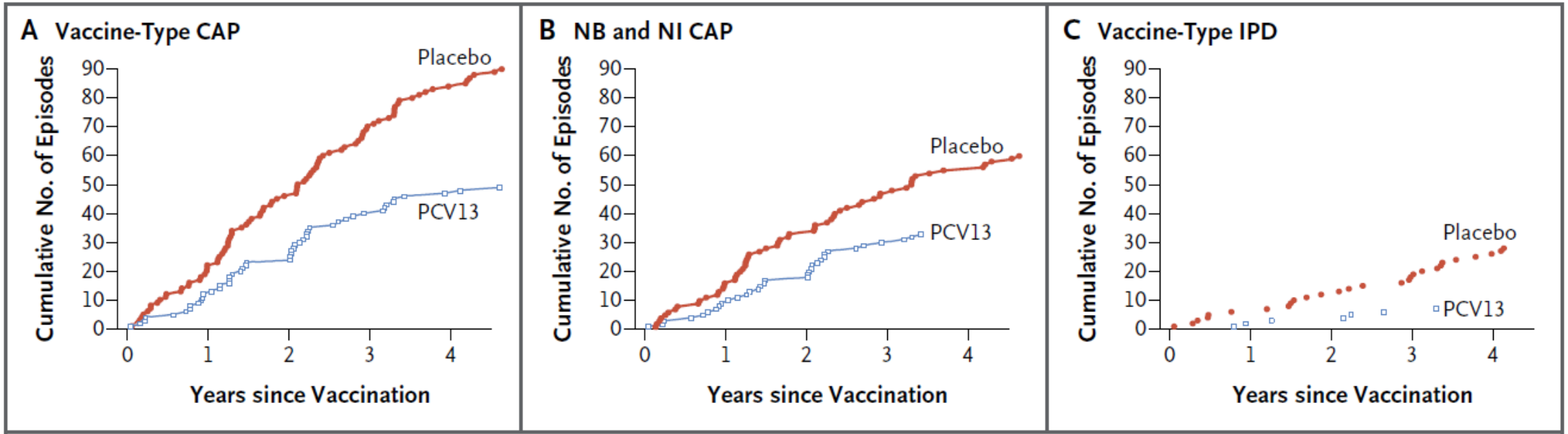


Figure 2. Post Hoc Analysis of the Cumulative Episodes of the Primary and Secondary Efficacy End Points in the Per-Protocol Population.

Bonton et al N ENGL J MED 372,March 2015

CAPITA Trial- limitations

- Homogeneous population of participants among whom there was a **low incidence** of pneumococcal disease
- Specifically **excluded** subjects who were regarded as immunocompromised
- Subjects who developed an immunocompromising condition or who were placed on some immunosuppressive therapy during the period of the study, PCV13 exhibited **no protective effect**
- **No comparative group** that received PPV23

Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine Against Hospitalization for Community-Acquired Pneumonia in Older US Adults: A Test-Negative Design

John M. McLaughlin,[1] Qin Jiang,[1] Raul E. Isturiz,[1] Heather L. Sings,[1] David L. Swerdlow,[1] Bradford D. Gessner,[1] Ruth M. Carrico,[2] Paula Peyrani,[2] Timothy L. Wiemken,[3] William A. Mattingly,[2] Julio A. Ramirez,[2] and Luis Jodar[1]

N= 2034 cases of CAP
Cases – 68(3.3%, PCV 13 serotypes) , controls -1966(96.7%,Non PCV 13 serotype)
Culture results(predominatly blood)- 1905/2304(93.7%)
Bacteremic(6/68 , 8.8%) , Non bacteremic (62/68- 91.2)

McLaughlin et al CID 2018:67 15 November

Logistic Regression Model[a]	All VT-CAP (n = 2034)	Nonbacteremic VT-CAP (n = 2014)
Cases, No.	68	62
Controls, No.	1966	1952
	VE, % (95% CI)	
Crude model[b]	72.8 (12.8–91.5)	70.1 (4.1–90.7)
Univariate adjustment		
Seasonality/time period	72.4 (11.4–91.4)	69.2 (.8–90.4)
Age group	72.8 (13.0–91.5)	70.2 (4.4–90.7)
Gender	72.3 (11.3–91.4)	69.8 (2.9–90.7)
Race	72.9 (13.3–91.6)	70.4 (4.9–90.8)
Ethnicity	72.8 (12.9–91.5)	70.2 (4.1–90.7)
Place of residence	73.3 (14.4–91.7)	70.5 (5.3–90.8)
Risk level	73.3 (14.2–91.7)	70.7 (5.9–90.9)
BMI category	72.1 (10.4–91.3)	69.3 (1.3–90.5)
PSI	72.3 (11.3–91.4)	69.8 (2.9–90.6)
Healthcare facility exposure in last 3 mo	72.6 (12.1–91.4)	69.9 (3.3–90.6)
Weekly exposure to children aged <5 y	72.8 (12.7–91.5)	70.4 (4.8–90.8)
Influenza vaccination within previous y	71.1 (6.9–91.0)	67.5 (–5.2 to 90.0)
History of PPSV23 in last 5 y	72.8 (12.7–91.5)	70.1 (4.1–90.7)
Fully adjusted[c]	71.2 (6.1–91.2)	67.6 (–6.2 to 90.1)

Vaccine effectiveness of 13-valent pneumococcal conjugate vaccine against hospitalized vaccine-type community-acquired pneumonia

McLaughlin et al CID 2018:67 15 November

Pneumococcal polysaccharide vaccine

Author	Study design	Intervention	Results
Inj. vaccines for preventing pneumococcal infection in patients with **COPD** (Review) Walters JAE et al 2010	RCTs -7 , n=1709	PPSV23 - 5 PCV-14 - 2	protection against pneumonia with pneumococcal vaccination (6 studies, OR 0.72(95% CI 0.51 to 1.01) And COPD exacerbations- (2 studies, OR 0.58; 95% CI 0.30 to 1.14)- not statistically significant Hosp. admission and emergency visits(n=238) All cause/cardiorespiratory mortality (n=888) } no diff.
Pneumococcal vaccines for preventing pneumonia in **COPD** Walters et al 2017	Meta analysis RCTs- 12 N -2171, Male-67% Mean FEV1-1.2 L(5)	PPV or PCV v/s control or alternative vaccine in COPD patients PPV23/PCV 14 in 9 /3 studies Influenza vaccine in 2 studies	Vaccine group: Lower likelihood of CAP (OR 0.62, 95% CI 0.43 to 0.89)/ COPD exacerbation (OR 0.60, 95% CI 0.39 to 0.93) **NNTB(CAP)- 21, NNTB(AE)- 8** No significant diff. in cardiovascular mortality/all cause mortality/hospital admission for any cause Only one study (n = 181) compared efficacy PPSV23/PCV7 - no differences for CAP, all-cause mortality, hospital admission or likelihood of a COPD exacerbation. More likelihood of some mild adverse effects of vaccination with PPV-23.

JAE walter et al Cochrane Database of Systematic Reviews 2017, Issue 1

Title and author	Study design	Intervention	Results
Long-term Comparative Immunogenicity of PCV and PPSV Vaccines in COPD, 2012 Dransfield et al	Randomised ,open label trial N=181 **Inclusion criteria** : >40 years of age ≥10 pack-year cigarette smoking Clinical diagnosis of moderate to very severe COPD (PBD FEV1/FVC <70% and FEV1<70% predicted). Never received PPSV23 or administered >5 years before randomization **Exclusion criteria** : Diagnosis of asthma, Use of immunosuppressive medications other than syst and ICS, conditions impairing pneumococcal vaccine response, Any illness within the month prior to enrollment that required antibiotics and/or systemic steroid	PPSV v/s PCV7	PCV 7 v/s PPSV23: greater OPK at both 1 and 2 years for 6 of 7 serotypes (not 19F) No differences in the frequency of acute exacerbations, pneumonia, or hospitalization

Darnsfield et al CID.2012

Tittle and author	Study design	Results
Comparative effectiveness of pneumococcal vaccination with PPV23 and PCV13 in COPD patients over a 5-year follow-up	open-label, prospective, observational cohort study N= **Inclusion** : • Male patients aged ≥45 years • Diagnosis of COPD (GOLD) • Current or past smokers with ≥10 pack-years history of smoking Exclusion • Undergone spirometry Society (ATS or ERS) **Exclusion** : • Clinically relevant respiratory comorbid condition along with COPD • Severe comorbid conditions. • Malignant tumors of any organ (either treated or not) in the medical history over the past 5 years • Oxygen therapy (>12 h per day). • Systemic corticosteroids within the past 3 months	Ist yr - Total rate of pneumonia significantly reduced (PPSV 23/PCV13) 2nd year- clinical effectiveness in PPV23 group decreased v/s PCV13 5 yrs after vaccination : **Pneumonia** – 47% , PPV23 group, v/s 3.3%, PCV13 group ($p < 0.001$) **COPD exacerbations** 81.3%, PPV 23 v/s 23.6%,PCV ($p < 0.001$). BODE index significantly reduced and maintained in PCV13 group

Ignatova et alSci Rep. 2021 Aug 5;11(1):15948

Pneumococcal vaccine in asthma

Title and author	Study design
Impact of pneumococcal vaccination on pneumonia rates in patients with COPD and asthma Lee Todd et al , 2007	Retrospective cohort Documented pneumococcal vaccination Follow up for 5 yrs COPD cases- 16,074;COPD control- 14,028 Asthma cases- 2746;Asthma control- 1345

Results – Prevaccination v/s Post vaccination

COPD :

Rate of pneumococcal pneumonia related hospitalizations (case) : 0.47→ 0.37/100 person years

Adjusted relative risk (case v/s control) : 8.02 (95% CI 4.44 to 14.48) →3.87 (95% CI 2.55 to 5.88)

Asthma :

Rate of pneumococcal pneumonia related hospitalizations (case) : 0.09→ 0.03/100 person years

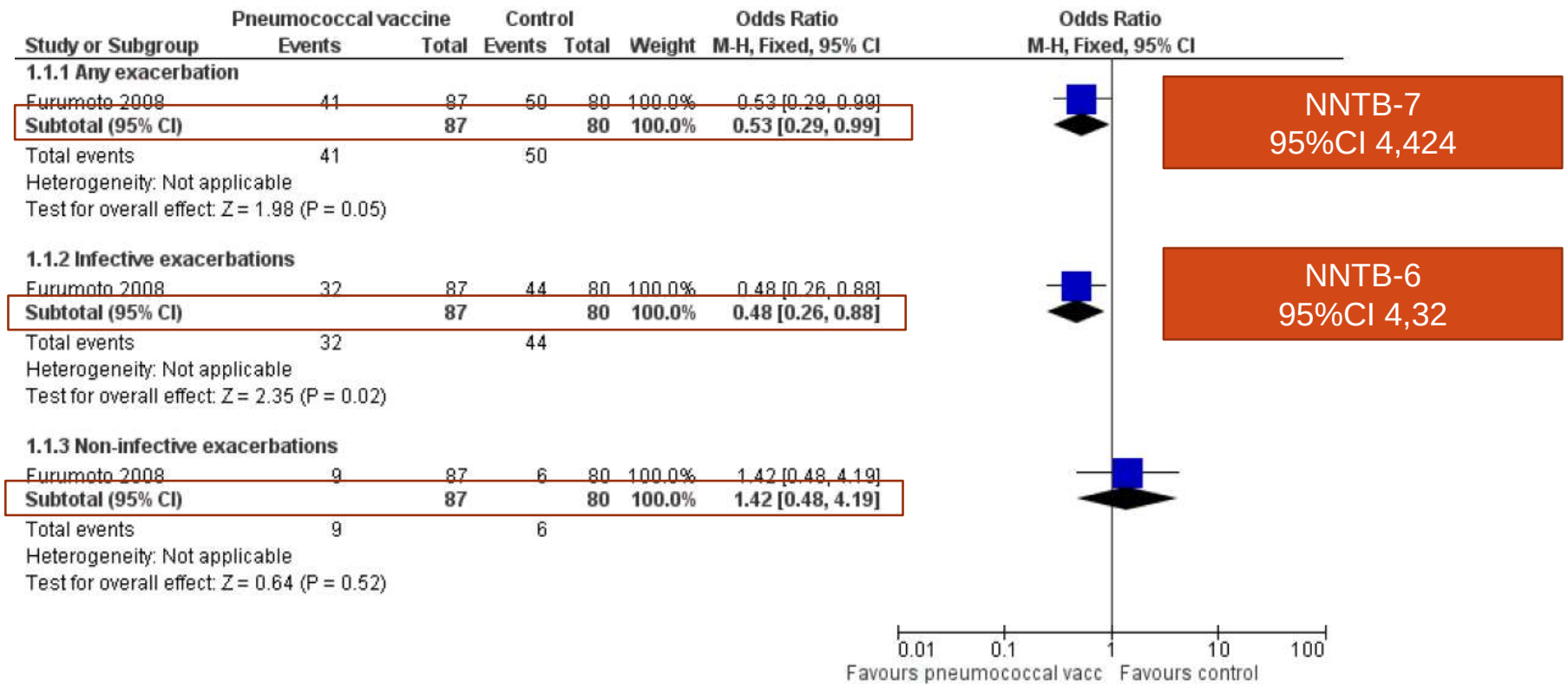
Adjusted relative risk (case v/s control) : 0.76 (95% CI 0.17 to 3.53) →0.30 (95% CI 0.04 to 1.99)

Lee Todd et al J Gen Intern Med. 2007 Jan; 22(1): 62–67

Pneumococcal vaccine in Bronchiectasis

Pneumococcal vaccines for children and adults with bronchiectasis (Review)

Chang CC, Singleton RJ, Morris PS, Chang AB



NNTB-7
95%CI 4,424

NNTB-6
95%CI 4,32

THE COCHRANE COLLABORATION®

RCT-1 ,
n=167 adults(COPD -55,Bronchiectasis -20, sequalae of pulmonary TB-50)
Intervention – PV23 +IV v/s IV
Follow up – 2yrs

C Chang et al Cochrane Database of Systematic Reviews 2009 issue 2

Pneumococcal vaccine in Bronchiectasis

	Univariable analysis		Multivariable analysis			
	OR (95% C.I.)	*P*-value	BSI model OR (95% C.I.)	*P*-value	FACED model OR (95% C.I.)	*P*-value
Age	1.07 (1.04–1.08)	<0.001	1.01 (0.99–1.04)	0.270	1.03 (1.01–1.07)	0.021
Male	2.68 (1.57–4.58)	<0.001	1.27 (0.57–2.82)	0.559	0.16 (0.53–2.54)	0.702
Pneumococcal vaccine	0.49 (0.29–0.80)	0.005	0.37 (0.19–0.70)	0.003	0.40 (0.21–0.74)	0.004
Diabetes Mellitus	3.64 (1.55–8.57)	0.003	1.62 (0.60–4.76)	0.355	1.57 (0.59–4.55)	0.380
Myocardial infarction	5.53 (1.24–24.60)	0.025	0.78 (0.14–6.92)	0.794	0.72 (0.13–6.06)	0.727
Heart failure	7.89 (2.34–26.54)	0.001	6.31 (1.55–43.07)	0.023	5.47 (1.36–37.23)	0.035
COPD	4.18 (2.06–8.47)	<0.001	2.06 (0.79–5.63)	0.145	2.42 (0.93–6.59)	0.074
Previous MDR colonization	2.27 (0.94–5.50)	0.070	0.97 (0.32–3.10)	0.956	1.16 (0.40–3.61)	0.791
Long-acting anticholinergic	2.54 (1.53–4.22)	<0.001	1.48 (0.74–2.92)	0.262	1.69 (0.87–3.30)	0.120
Proton pump inhibitor	4.78 (2.77–8.24)	<0.001	2.64 (1.35–5.26)	0.005	2.85 (1.48–5.59)	0.002
Chronic oxygen therapy	4.52 (1.52–13.39)	0.007	1.82 (0.46–9.47)	0.427	2.73 (0.70–14.05)	0.179
Previous hospitalization due to BE at any time	3.25 (1.93–5.46)	<0.001	–	–	2.63 (1.36–5.17)	0.005
Previous history of pneumonia	1.81 (1.095–3.00)	0.021	1.55 (0.81–2.99)	0.185	1.41 (0.73–2.75)	0.307
FACED	5.22 (2.97–9.20)	<0.001	–	–	0.97 (0.78–1.22)	0.810
BSI	13.79 (6.53–29.13)	<0.001	1.20 (1.09–1.32)	<0.001	–	–

Predictors of hospital admission: univariable and multivariable analysis

- Prospective observational study
- Bronchiectasis patients
- Included in study-319
- Exacerbation-265
- OPD-103
- Hosp admission -162
- Follow up period -1 yr
- Pneumococcal vaccine: Hospitalized -64/162(40%), OPD -59/103(60%)

Menéndez et al. Respiratory Research (2017) 18:176

Pneumococcal vaccine in CPA and ABPA

Title and author	Study design
Response to pneumococcal polysaccharide vaccination in patients with chronic and allergic aspergillosis(n=318)	Prospective observational study. Pre and post vaccination antibody concentrations)PPV-23) Study population – consecutive patients of CPA(n=156), bronchiectasis(n=36),SAFS(n=43) and ABPA(n=43). 40% never received pneumococcal vaccination **Results** : Patients with CPA and ABPA exhibited **poorer response** to PPV -23 as compared to healty adults
Pneumococcal 13-valent conjugate vaccination (PCV13)response in patients with pulmonary aspergillosis. Retrospective study Site -National Aspergillosis Centre, Manchester University NHS Foundation Trust **Inclusion Criteria** 1. Diagnosis of pulmonary aspergillosis (CPA, ABPA, SAFS, Aspergillus bronchitis or mixed CPA/ABPA) 2. Have non-protective serology 3. Received one or two doses of PCV13 4. Had pneumococcal serology checked within 3 months following last PCV13 dose	**Primary Outcome**: Percentage of patients with protective serology following PCV13. Protective serology post-vaccine defined as: post vaccine serology >1.3µg/mL OR ≥4 fold increase to 9 or more serotypes within 3 months after vaccine **Results**: • 2 doses of PCV13 give better response than 1 dose , however not superior to PSV 23 • Patients with ABPA respond better than CPA to PCV13 • Response to PCV13 may wane after 3 months, PPSV23 response appears to be more sustained over 2 years post vaccination

Kosmidis Chris et al Observational Study Vaccine 2015 Dec 16;33(51)
Aggarwal S et al Access microbiology volume 2 issue 2 2020 Feb 28

Newer pneumococcal conjugate vaccine

PCV13

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

PCV15

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F + 22F & 33F

PCV20

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F + 8, 10A, 11A, 12F, 15B, 22F, and 33F

PCV 15

Study	Intervention	Results
PNEU-DAY Immunogenicity, safety, and tolerability of V114(15-valent PCV) in immunocompetent adults aged 18–49 years with or without risk factors for pneumococcal disease Phase III trial N=1515	PCV13 or V114 followed 6 months later by PPSV 23	D30 - both V114 and PCV13 were immunogenic for all serotypes based on opsonophagocytic activity(OPA) geometric mean titres(GMT) . PPSV23 was immunogenic for all serotypes V114(22F and 33F) Most common adverse effect – injection site pain and fatigue
PNEU-AGE safety, tolerability, and immunogenicity of V114(15-valent PCV), compared with PCV13 in adults 50 years of age and older	PCV13 or V114 (randomised 1:1)	**Non inferiority** for 13 shared serotypes Superiority for serotypes 3,22F , 33F Most common adverse effect – injection site pain , fatigue and myalgia
PNEU-PATH Safety, tolerability, and immunogenicity of V114(15-valent PCV), followed by sequential PPSV23 vaccination in healthy adults aged >50 years; randomized phase III trial	PCV13 or V114, followed 12 months later by PPSV23	D30 and 12 months post-vaccination **comparable immune response** Higher in the V114 group for 22F and 33F Most common adverse effect – injection site pain and swelling

Hamitt Laura et alOpen Forum Infectious Diseases 2022
Platt et alVaccine. 2022 Jan 3;40(1):162-172
Song et al Vaccine. 2021 Oct 15;39(43):6422-6436

PCV 20

Study	Intervention	Results
Phase 3, randomized, double-blind study to evaluate the immunogenicity and safety of 3 lots of 20-valent PCV in pneumococcal vaccine-naive adults 18 through 49 years of age Phase III trial N=1710	3 lots of PCV20 or PCV 13, randomised 2:2:2:1	similar and robust immune responses elicited at 1 month after vaccination by 3 lots of PCV20 against the 20 vaccine serotypes **noninferiority** of OPA GMRs for the pooled PCV20 lots compared to PCV13 for all 13 serotypes at D30 Adverse event profile – similar in both groups
Pivotal Evaluation of 20-valent,PCV20 Safety, Tolerability, and Immunologic Noninferiority in Participants 18 Years and Older Phase III, N=3889 Adult naïve to pneumococcal vaccination	>60 yrs: PCV20/saline(n=1507) or PCV13/PPSV 23(1490) randomised 1:1 50-59 yrs & 18-49 yrs: PCV20/PCV13 randomised 3:1	All serotypes in PCV 20 induced robust responses OPA geometric mean titers (GMTs) to all 13 matched serotypes were noninferior to PCV13. OPA GMTs to 6 /7 additional serotypes 1 month after PCV20 - **noninferior** compared to the same serotypes in PPSV23. GMTs after PCV20 in (18–49 years, 50–59 years) were **noninferior** to cohort of 60–64 years. Similar tolerability and safety profile

Klein etal , vaccine Jul21

Routine Vaccination

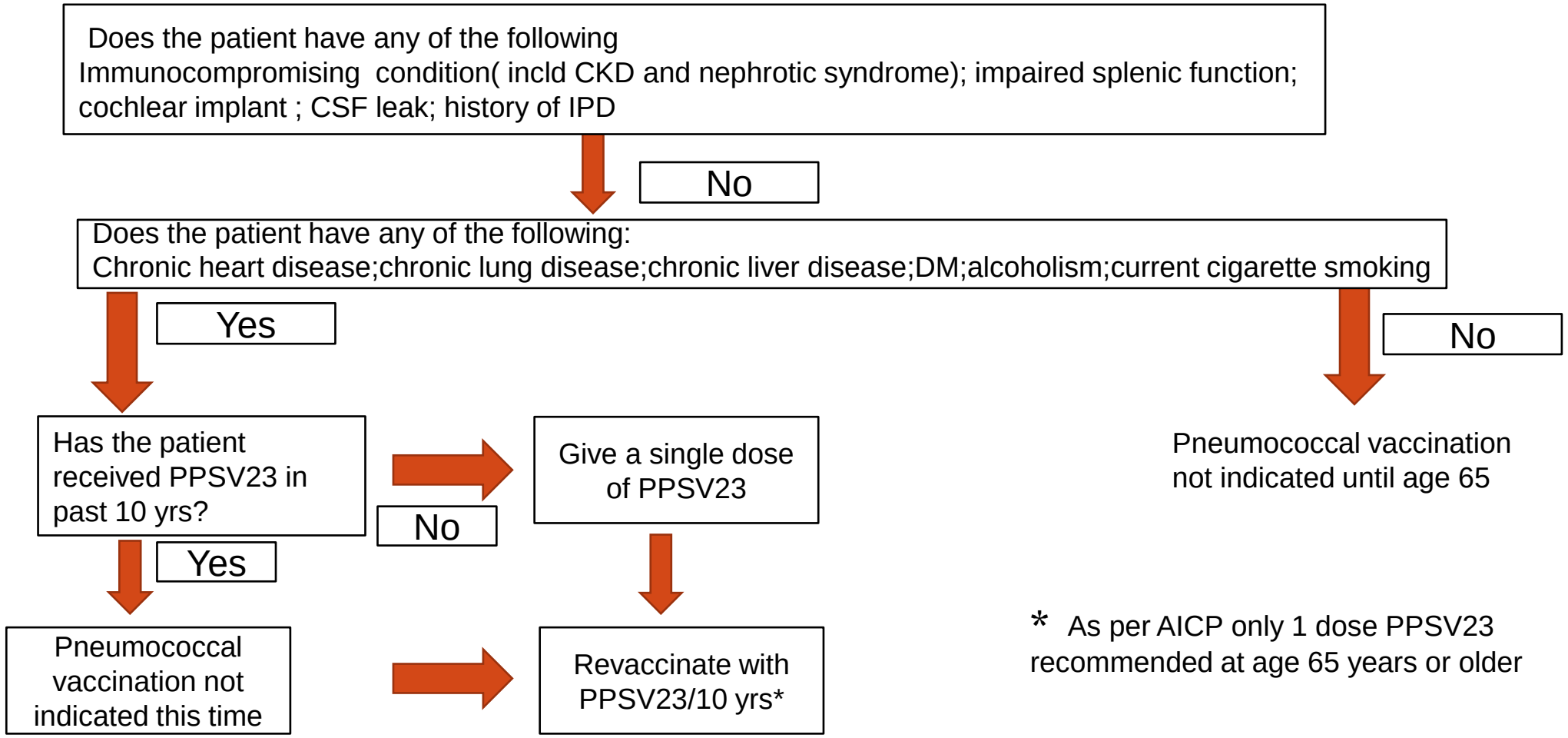
- Age 65 years or older (immunocompetent):
  - 1 dose PCV13 if previously did not receive PCV13, followed by 1 dose PPSV23 at least 1 year after PCV13 (at least 5 years after last dose PPSV23)
  - Previously received PPSV23 but not PCV13 : 1 dose PCV13 at least 1 year after PPSV23
  - When both PCV13 and PPSV23 are indicated, administer PCV13 first

PCV13 not administered routinely to >65 yrs unless

another indication for PCV 13 (and not previously received PCV 13) or

presence of chronic conditions which places these individuals at higher risk for pneumococcal disease

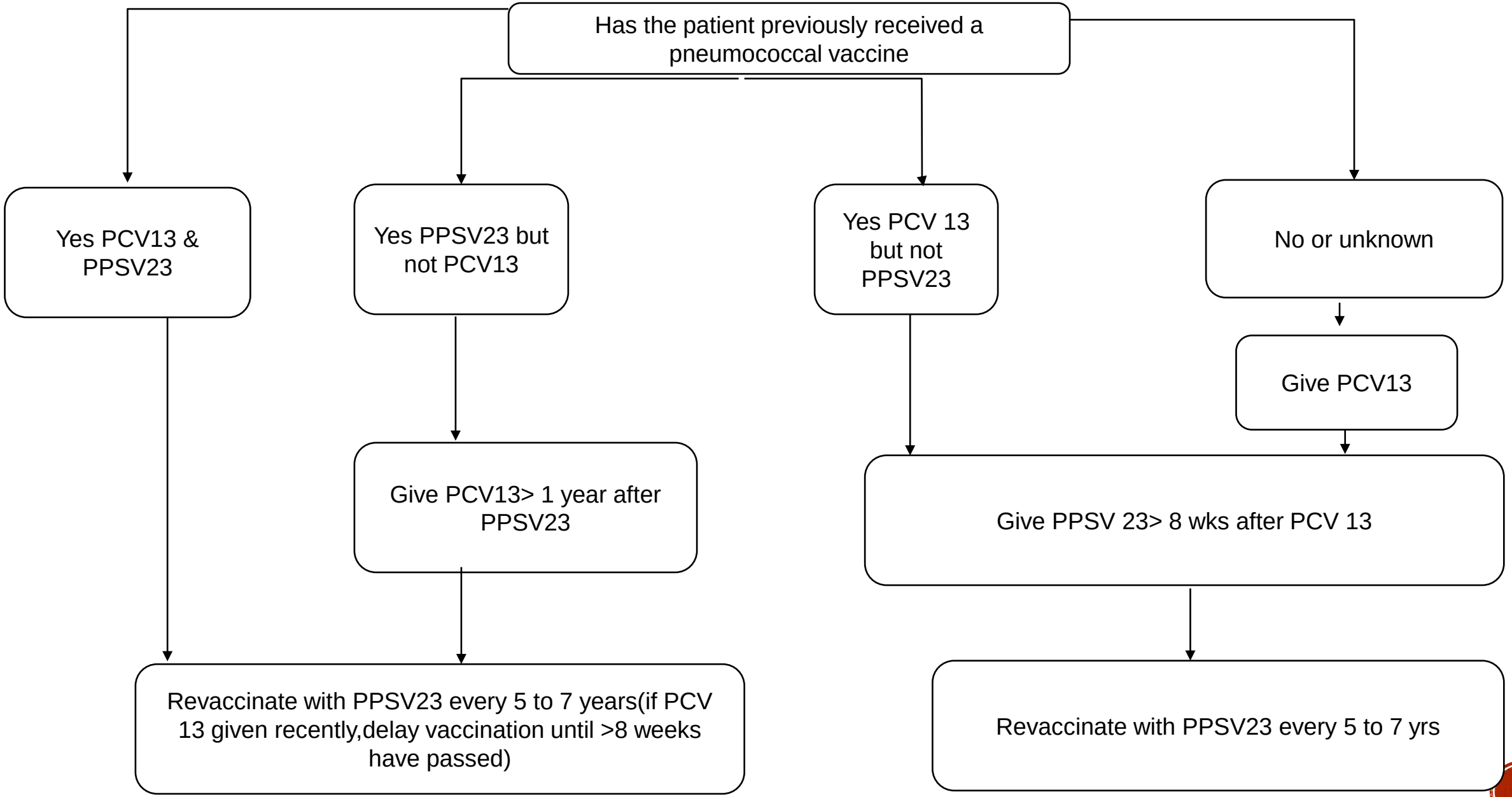
Pneumococcal vaccination in immunocompetent adults(19-65 yrs)



* As per AICP only 1 dose PPSV23 recommended at age 65 years or older

Musher Daniel M (2022).Pneumococcal vaccination in adults .In T.W.Post,T M File & M Bogorodskaya (Eds),UpToDate

Pneumococcal vaccination for adults(any age) with cochlear implant,CSF leak ,asplenia , immunocompromised



Musher Daniel M (2022).Pneumococcal vaccination in adults .In T.W.Post,T M File & M Bogorodskaya (Eds),UpToDate

Updated Recommendations of the Advisory Committee on Immunization Practices (2021-22)

For those who have never received a pneumococcal vaccine or those with unknown vaccination history (age >65 yrs)	**1 dose of PCV 20 - Immunisation complete OR 1 dose of PCV15 , followed one year later(or 8 wks) 1 dose of PPSV 23- Immunisation complete**
For those who previously received PPSV23 but who have not received any pneumococcal conjugate vaccine (e.g., PCV13, PCV15, PCV20) (age > 65 yrs)	At least one year later one dose of either PCV15/PCV 20* Immunisation complete
Age 19-64 yrs , no underlying medical condition or risk factor	None
Age 19-64 yrs with underlying medical condition or risk factor	1 dose of PCV20 OR 1 dose of PCV15 followed by 1 dose of PPSV23 at least 1 year later The minimum interval (8 weeks) can be considered in adults with an immunocompromising condition

*Not to repeat dose of PPSV 23
In individuals > 65 yrs of age with underlying risk factor and already received PCV 15/PCV 20 earlier at a younger age no additional doses required
Adults with previous PCV13- should complete the previously recommended PPSV23 series

Pneumococcal Vaccine

	PPSV 23	PCV13	PCV15	PCV20
Dose	0.5 ml			
Route	I.M or S.C	I.M	I.M	I.M
Local side effects	Injection-site pain and swelling, muscle pain, fatigue, headache, and arthralgia			
Contraindication	History of severe allergic reaction to vaccine or any of its component			
Availability in India	yes	yes	-	-
Cost/dose	Pneumovax 23 $ 74.503(CDC)	Prevnar 13 $ 137.22(CDC)	Vaxenuvance $215(0.5ml)	Prevnar 20 $232(0.5ml)

Women of reproductive age group:
PPSV23 -who have lung disease ,heart disease, sickle cell disease ,DM and other chronic illnesses
PCV13 – HIV/asplenia /immunocompromised

Influenza

- Infectious vaccine preventable respiratory disease caused by Influenza A and B viruses
- Illness can range from mild symptoms to lethal pneumonia, besides causing extrapulmonary involvement too
- Characterized by seasonal epidemics, sporadic and unpredictable pandemics
- Viral surface proteins HA(hemagglutinin) and NA (neuraminidase) are antigenically variable and classified into antigenically diverse subtypes
- Antigen shift – major changes in HA/NA responsible for epidemics and pandemics
- Antigen drift –Minor changes in HA/NA associated with more localised outbreaks of varying extent

Influenza burden

- Every year, 3–5 million cases of severe illness caused by seasonal influenza virus infection in the world
- In US as per CDC , from 2010 to 2017,influenza virus infection has resulted in 9.2 million to 35.6 million illnesses and 1.4 to 7 lac hospitalizations
- 70% of COPD exacerbation are due to infections with 30% caused by viruses
- Influenza virus second most common virus associated with AECOPD(prevalence 2.5 – 11.6%)
- CFR – 7.6%, influenza hospitalization – 46.8/10000 patients(Indian studies)

Krammer et al Nature Reviews Disease Primers 2018
Mohan Anant et al Respirology. 2010 Apr
Chadha Mandeep et al PLoS One. 2013 May 15
Chaterjee et al American Journal of Respiratory and Critical Care Medicine 2018

Influenza Vaccines

Factor	LAIV	IIV	RIV
Route	Intranasal spray	I.M or needle free injector	I.M
Type	Live virus	Killed virus	Recombinant HA proteins
Frequency	Annually	Annually	Annually
Approved age	2-49 yrs	>6 months	>18 yrs
Co administration with other vaccines	Yes(can be administered with other live vaccine simultaneously ,if not to be administered 4 weeks apart)	yes	yes
Can be given to persons who have received : Oseltamivir/zanamivir within 48 hrs or Peramivir within the past 5 days or Baloxavir within past 17 days	No	yes	yes

LAIV not to be administered to persons who live with an immunocompromised person who received HSCT in previous 2 months, GVHD, SCID

Hibberd Patricia L(2022). Seasonal influenza vaccination in adults .In T.W.Post,M S Hirsch & E L Baron(Eds),UpToDate

Egg based influenza vaccine	Influenza A/Victoria/2570/2019 (H1N1)pdm09-like virus Influenza A/Cambodia/e0826360/2020 (H3N2)-like virus Influenza B/Washington/02/2019 (Victoria lineage)-like virus Influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus.
ccIIV4/RIV 4	Influenza A/Wisconsin/588/2019 (H1N1)pdm09-like virus Influenza A/Cambodia/e0826360/2020 (H3N2)-like virus Influenza B/Washington/02/2019 (Victoria lineage)-like virus Influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus.
Vaccine	Per dose
IIV4/aIIV4/ccIIV4	15µg HA/vaccine virus per 0.5 ml
HD-IIV4	60µg HA/vaccine virus per 0.7 ml
RIV4	45µg HA/vaccine virus per 0.5 ml
LAIV	$10^{6.5–7.5}$ fluorescent focus units/0.2 ml

Grohskopf Lisa Aet al MMWR / August 27, 2021 / Vol. 70 / No.5

Adult immunisation schedule

Routine vaccination

- **Persons aged 6 months or older:** 1 dose IIV, RIV, or LAIV appropriate for age and health status annually

Special situations

- **Egg allergy, hives only:** 1 dose IIV, RIV, or LAIV appropriate for age and health status annually
- **Egg allergy more severe than hives** (e.g., angioedema, respiratory distress): 1 dose IIV, RIV, or LAIV appropriate for age and health status annually in medical setting under supervision of health care provider who can recognize and manage severe allergic conditions
- **Immunocompromising conditions (including HIV infection), anatomical or functional asplenia, pregnant women, close contacts and caregivers of severely immunocompromised persons in protected environment, use of influenza antiviral medications in previous 48 hours, cerebrospinal fluid leak or cochlear implant:** 1 dose IIV or RIV annually (LAIV not recommended)
- **History of Guillain-Barré syndrome within 6 weeks of previous dose of influenza vaccine:** Generally should not be vaccinated

ACIP

Table 2: Recommendations for influenza vaccination in the Indian population

Age group (years)	Influenza vaccination recommendations
18-49	**1 dose (IIV/LAIV) annually** The decision to vaccinate individuals aged 18-49 years should be based on the discretion of the doctor and the choice of the patient
>50	**1 dose annually** Vaccination is strongly recommended for patients at high risk for influenza

Indian

Influenza vaccine contraindications and precautions for persons with a history of severe allergic reaction to a previous dose of an influenza vaccine

Vaccine (of any valency) associated with previous severe allergic reaction (e.g., anaphylaxis)	Egg based IIV4/LAIV4	ccIIV4	RIV4
Any egg-based IIV or LAIV	contraindication	precaution	Precaution
Any ccIIV	contraindication	contraindication	Precaution
Any RIV	contraindication	precaution	contraindication
Unknown influenza vaccine	Allergist confirmation recommended		

Hibberd Patricia L(2022). Seasonal influenza vaccination in adults .In T.W.Post,M S Hirsch & E L Baron(Eds),UpToDate

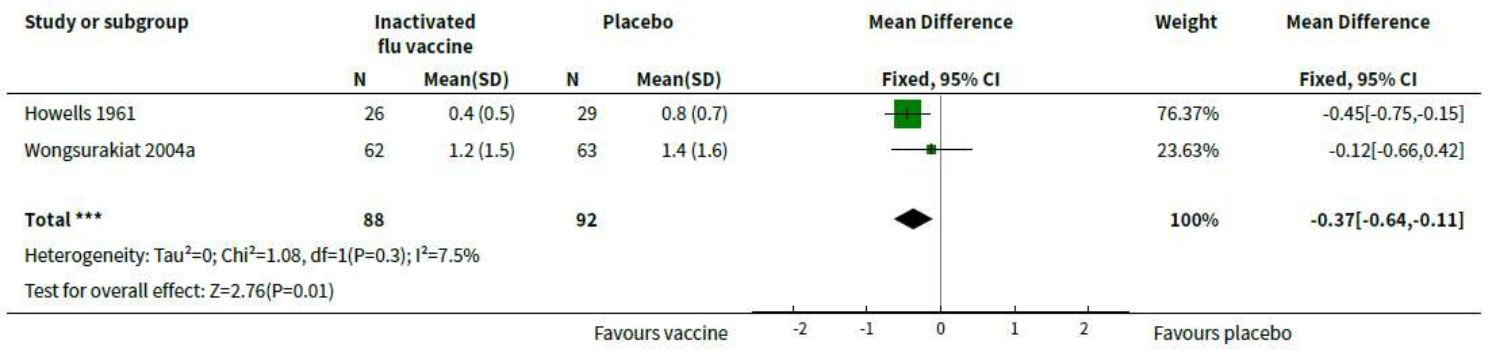
Cochrane Library

Cochrane Database of Systematic Reviews

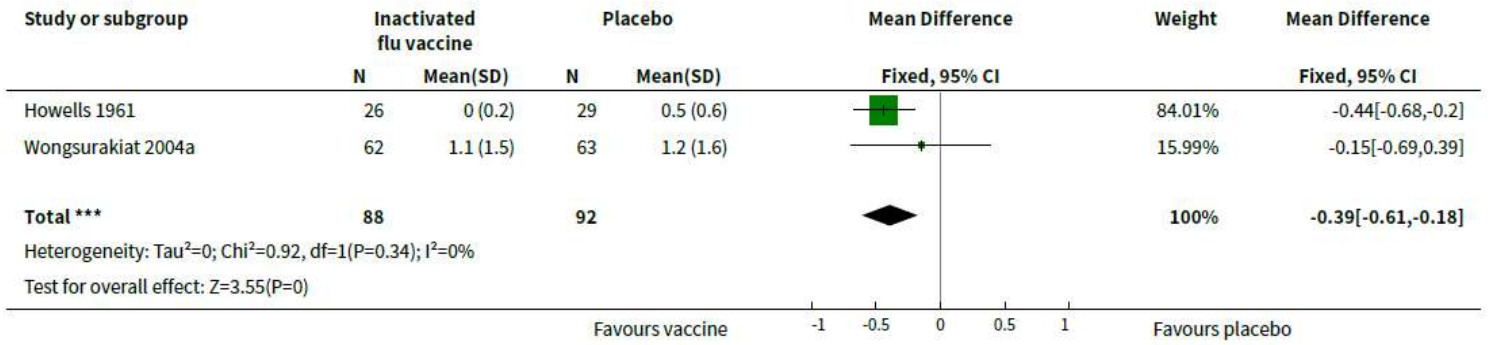
Influenza vaccine for chronic obstructive pulmonary disease (COPD) (Review)

Kopsaftis Z, Wood-Baker R, Poole P

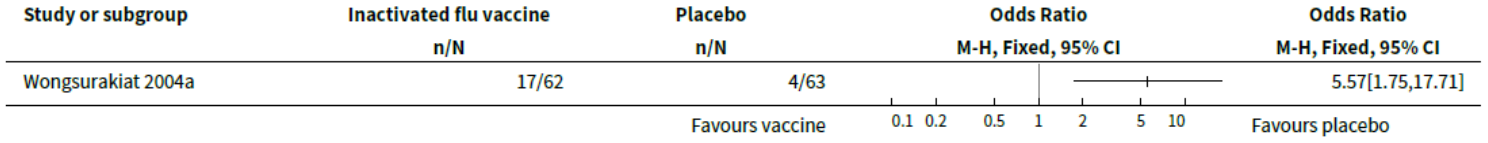
- Systemic review and meta analysis
- Included study that compared live or inactivated virus vaccines with placebo, either alone or with another vaccine ,in people with COPD
- 11 RCTs (6 studies people with COPD, n=2469)
- Intervention : LAIV -4; IIV -2; LAIV +IIV v/s IIV -2



IIV v/s placebo: Total exacerbations per participant



IIV v/s placebo: late exacerbations per participant



IIV v/s placebo: Local effects at injection site

Kofsaftis et al Cochrane Database of Systematic Reviews,Jun 2018

Influenza vaccine in Chronic obstructive pulmonary disease

Title & Author	Study design	Intervention	Results
Seasonal influenza vaccination in patients with COPD Berkani Rafik et al 2017	RCTs – 4, Prospective cohort- 2 Retrospective cohort-5 Case controlled -2	Seasonal influenza vaccine (TIVs)	4 RCTs + 1 observational -seasonal influenza vaccination is **immunogenic** in patients with COPD 6 /7studies (observational) on **VE** - reduced number of exacerbations, hospitalisations and OPD visits, and decreased all-cause and respiratory mortality. Adverse effect profile similar b/w vaccinated and placebo
Effectiveness of Influenza Vaccination for Individuals with COPD in Low- and Middle-Income Countries Lall Dorothy et al , 2015	RCTs- 9, Analytic -10	IIV/LAIV	RCTs- immunogenic response in all studies(**4 fold rise in antibody**) Significantly lower rates of lab diagnosed influenza, ARI and acute exacerbation of chronic lung disease in vaccinated Observational – reduced hospitalisations(34-75%)/mortality(18-45%)/ exacerbations 6 studies from low –middle income countries – similar results to high income countries

Bekkat-Berkani et al. BMC Pulmonary Medicine (2017) 17:79
Lall Dorothy et al COPD. 2016;13(1):93-9

Influenza vaccine in asthma

	2002/2003 season		
	Vaccinated Subject	Not-vaccinated Subject	*p* Value
Person	57	58	
No. of exacerbations	8	20	
Mean±S.D.	0.14±0.4	0.35±0.61	0.037
	2001/2002 season		
	Vaccinated Subject	Not-vaccinated Subject	*p* Value
Person	24	43	
No. of exacerbations	2	12	
Mean±S.D.	0.08±0.41	0.27±0.59	0.143

Effect of Influenza vaccination on the asthma exacerbations

	Vaccinated Subjects	Not-vaccinated Subjects	*p* Value
Patients controlled within Green-zone	32	31	
No. of exacerbations	2	10	
Mean±S.D.	0.06±0.25	0.32±0.65	0.049

Effect of Influenza vaccination on the exacerbations of asthma who were controlled within Green-Zone(**included patients whose asthma was stably controlled for 3 months before the winter season**) before winter season in 2002/2003

Adult asthmatic patients
115(2001-02);57 vaccinated
67(2002-03) ;24 vaccinated
Majority cases – moderate to severe persistent asthma

Watanabe shin et al Allergology International. 2005;54:305-309

Influenza vaccine in asthma

	Group 1 (vaccinated)	Group 2 (not vaccinated)
No. of viral upper respiratory tract infection, n (%)		
0	64 (66.7)	2 (6.3)
1	17 (17.7)	19 (59.4)
2	9 (9.4)	6 (18.8)
≥3	6 (6.3)	5 (15.6)
Rate of asthma exacerbations, n (%)		
0	71 (82.6)	34 (81.0)
1	9 (10.5)	7 (16.7)
2	4 (4.7)	1 (2.4)
≥3	2 (2.3)	—

p->0.05

p->0.05

Outcome measures in vaccinated and non vaccinated

Randomly selected asthma patients in age group(22-84 years)
Vaccinated-86 , Non vaccinated -42
Vaccine – trivalent inactivated split virus vaccine
Primary outcome -frequency of URTI and exacerbations of asthma during the winter following vaccination

Abadoglu Oznur et al,JOURNAL OF ASTHMA Vol. 41, No. 3, pp. 279–283, 2004

COVID-19

- Caused by novel beta-coronavirus SARS-CoV-2 ,
- As of 20 February 2022, over 422 million confirmed cases and over 5.8 million deaths have been reported globally.
- Contagious virus spreads via respiratory aerosols, human contact and fomites
- Illness ranges from mild asymptomatic presentation to severe ARDS and respiratory failure
- Vaccines against SARS-CoV-2 infection essential for limiting transmission and reducing mortality and morbidity

COVID 19 in asthma and COPD

- Systematic review and meta-analysis of people hospitalized with COVID-19 suggested COPD associated with a four-times higher risk of severe disease
- Population cohort study (n= 8,2,56,161) to assess affect of chronic lung disease on contracting severe COVID19
  - respiratory disease: 15.4%
  - hospital admission : 25.5% underlying respiratory disease
  - All respiratory disease: increased risk for hospitalization with COVID 19
  - COPD and most ILDs : increased risk(>50%) of death due to COVID 19

DC Sanchez ramirez et al :Respir Med 2020;171: 106096
Aveyard paul et al Lancet Respir Med 2021; 9: 909–23

Approved COVID 19 Vaccines(WHO)

Manufacturer	Name of Vaccine	Type of vaccine [1]	WHO EUA qualified	Approved schedule [2, 3]	Second dose options for completion of series in BC [4]
Pfizer-BioNTech	BNT162b2 / COMIRNATY / Tozinameran (INN)	mRNA	✓	Two doses, 21-28 days apart	- Moderna - Pfizer-BioNTech
Moderna	mRNA-1273	mRNA	✓	Two doses, 28 days apart	- Moderna - Pfizer-BioNTech
AstraZeneca	AZD1222 Vaxzevria	Adenovirus (CHAdOx1) vector	✓	Two doses, 4-12 weeks apart	- AstraZeneca - Moderna - Pfizer-BioNTech
Serum Institute of India	COVISHIELD	Adenovirus (CHAdOx1) vector	✓	Two doses, 4-12 weeks apart	- AstraZeneca - Moderna - Pfizer-BioNTech
Janssen (Johnson & Johnson)	Ad26.COV2.5	Adenovirus type 26 vector	✓	One dose	N/A – one dose series
SinoPharm / Beijing Institute of Biological Products (BIBP)	Covilo / BBIBP-CorV	Whole inactivated Coronavirus	✓	Two doses, 21-28 days apart	- Moderna - Pfizer-BioNTech
Sinovac	CoronaVac	Whole inactivated Coronavirus	✓	Two doses, 14-28 days apart	- Moderna - Pfizer-BioNTech
Bharat Biotech, India	COVAXIN	Whole inactivated Coronavirus	✓	Two doses, 28 days apart	- Moderna - Pfizer-BioNTech
Novavax	NVX-CoV2373 / Nuvaxovid	Protein subunit	✓	Two doses, 21-28 days apart	- Moderna - Pfizer-BioNTech
Serum Institute of India	NVX-CoV2373 / Covovax	Protein subunit	✓	Two doses, 21-28 days apart	- Moderna - Pfizer-BioNTech
The Gamaleya National Center	Sputnik V	Human adenovirus vector	pending		
SinoPharm / Wuhan Institute of Biological Products (WIBP)	Inactivated SARS-CoV-2 Vaccine (Vero Cell)	Whole inactivated Coronavirus	pending		
CanSinoBio	Ad5-nCoV	Adenovirus Type 5 vector	pending		
CureVac	CVnCoV/CV07050101 Zorecimeran (INN)	mRNA	pending		

COVID 19 vaccines in India

Title & Author	Study design	Intervention	Results
RCT to assess the safety and immunogenicity of SII-ChAdOx1 nCoV-19 (**Covishield**) in adults in India	n=1601 Phase 2/3 Double blinded 14 hospitals in India	3:1 to Covishield or AZD1222 (Immunogenicity cohort) n=401 and 3:1 to Covishield or placebo (safety cohort) n=1200 2 doses 4 wks apart	Covishield was non-inferior to AZD1222 (GMT ratio 0.98; 95% CI 0.78- 1.23). SAEs were reported in <2.0% participants across the three groups
Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152) Covaxin	randomised, double-blind, placebo-controlled, multicentre, phase 3 clinical trial in 25 Indian hospitals n= 25798	BB152 vaccine(n=12221) v/s placebo(12 198) 2 doses 4 wks apart	130 cases total in 16973(per protocol) 24 (0·3%) cases in vaccine recipients(n=8471) 106 (1·2%) in placebo recipients(n= 8502) estimated vaccine efficacy of 77·8% Adverse events : 12.4% in the both arms

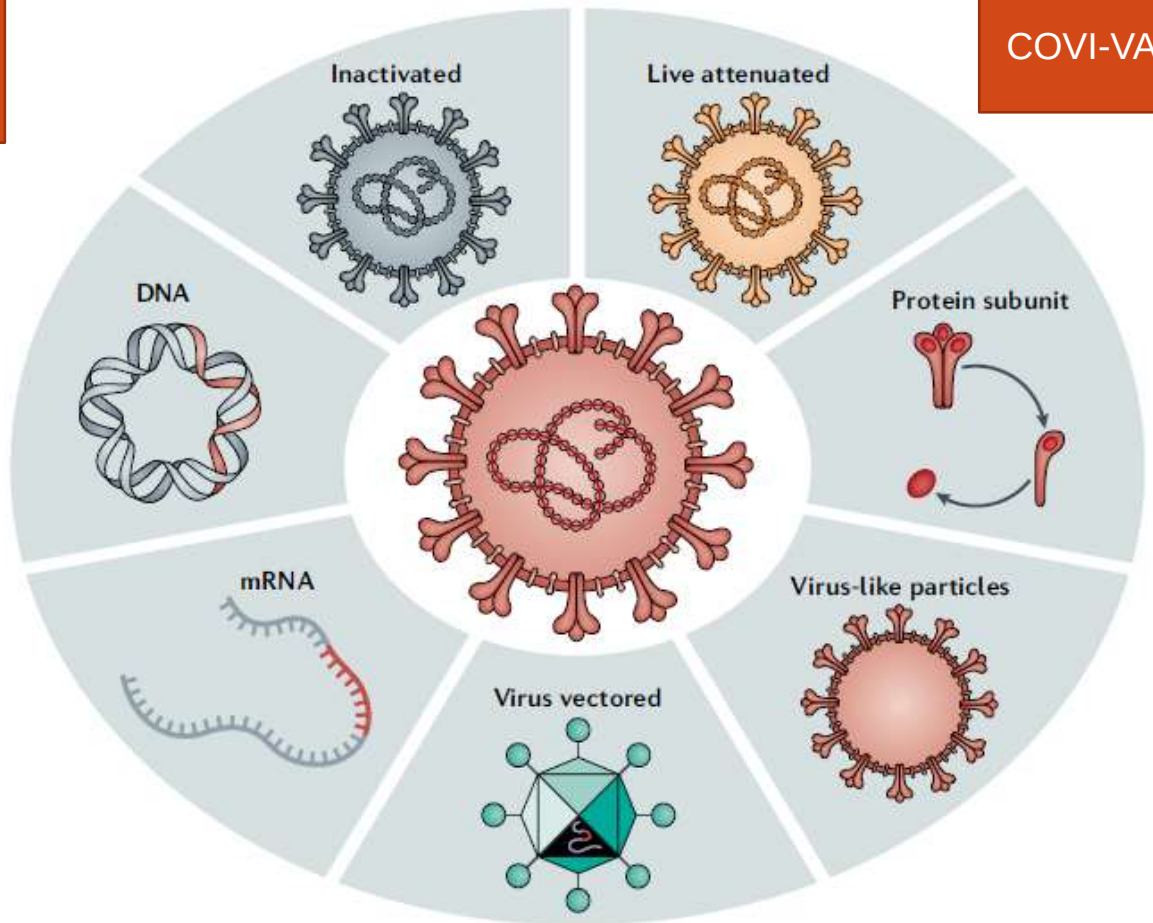
Kulkarni Prasad et al EClinicalMedicine 42 (2021) 101218
Raches Ella et al Lancet. 2021 Dec 11;398(10317):2173-2184

COVID vaccines

Covaxin,Bharat Biotech
CoronaVac,Sinovac Biotech

ZYCOV-D,Zydus cadilla

BNT16b2 Pfizer/Biotech
mRNA1273, Moderna



Gamaleya,Sputnik V
AstraZeneca ChAdOX1
Ad26.COV2.S Johnson & Johnson

COVI-VAC,Codagenix/SII

NVX-CoV2373, Novavax
Co-VLP,Medicago/GSk

Dai Lainpan et al Nature Reviews Immunology volume 21, pages73–82 (2021)

COVID Vaccines

Vaccine	Age	Dose	Route	Cost
Pfizer-BioNTech	>5yrs	30µg/0.3mlper dose	I.M 2 doses 21days apart	$ 20
Moderna	>18yrs	100µg/0.5mlper dose	I.M 2 doses 28 days apart	$ 15
Johnson and Johnson's Janssen	>18yrs	$5x10^{10}$ viral particles	I.M single dose	$10
Astrazenca/Covishield	>18 yrs	$5x10^{10}$ viral particles	I.M 2 doses 4-12 wks apart	$ 4-6
COVAXIN	>18 yrs	6µg/0.5 ml/dose	I.M 2 doses 28 days apart	$ 3-5
ZYCOV-D	>12 yrs	Total dose -6mg	3 doses 28 days apart,needle free injector ,I.D	$ 3-5

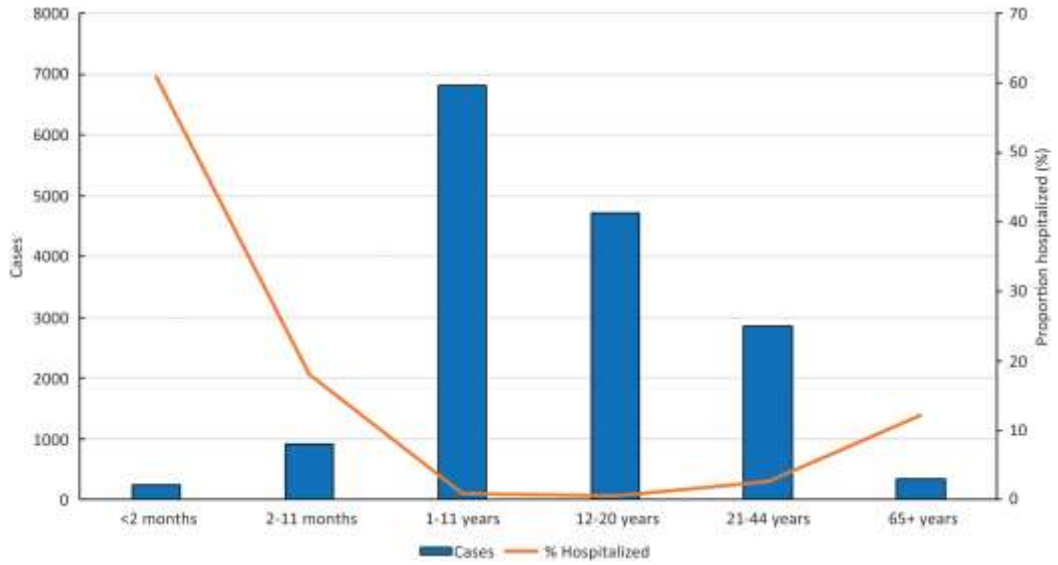
FioletThibault Clinical Microbiology and Infection 28 (2022) 202-221

Bordetella pertussis

- Exclusively human pathogen causing a highly contagious respiratory illness
- Incidence dropped significantly following introduction of pertussis vaccine
- Increase in incidence of cases reported to CDC (6.1/lac population in 2011 to 15.4 /lac in 2012) with more than half cases in persons >11 yrs
- More than 1.5lac cases globally in 2018

Macina Denis et al Infect Dis Ther (2021) 10:1141–1170
Mbayei sarah et al Clin Infect Dis. 2019 Jul 2;69(2):218-226

Bordetella pertussis



Number of pertussis cases and the proportion hospitalized by age group at enhanced pertussis surveillance sites, united states, 2011–2015.

Enhanced pertussis surveillance (EPS) as part of the emerging infections program network in 7 US states

N=15,942 pertussis cases
Hospitalized- 515(3.2%)
>21 yrs – 117/515(23%)
Asthma – 31/117(27%)
COPD - 22/117(19%)

Mbayei sarah et al Clin Infect Dis. 2019 Jul 2;69(2):218-226

Bordetella pertussis vaccine recommendation

- Age :10-64 yrs
- Routine booster ≥5 years after a dose of DTaP or Td vaccine, with a second dose ≥8 years after first (any) Tdap dose
- Tetanus prophylaxis if ≥5 years have elapsed since the last tetanus-containing vaccine

Havers. Fiona P et al Weekly / January 24, 2020 / 69(3);77–83

Pseudomonas vaccine in CF

Cochrane Library
Cochrane Database of Systematic Reviews

Vaccines for preventing infection with Pseudomonas aeruginosa in cystic fibrosis (Review)

Johansen HK, Gøtzsche PC

Study	Intervention	Adverse effects	Outcome
Doring etal, 2007 N=476 Double blind, randomised,placebo controlled, phaseIII	Pseudomonal vaccine v/s placebo Flagella proteins of subtypes a0a1a2 and b from strains 1210 and 5142,respectively,	227 events, 4 severe	No decrease in risk of chronic infection Lung function similar in both groups
Langford et al,1983 N= 37	No comparison group polysaccharide vaccine of 16 international serotypes of *P. aeruginosa* (Lot PEV01,Wellcome)	91 events , 1 severe	

Doring et al Proc Natl Acad Sci U S A. 2007 Jun 26;104(26):11020-5
Langford et al Arch Dis Child. 1984 Dec;59(12):1131-4.

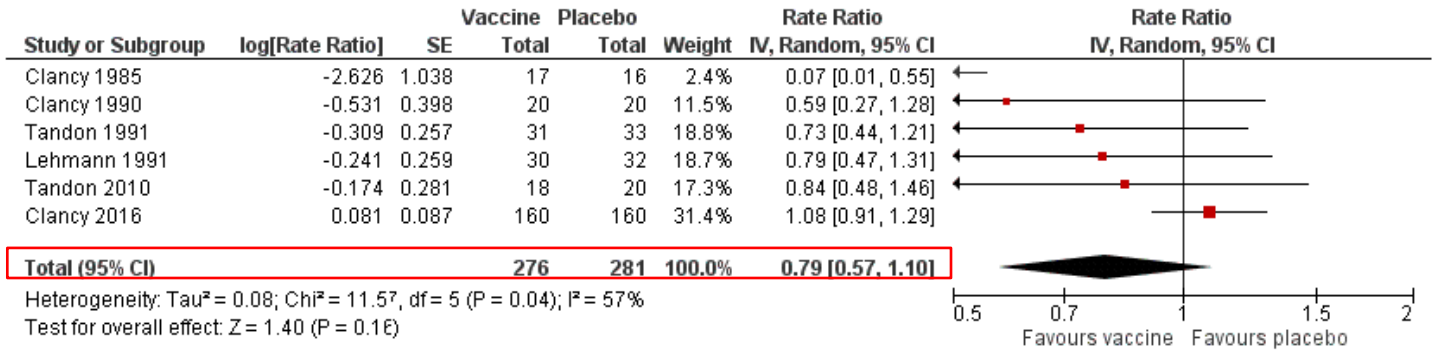
Haemophilus influenza vaccine

RCTs- 6 ,placebo controlled;5 double blinded
Participants – COPD/chronic bronchitis,
Mean age -40-80 yrs; Trial duration – 3-12 months
Vaccine- enteric coated,killed preparation(two tablets for 3 consecutive days on D 0,28,56)

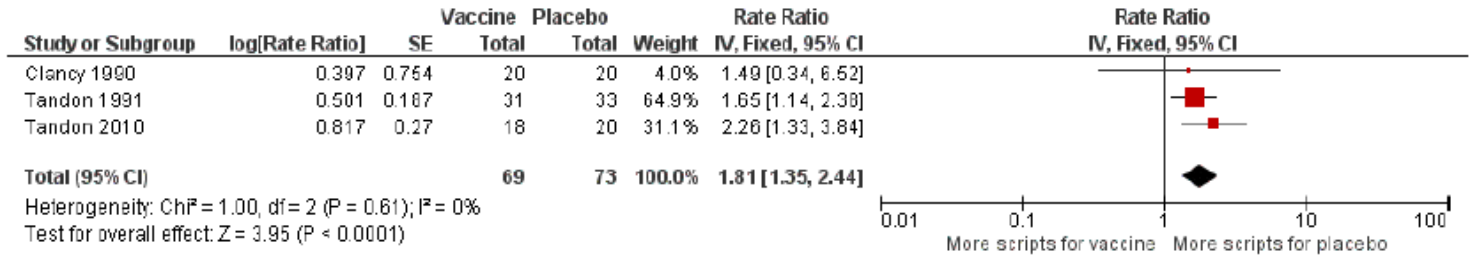
Cochrane Library
Cochrane Database of Systematic Reviews

Haemophilus influenzae oral vaccination for preventing acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease (Review)

Teo E, Lockhart K, Purchuri SN, Pushparajah J, Cripps AW, van Driel ML



Outcome – exacerbations
Non significant decrease of 2.084%



Outcome – antibiotic prescriptions
80% increase in placebo group

E Teo et al Cochrane Database of Systematic Reviews 2017, Issue 6.

Haemophilus influenza and Moraxella catarrhalis vaccine

Study	Intervention	Outcome
Phase2 trial Observer blind N=145 COPD(mod – severe disease with prior exacerbations)	NTHi vaccine (Protein D ,ProteinE-PilinA,AS01 adjuvant) 1:1 randomisation 2 I.M doses of vaccine 60 days apart v/s placebo	acceptable safety and reactogenicity profile and good immunogenicity in adults with COPD.
Randomised , observer blind, placebo controlled N=90, age-50 to 71yrs Smoking history(at least 10 pack years)	Multi component vaccine NTHi (PD and PE-PilA) and Mcat (UspA2) surface proteins 1:1:1 randomization 10-10-AS01(n=27) 10-3-AS01(n=26) Placebo(n=28) 2 doses 60 days apart	immune responses against NTHi antigens persisted for 4 years after two-doses No persistent response against the Mcat antigen. No safety concerns were identified during follow-up

Wilkinson et al Vaccine 37 (2019) 6102–6111
Smedt et al Vaccine: X 9 (2021) 100124

Coadministration of different vaccines

- PCV15 , PCV20 and PPSV 23 can be co administered with QIV
- Influenzae vaccine may be co administered with COVID 19 vaccine at separate anatomic sites to avoid local reactions
- Co administration of PCV15,PCV20 or PPSV23 with COVID19 vaccines is under evaluation

Summary

Respiratory disorder	Vaccine Recommendations
Bronchial asthma	COVID vaccine for all Influenzae vaccine for moderate to severe asthma cases Pneumococcal Vaccine in asthma routinely not advised
COPD	COVID and Influenzae vaccine for all Pneumococcal Vaccine(PCV 13 & PPSV 23) for all >65 yrs PCV 13 for young individuals with significant comorbid conditions
Bronchiectasis	Limited studies/evidence
Other chronic respiratory disorders	Lacking relevant studies