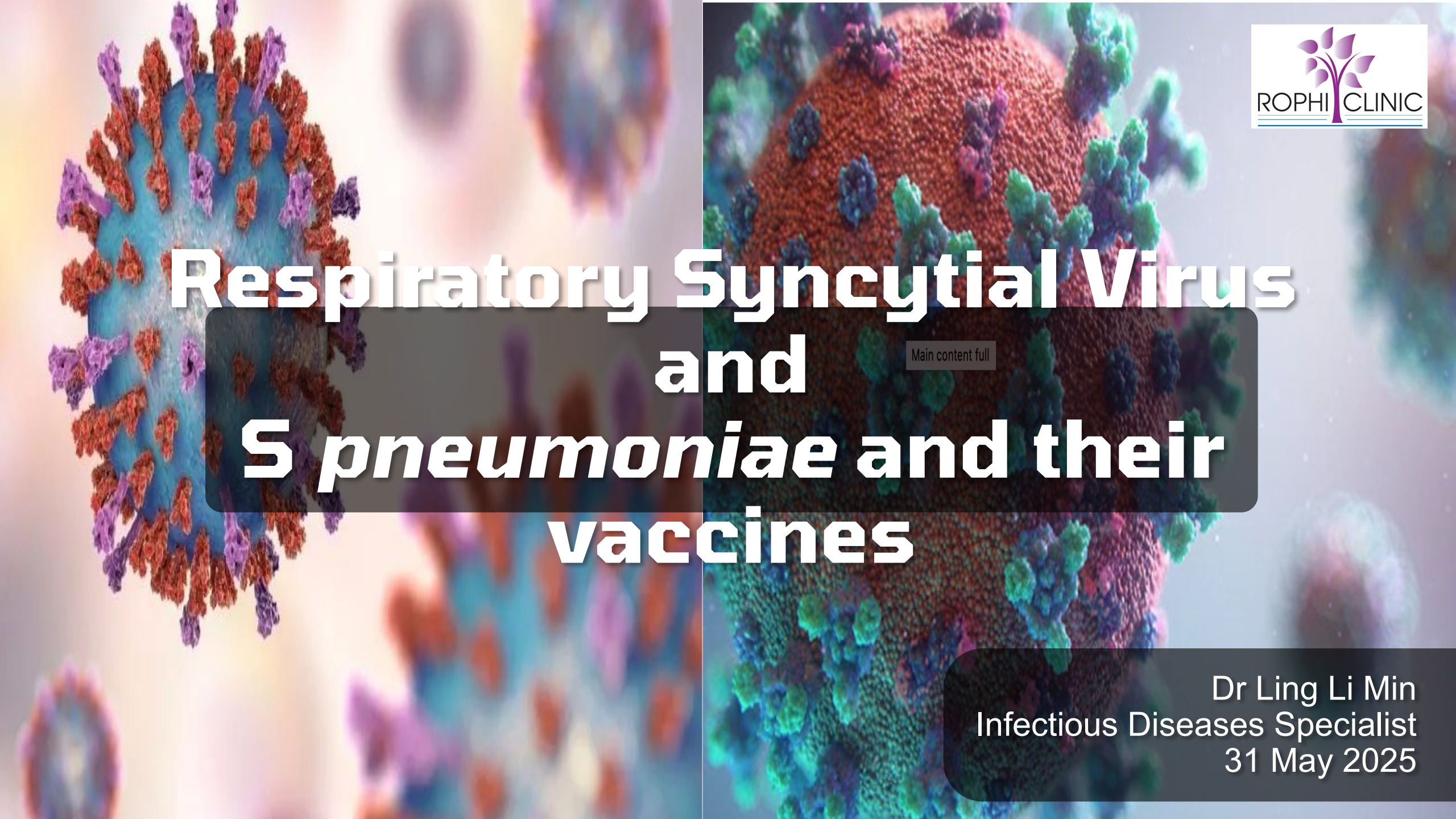

Respiratory Syncytial Virus and *S pneumoniae* and their vaccines

Main content full

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Infectious Diseases Specialist
31 May 2025

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Respiratory Syncytial Virus(RSV)

- Respiratory syncytial virus epidemiology
- 2 Pivotal trials
- ACIP Guidelines & Recommendations
- Real World Data

Who Gets RSV?

Young Infants/Young Children

- In children < 5 years of age,
  - RSV leads > 2 million outpatient visits and between 58,000 and 80,000 hospitalizations.
- Babies : 6 weeks and 6 months of age
  - are the most likely to be hospitalized. Between 100 and 300 children die each year from RSV and its complications.

Adults over 65:

- Annually, in the U.S., between 60,000 and 160,000 adults are hospitalized, and 6,000 to 10,000 deaths

Individuals with chronic conditions: Older children and adults with chronic diseases of the lungs or heart and those with immune-compromising conditions are at increased risk for severe disease if infected with RSV.

https://www.chop.edu/vaccine-education-center/vaccine-details/rsv-vaccine-monoclonal-antibody Accessed 6 Oct 2024

Seasonal Variability

- The Southern Hemisphere between March and June
- The Northern Hemisphere between September and December
- Most seasons last 5 to 6 months
- More humid countries, RSV tend to linger up to 10 months

Country	Start (season week)	Peak (season week)	End (season week)	Season length (weeks)	Period studied	Region variability
Southern Asia						
Malaysia	July	September–December	March	36	1982–2008	No
Philippines	October	November–December	February	20	2010–2013	Yes
Thailand	April–May	September	November	24	2005–2011	No
East Asia						
China	November	December–February	April	24	2010–2015	Yes
Japan	30–45	41–50	45–9**	14–27	2010–2017	No data
South Korea	August–October	Mid-October–November	December	14–20	2008–2016	No data

Obando-Pacheco et al JID 2018:217 (1 May)

Virus	Peak Incidence	R0	Incubation	Duration of Viral Shedding
Influenza	Seasonal influenza: winter months H1N1: winter months, but infection occurs year round	Seasonal: 1.3 H1N1: 1.3-1.7	1-4 days	1-2 weeks
Rhinovirus	Early fall, but infections occur year round	Not well studied	2-4 days	5 days to 3 weeks
Coronavirus	Winter, but infections occur year round	Non-SARS/MERS: unknown SARS: pandemic ~3, prepandemic <1 MERS: <1	Non-SARS/MERS: 2-5 days SARS: 2-10 days MERS: 2-14 days	Non-SARS/MERS: 1-week to 1 month SARS: 1-2 weeks MERS: unknown
Respiratory syncytial virus	November to April	1.2-7.1	3-7 days	1-2 weeks
Human metapneumovirus	Late winter and spring, but infections occur year round	Not well studied	3-6 days	Unknown, but peak titers 7-9 days after infection
Parainfluenza	PIV1: fall and winter PIV2: fall and winter PIV3: spring and summer, but infections occur year round PIV4: not well studied	Not well studied	2-6 days	1-3 weeks
Adenovirus	No seasonal variation	Not well studied	4-8 days	1-3 weeks
Enterovirus	Summer and fall, but infections occur year round	Not well studied	2-7 days	1-3 weeks

Nguyen C et al. J of Intensive Care Med 2016;3:427

Virus	Transmission	Clinical Presentation	Established Treatment	Investigational Treatment
Influenza	Large particle droplets	• Common: fever, cough, sore throat, headache, myalgia, malaise, and gastrointestinal complaints • Uncommon: respiratory failure, ARDS, myositis, meningoencephalitis, transverse myelitis, and cardiomyopathy	• Zanamivir and oseltamivir • Supportive care • Vaccination	• Peramivir • Combination antiviral therapy
Rhinovirus	• Large particle droplets • Direct contact	• Common: cough, sore throat, rhinorrhea, and myalgias • Uncommon: respiratory failure and severe LRTI	Supportive care	Intranasal interferon
Coronavirus	• Large particle droplets • Direct contact • Fecal oral contamination	• Common: fever, chills, rigors, cough, chest pain, and gastrointestinal symptoms • Uncommon: severe LRTI, ARDS	Supportive care	• Ribavirin for MERS-CoV • Vaccination
Respiratory syncytial virus	• Direct contact • Fomites • Large particle droplets	• Common: cough, coryza, rhinorrhea, and conjunctivitis • Uncommon: severe LRTI, ARDS, SIADH, hepatitis, myocarditis, and neurologic deficits	Supportive care	• Ribavirin • IVIG • Corticosteroids
Human metapneumovirus	• Large particle droplets • Fomites • Direct contact	• Common: cough, nasal congestion, rhinorrhea, dyspnea, hoarseness, and wheezing • Uncommon: severe LRTI, ARDS, and respiratory failure	Supportive care	Ribavirin
Parainfluenza	• Large particle droplets • Direct contact	• Common: fever, rhinorrhea, cough, sore throat, and myalgias • Uncommon: respiratory failure and ARDS	Supportive care	• Ribavirin • IVIG • Hemaglutinin-neuraminidase inhibitors • Recombinant sialidase
Adenovirus	• Large particle droplets • Fecal oral contamination • Fomites	• Common: URTI, gastroenteritis, keratoconjunctivitis, and meningitis • Uncommon: severe LRTI, respiratory failure, ARDS, and encephalitis	Supportive care	• Cidofovir • Ganciclovir • IVIG

Nguyen C et al. J of Intensive Care Med 2016;3:427

Burden and Cost of RSV in Singapore

A) Estimated RSV-associated hospitalisations and primary care consults, SG 2014

Age, mo	Outcome	Total no. cases (95% CI)	No. cases/1,000 person-years (95% CI)
Hospitalizations			
<6	All diagnoses	708 (664–765)	33.5 (31.4–36.2)
	Bronchiolitis	637 (604–671)	30.2 (28.6–31.8)
	Pneumonia	54 (30–99)	2.6 (1.4–4.7)
	Pneumonia with complications	15 (7–29)	0.7 (0.3–1.4)
6–29	All diagnoses	1,096 (994–1,269)	13.2 (12–15.3)
	Bronchiolitis	826 (793–862)	9.9 (9.5–10.4)
	Pneumonia	203 (115–372)	2.4 (1.4–4.5)
	Pneumonia with complications	63 (38–110)	0.8 (0.5–1.3)
Primary care consultations			
<6	ARI	3,600 (3,120–4,130)	170.5 (147.8–195.6)
6–29	ARI	5,700 (5,010–6,450)	68.6 (60.3–77.6)

*Estimates are expressed as the medians from 10,000 Monte Carlo simulations. Note that the sum of medians from individual diagnoses does not equal the median for all diagnoses combined. ARI, acute respiratory illness; RSV, respiratory syncytial virus.

Tam CC et al. Emerg Infect Dis. 2020 Jul;26(7):1489-1496.

B) Cost of RSV-associated hospitalisations and primary care consults, SG 2014

Age, mo	Outcome	Full cost (95% CI)	Subsidized cost (95% CI)
Hospitalizations			
<6	All	$2,160,000 ($2,002,000–$2,352,000)	$1,321,000 ($1,168,000–$1,492,000)
	Bronchiolitis	$1,881,000 ($1,771,000–$1,995,000)	$1,127,000 ($1,006,000–$1,250,000)
	Pneumonia	$152,000 ($82,000–$278,000)	$106,000 ($53,000–$198,000)
	Pneumonia with complications	$119,000 ($55,000–$220,000)	$80,000 ($25,000–$167,000)
6–29	All	$3,554,000 ($3,175,000–$4,118,000)	$2,236,000 ($1,932,000–$2,651,000)
	Bronchiolitis	$2,436,000 ($2,319,000–$2,563,000)	$1,459,000 ($1,328,000–$1,600,000)
	Pneumonia	$573,000 ($321,000–$1,041,000)	$401,000 ($217,000–$729,000)
	Pneumonia with complications	$523,000 ($322,000–$857,000)	$358,000 ($191,000–$610,000)
Primary care consultations			
<6	Primary care attendances	$177,000 ($153,000–$203,000)	$118,000 ($102,000–$136,000)
6–29	Primary care attendances	$280,000 ($246,000–$317,000)	$187,000 ($163,000–$213,000)
Hospitalizations and primary care consultations			
<6	All	$2,337,000 ($2,175,000–$2,530,000)	$1,440,000 ($1,285,000–$1,611,000)
6–29	All	$3,833,000 ($3,454,000–$4,399,000)	$2,423,000 ($2,115,000–$2,838,000)
<30	All	$6,228,000 ($5,734,000–$6,950,000)	$3,899,000 ($3,506,000–$4,432,000)

*Estimates are expressed as the medians from 10,000 Monte Carlo simulations. Note that the sum of medians from individual diagnoses does not equal the median for all diagnoses combined. All costs are in Singapore dollars. RSV, respiratory syncytial virus.

Tam CC et al. Emerg Infect Dis. 2020 Jul;26(7):1489-1496.

Burden of RSV- associated Acute Respiratory Infections in Pregnancy

- Proportion with ARI that tested positive for RSV ranged from 0.9% to 10.7%, with a meta-estimate of 3.4% (95% confidence interval [CI], 1.9%– 54%).
- The pooled incidence rate of RSV among pregnant individuals was 26.0 (95% CI, 15.8–36.2) per 1000 person-years.
- RSV hospitalization rates reported :2.4 and 3.0 per 1000 person-years.
- No deaths (5 studies)
- RSV-positive vs RSV-negative pregnant individuals : no difference in the odds of miscarriage, stillbirth, low birth weight, and small size for gestational age.
- RSV-positive pregnant individuals had higher odds of preterm delivery (odds ratio, 3.6 [95% CI, 1.3–10.3]).

Sebastien Kenmoe et al. The Journal of Infectious Diseases 2024;229(S1):S51–60

In Pregnancy

- 43 per 1000 person-months among HIV-uninfected women
- Cough (72.1%), rhinorrhea (39.5%), sore throat (37.2%), and headache (42%), NO FEVER
- NO adverse pregnancy outcomes
- Postpartum, concurrent infection among 51.9% of their infants and, conversely, 29.8% of mothers investigated within 7 days of their infants having an RSV illness also tested positive for RSV.

Madhi et al. Clinical Infectious Diseases 2017; 66:1658

Older Adults > 60y/o In Higher Income Countries

	RSV-ARI	RSV hospitalizations	RSV in-hospital deaths
Overall (point estimates, 95% CI)	Attack rate 1.62% (0.84–3.08)	Hospitalization rate 0.15% (0.09–0.22)	hCFR 7.13% (5.40–9.36)
Population ≥60 years of age in 2019	Number of cases (95% CI)	Number of hospitalizations (95% CI)	Number of in-hospital deaths (95% CI)
 High-income countries 321,292,000	5,188,866 (2,698,853–9,899,007)	465,873 (302,014–719,694)	33,231 (16,321–67,371)
 Europe 188,795,000	3,049,039 (1,585,878–5,816,774)	273,753 (177,467–422,901)	19,527 (9,590–39,588)
 United States 75,058,081	1,212,188 (630,488–2,312,539)	108,834 (70,555–168,130)	7,763 (3,813–15,739)
 Japan 43,191,000	697,535 (362,804–1,330,715)	62,627 (40,600–96,748)	4,467 (2,194–9,057)

Savic M et al. Influenza Other Respir Viruses. 2023 Jan;17(1):e13031

RSV-NET, 12 States - July 2022 to 2023

Among a random sample of 1,634 older adult patients (≥60 years old) with RSV-associated hospitalization

- **54.1%** were aged ≥75 years; 17.2% (95% CI = 14.9%–19.8%) of all cases occurred in long-term care facility residents
- Most common underlying medical conditions were **obesity**, **chronic obstructive pulmonary disease, congestive heart failure**, and **diabetes**.
- **Severe outcomes** occurred in **18.5%** (95% CI = 15.9%–21.2%) of hospitalized patients aged
  ≥ 60 years.
  - 17.0% (95% CI = 14.5%–19.7%) were admitted to an intensive care unit,
  - 4.8% (95% CI = 3.5%–6.3%) required mechanical ventilation,
  - 4.7% (95% CI = 3.6%–6.1%) died

Havers et al RSV-NET surveillance team US CDC Morbidity and Mortality Weekly Report Oct 6 2023

In Older Adults

- The pre-pandemic incidence rate of RSV-positive ARI was 48.6 (95% CI, 36.9-62.9) per 1000 person- years with a 2.50% (95% CI, 1.90%-3.21%) attack rate.
- reported **significantly lower QOL within 2 to 4 weeks of infection:**
- physical health; fatigue, difficulty in social functioning

Young J Juhn JAMA Network 2023;6(1):e2250634

RSV vs COVID vs Flu

Between February 1, 2022 and May 31, 2023, a total of 9,117 adults > 18 years old
Lab confirmed RSV, SARS-CoV-2, or influenza

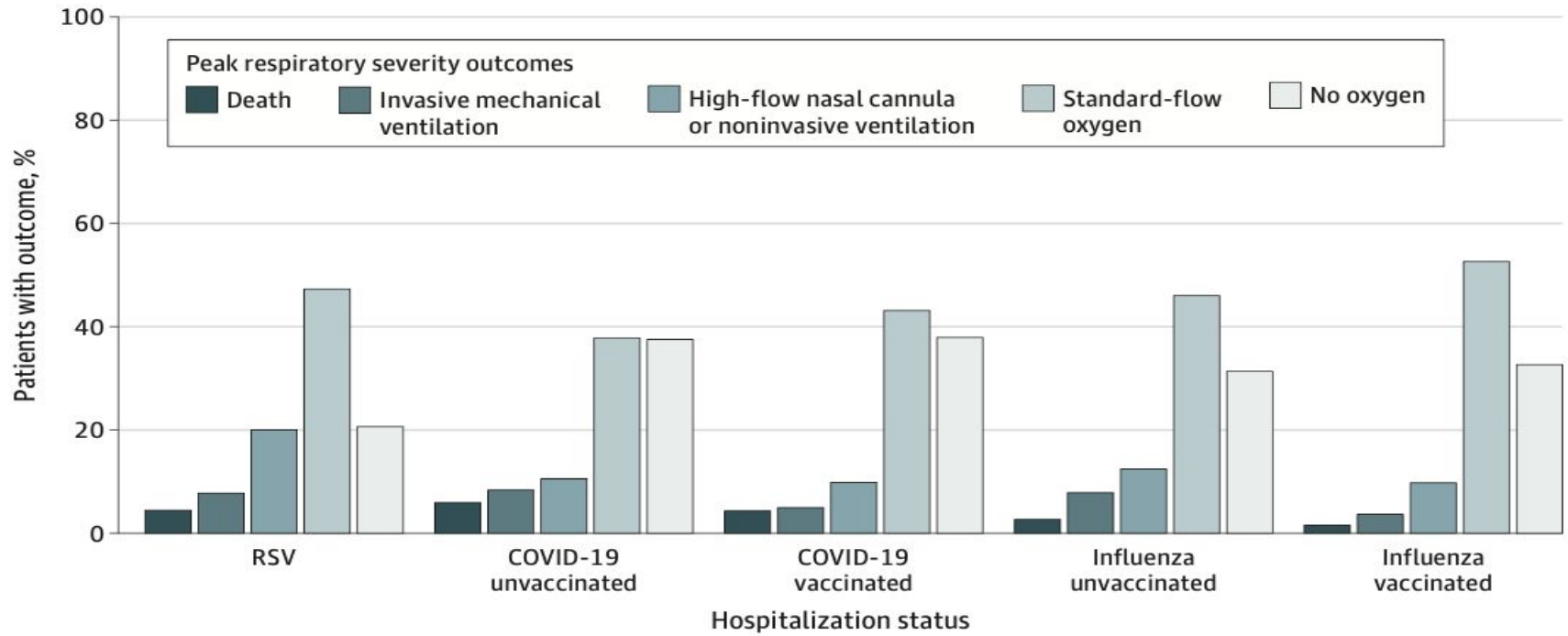
Characteristic	Patients, No. (%)		
	RSV (n = 484)	COVID-19 (n = 6422)	Influenza (n = 1092)
Influenza vaccination status[h]			
Unvaccinated	226 (46.7)	3060 (47.7)	699 (64.0)
Vaccinated[i]	216 (44.6)	2882 (44.9)	393 (36.0)

Sure et al. JAMA Network Open. 2024;7(4):e244954.
doi:10.1001/jamanetworkopen.2024.4954

Table 3. Disease Severity of RSV, SARS-CoV-2, and Influenza by Subtype or Lineage Among US Adults

In-hospital outcome	RSV subtypes Patients, No. (%) A (n = 250)	B (n = 118)	*P* value	SARS-CoV-2 Omicron lineages Patients, No. (%) BA.1 (n = 217)	BA.2 (n = 691)	BA.4/5 (n = 1310)	BQ.1 (n = 467)	XBB.1.5 (n = 781)	*P* value	Influenza A Subtypes Patients, No. (%) A(H3N2) (n = 474)	A(H1N1) (n = 175)	*P* value
Supplemental oxygen therapy[a]	188 (75.2)	84 (71.2)	.41	158 (72.8)	372 (53.8)	751 (57.3)	275 (58.9)	443 (56.7)	<.001	297 (62.7)	121 (69.1)	.13
Advanced respiratory support[b]	71 (28.4)	32 (27.1)	.80	70 (32.3)	87 (12.6)	238 (18.2)	77 (16.5)	136 (17.4)	<.001	76 (16.0)	42 (24.0)	.02
Acute organ failure[c]	74 (29.6)	32 (27.1)	.62	76 (35.0)	102 (14.8)	258 (19.7)	87 (18.6)	159 (20.4)	<.001	84 (17.7)	44 (25.1)	.04
ICU admission	62 (24.8)	22 (18.6)	.19	59 (27.2)	93 (13.5)	213 (16.3)	75 (16.1)	108 (13.8)	<.001	68 (14.4)	32 (18.3)	.22
IMV or death	28 (11.2)	11 (9.3)	.58	34 (15.7)	49 (7.1)	126 (9.6)	40 (8.6)	60 (7.7)	.002	33 (7.0)	14 (8.0)	.65

Figure 1. Peak Respiratory Severity of Adults Hospitalized With Respiratory Syncytial Virus (RSV), COVID-19, or Influenza by Vaccination Status



RSV

The RSV virion surface consists of three integral proteins – a receptor attachment glycoprotein, a fusion (F) glycoprotein, and a small hydrophobic protein.

The F protein plays a critical role in viral fusion and entry into host cells.

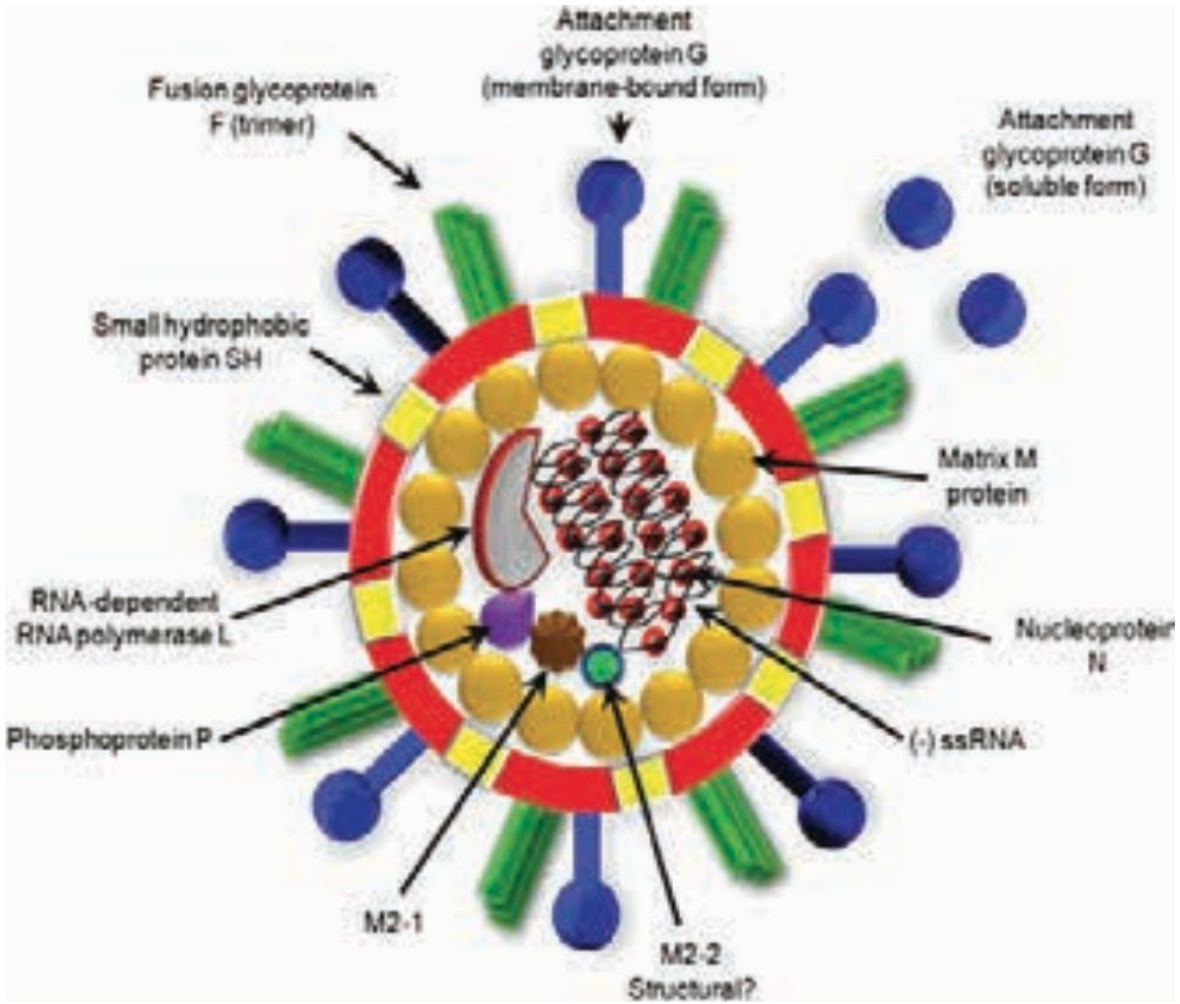


Figure adapted from González et al. Rev Med Virol. 2012 Jul;22(4):230- 44.

McLellan JS, Ray WC, Peeples ME. Curr Top Microbiol Immunol. 2013;372:83-104

RSV Vaccines

Vaccine	Target Group	Details of Vaccine Administration	Regulatory Approval by the U.S. FDA	Regulatory Approval by the EMA
RSVpreF vaccine (Abrysvo™, Pfizer Inc.), a non-adjuvanted, bivalent recombinant stabilized prefusion F protein subunit vaccine	Infants (via maternal immunization at 32–36 weeks gestation for U.S. FDA, and at 24–36 weeks gestation for EMA)	Single intramuscular dose of 120 mcg (0.5 mL). Coadministration with Tdap, influenza, and COVID-19 vaccines is possible	21 August 2023 [10,59]	23 August 2023 [58]
RSVpreF vaccine (Abrysvo™, Pfizer Inc.), a non-adjuvanted, bivalent recombinant stabilized prefusion F protein subunit vaccine	Individuals aged ≥ 60 years	Single intramuscular dose of 120 mcg (0.5 mL). Coadministration with influenza vaccine is possible	31 May 2023 [11]	23 August 2023 [58]

1 Nov 2024: in SG, pregnant women(32 to 36 weeks)
22 Oct 2024U.S. FDA Approves ABRYSVO® for Adults Aged 18 to 59 at Increased Risk for Disease

Table adapted from See KC Vaccination for Respiratory Syncytial Virus: A Narrative Review and Primer for Clinicians Vaccines 2023, 11, 1809
Straits Times 22 Oct 2024Pfizer Press Release 22 Oct 2024

Guideline Agency	Target Group	Details	Reference
American College of Obstetricians and Gynecologists (ACOG)	Pregnant women at 32 through 36 weeks gestation	Seasonal administration of one dose of RSV vaccine (Abrysvo, Pfizer Inc.) to prevent RSV LRTD in infants	ACOG (2023) [59]
U.S. Centers for Disease Control and Prevention	Pregnant women at 32 through 36 weeks gestation	Seasonal administration of one dose of RSV vaccine (Abrysvo, Pfizer Inc.) to prevent RSV LRTD in infants	Fleming-Dutra (2023) [10]
U.S. Centers for Disease Control and Prevention	Adults 60 years and older	Single dose of RSV vaccine with either Abrysvo™, (Pfizer Inc.) or Arexvy™, (GSK Inc.) to prevent RSV LRTD	Melgar (2023) [11]

GSK: GlaxoSmithKline; LRTD: Lower respiratory tract disease; RSV: Respiratory syncytial virus; U.S.: United States.

Table adapted from See KC Vaccination for Respiratory Syncytial Virus: A Narrative Review and Primer for Clinicians Vaccines 2023, 11, 1809

ACIP / US CDC

A single dose of any FDA-licensed RSV vaccine for

- all adults 75 years and older
- adults ages 60 to 74 years at increased risk of severe RSV

Eligible adults can have the vaccine anytime

ACIP; Advisory Committee on Immunization Practices, US CDC; United States Centers for Disease Control and Prevention, FDA; Food and Drug Administration

Britton et al. MMWR Aug 2024

Risk factors for severe RSV infections among adults 60 to 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/m^2)
- Moderate or severe immune compromise[†]
- Residence in a nursing home
- Other chronic medical conditions or risk factors that a health care provider determines would increase the risk for severe disease due to viral respiratory infection (e.g., frailty,[§] situations in which health care providers have concern for presence of undiagnosed chronic medical conditions, or residence in a remote or rural community where transportation of patients with severe RSV disease for escalation of medical care is challenging[¶])

Britton et al. MMWR Aug 2024

2024 GINA Guidelines for Asthma

- RSV vaccines prevent RSV-related acute respiratory infection; an adjuvanted RSV-subunit vaccine reduced upper and lower respiratory tract disease in adults 60 years or older, including in those with underlying coexisting conditions such as asthma.

2024 GOLD Guidelines for COPD

- RSV vaccines for patients > 60 years old (Evidence Level A)
- Influenza, pneumococcal vaccines, COVID -19 vaccines (Evidence Level B)

https://ginasthma.org/2024-report/ Page 106 Accessed 6 Oct 2024
https://www.pulmonologyadvisor.com/features/2024-gold-guidelines-recommend-patients-with-copd-receive-all-vaccines/ Accessed 6 Oct 2024

RENOIR study

ORIGINAL ARTICLE

Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

E.E. Walsh, G. Pérez Marc, A.M. Zareba, A.R. Falsey, Q. Jiang, M. Patton, F.P. Polack, C. Llapur, P.A. Doreski, K. Ilangovan, M. Rämet, Y. Fukushima, N. Hussen, L.J. Bont, J. Cardona, E. DeHaan, G. Castillo Villa, M. Ingilizova, D. Eiras, T. Mikati, R.N. Shah, K. Schneider, D. Cooper, K. Koury, M.-M. Lino, A.S. Anderson, K.U. Jansen, K.A. Swanson, A. Gurtman, W.C. Gruber, and B. Schmoele-Thoma, for the RENOIR Clinical Trial Group*

Walsh et al. NEJM April 2023;388:1465

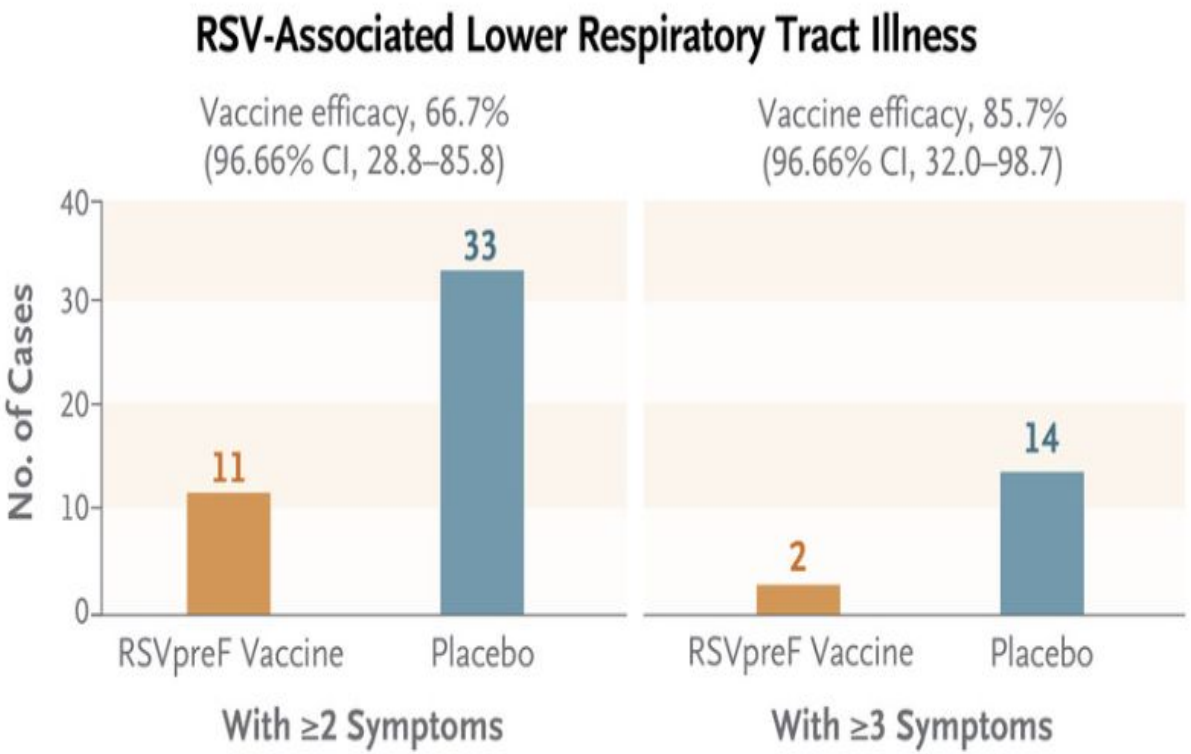
RENOIR - Methodology

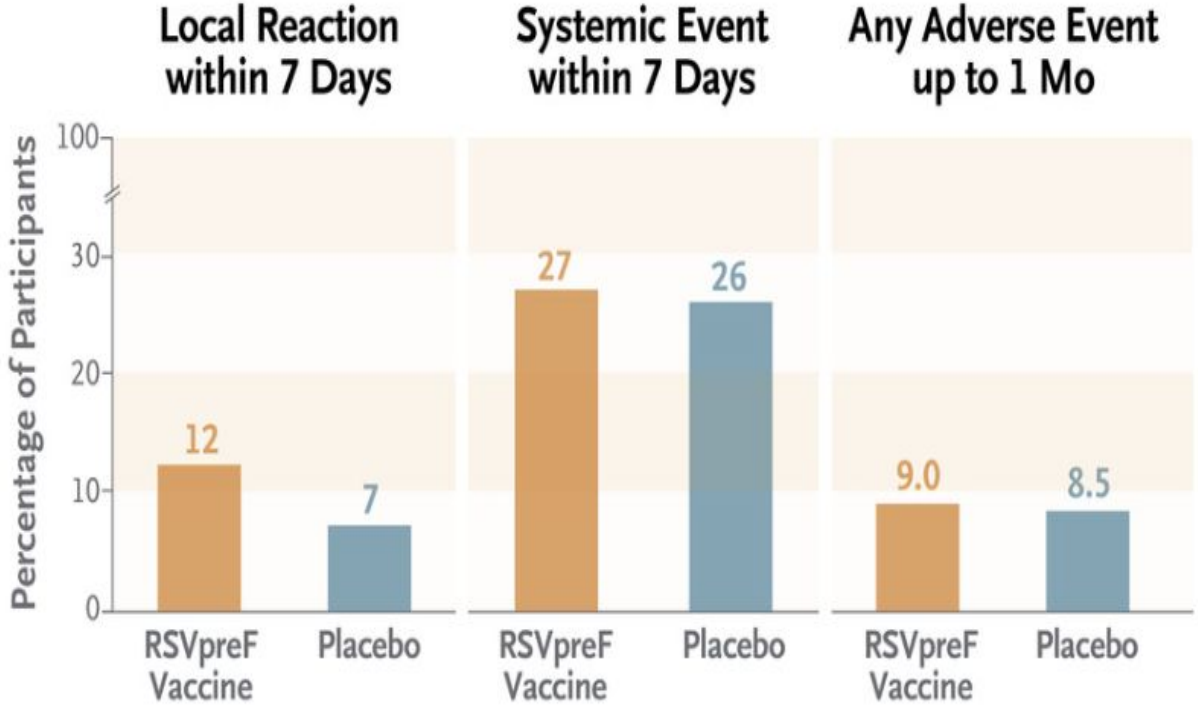
- 17,125 received RSVpreF vaccine vs 17,069 placebo
- ≥60 years old

- VE against RSV associated LRTI with
  - 2 signs or symptoms
  - 3 signs or symptoms
  - Starting on day 15 after injection

Walsh et al. NEJM April 2023;388:1465

RENOIR – Vaccine Efficacy and Safety





Walsh et al. NEJM April 2023;388:1465

Efficacy sustained across 2 seasons

End Point	End of Season One			End of Season Two			Seasons One and Two		
	RSVpreF Vaccine	Placebo	Vaccine Efficacy (95% CI)	RSVpreF Vaccine	Placebo	Vaccine Efficacy (95% CI)	RSVpreF Vaccine	Placebo	Vaccine Efficacy (95% CI)
	no. of cases/ no. at risk		%	*no. of cases/ no. at risk*		%	*no. of cases/ no. at risk*		%
RSV LRTI, ≥3 symptoms	2/18,050	18/18,074	88.9 (53.69–8.7)	8/16,164	36/16,059	77.8 (51.4–91.1)	10/18,050	54/18,074	81.5 (63.3–91.6)
RSV LRTI, ≥2 symptoms	15/18,050	43/18,074	65.1 (35.9–82.0)	39/16,164	88/16,059	55.7 (34.7–70.4)	54/18,050	131/18,074	58.8 (43.0–70.6)
RSV-associated ARI	37/18,050	98/18,074	62.2 (44.4–74.9)	149/16,164	236/16,059	36.9 (22.2–48.9)	186/18,050	334/18,074	44.3 (33.2–53.7)

* ARI denotes acute respiratory illness, LRTI lower respiratory tract illness, RSV respiratory syncytial virus, and RSVpreF RSV prefusion F protein–based.

Walsh et al. NEJM Oct 2024;391(15):1459-1461

MATISSE study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

Kampmann et al. N Engl J Med 2023; 388:1451-1464

MATISSE - Methodology

RSVpreF Vaccine (N=3495) vs Placebo (N=3480)

Women with uncomplicated singleton pregnancy at 24 to 36 weeks gestation

VE in preventing RSV associated illness in infants

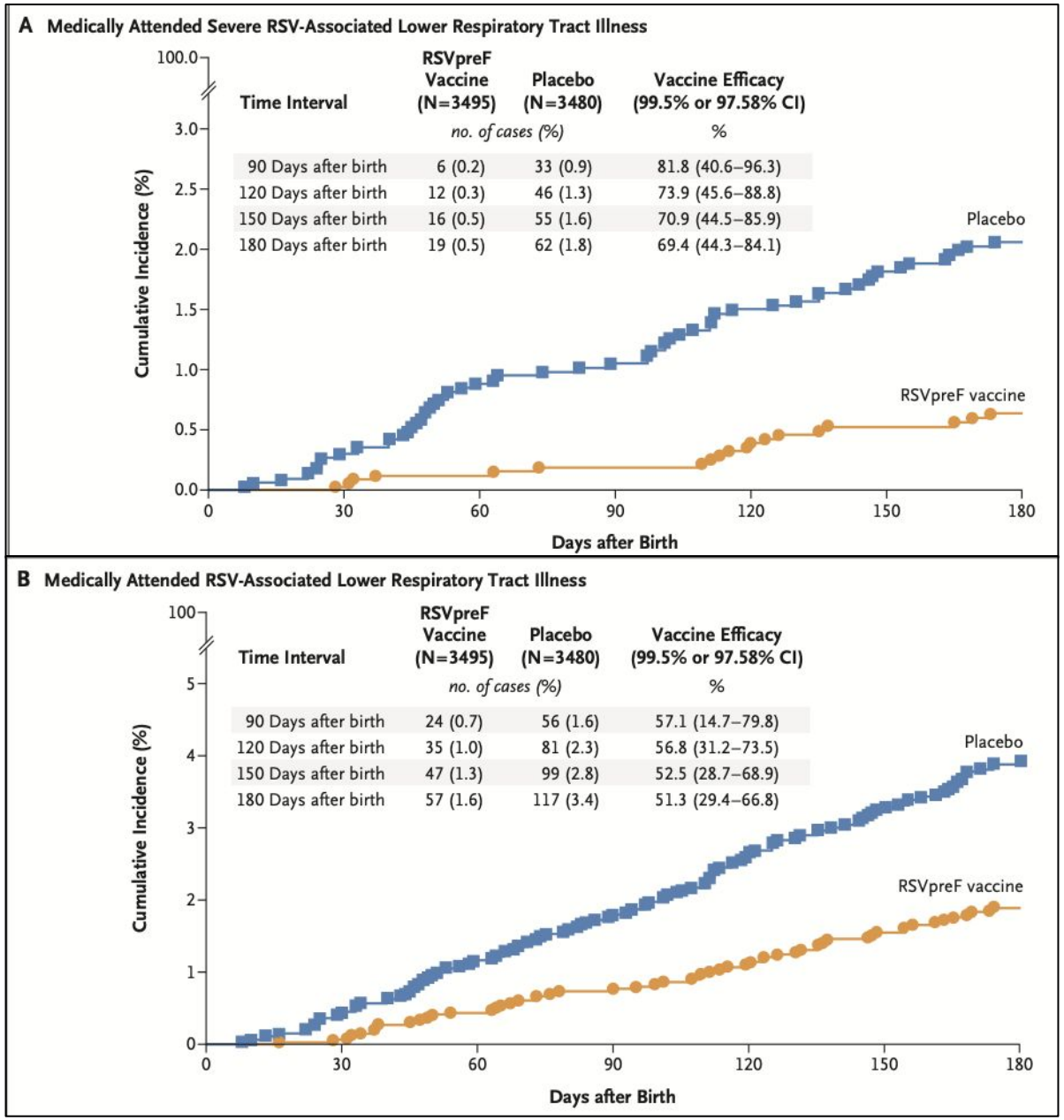
Safety of vaccine

End Points:

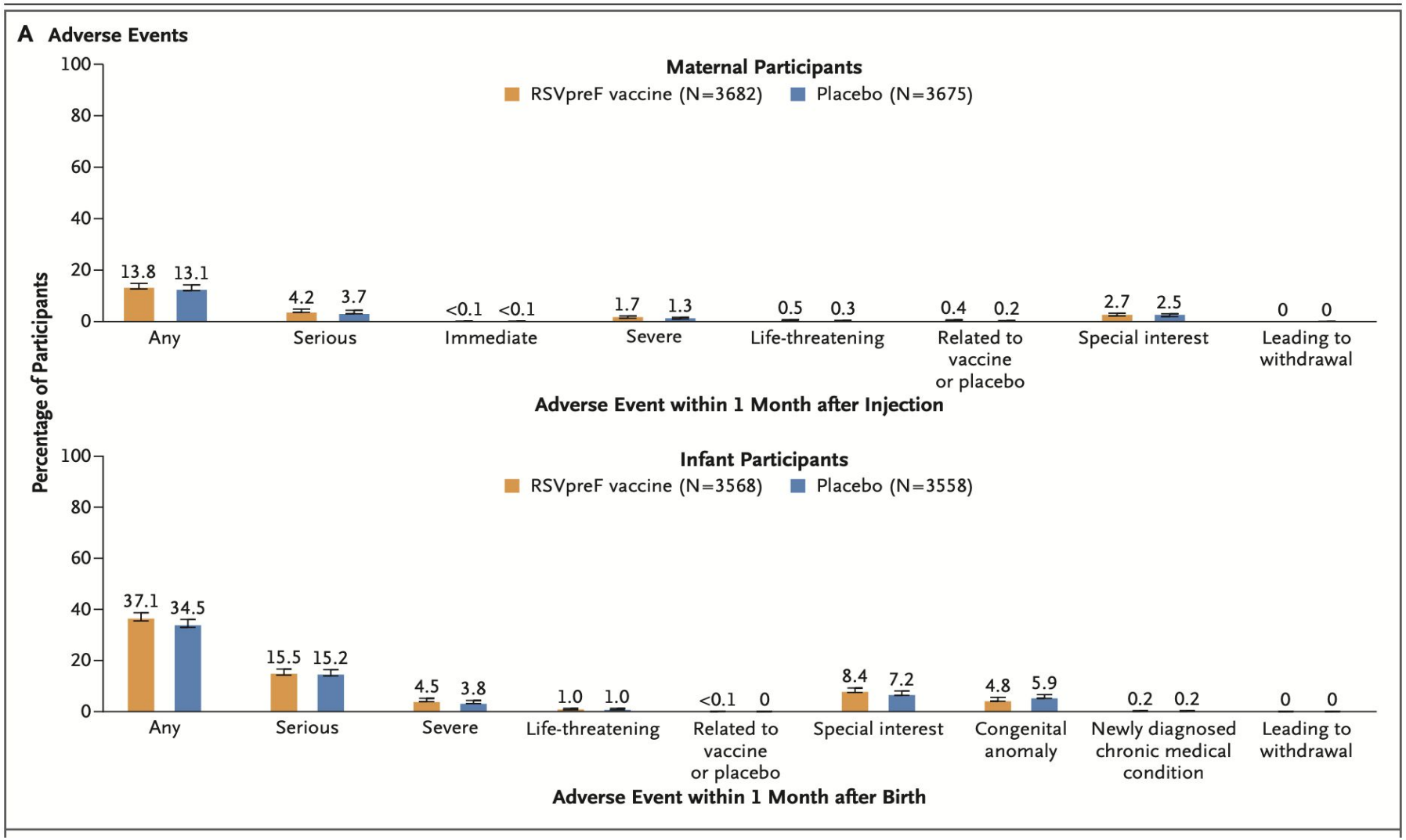
In infants within 90, 120, 150 and 180 days after birth

- Medically attended Severe RSV-associated LRTI
- Medically attended non-severe RSV-associated LRTI

Kampmann et al. N Engl J Med 2023; 388:1451-1464



Kampmann et al. N Engl J Med 2023; 388:1451-1464



No safety signals were detected in infants up to 24 months old

Kampmann et al. N Engl J Med 2023; 388:1451-1464

REAL WORLD Vaccine Effectiveness

Adverse Events

JAMA Network Open

Original Investigation | Infectious Diseases

Effectiveness and Safety of Respiratory Syncytial Virus Vaccine for US Adults Aged 60 Years or Older

Sarah E. Fry, BS; Pauline Terebuh, MD, MPH; David C. Kaelber, MD, PhD, MPH; Rong Xu, PhD; Pamela B. Davis, MD, PhD

- Case control
- Participants > 60 years old with ARI and tested for RSV between Oct 1 , 2023 and April 30, 2024
- Cases : RSV +, controls RSV -
- Vaccinated if there was vaccination done in at least past 14 days before testing
- VE against ARI, ED visits and hospitalization
- Risks of ITP and GBS were reviewed for 6 weeks postvaccination

Findings

Figure 1. Estimated Vaccine Effectiveness Against Respiratory Syncytial Virus-Associated Medically Attended Respiratory Illness, Emergency Department or Urgent Care Visits, or Hospitalizations, October 1, 2023, to April 30, 2024

Age group, y	No. of vaccinated cases/total No. (%)	No. of vaccinated controls/total No. (%)	Vaccine effectiveness, % (95% CI)
ARI			
≥60	1318/53 963 (2.4)	66 928/733 859 (9.1)	75.1 (73.6-76.4)
60-74	561/27 923 (2.0)	30 496/400 012 (7.6)	75.2 (73.0-77.2)
≥75	757/26 040 (2.9)	36 429/333 847 (10.9)	75.6 (73.7-77.3)
ED/UC			
≥60	391/18 831 (2.1)	19 139/237 864 (8.0)	75.8 (73.2-78.1)
60-74	157/10 181 (1.5)	8842/139 502 (6.3)	76.9 (72.9-80.3)
≥75	234/8650 (2.7)	10 297/98 362 (10.5)	76.2 (72.9-79.2)
Hospitalization			
≥60	469/22 125 (2.1)	26 340/324 563 (8.1)	75.5 (73.1-77.6)
60-74	161/9266 (1.7)	9729/146 207 (6.7)	75.2 (71.0-78.8)
≥75	308/12 859 (2.4)	16 611/178 356 (9.3)	76.1 (73.2-78.7)

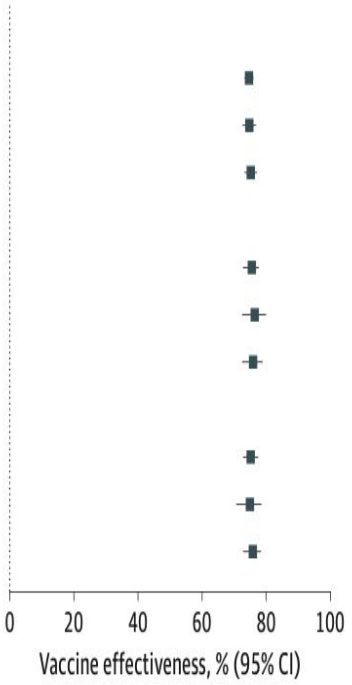


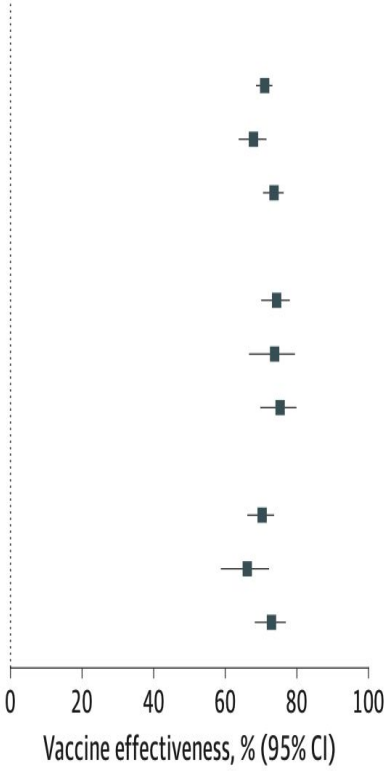
Table 1. Characteristics of Case Participants and Control Participants for Vaccine Effectiveness Analysis

Characteristic	Cases (n = 53 963)	Controls (n = 733 859)
Age, median (IQR), y	74 (67-82)	73 (67-81)
Age group, No. (%), y		
60-74	27 923 (51.7)	400 012 (54.5)
≥75	26 040 (48.3)	333 847 (45.5)
Race and ethnicity, No. (%)[a]		
White	44 929 (83.3)	590 499 (80.5)
Black	6257 (11.6)	104 971 (14.3)
Asian	1326 (2.5)	17 700 (2.4)
American Indian or Alaska Native	440 (0.8)	6306 (0.9)
Native Hawaiian or Pacific Islander	153 (0.3)	2178 (0.3)
Other[b]	4087 (7.6)	57 349 (7.8)
Immunocompromised, No. (%)	16 744 (31.0)	234 799 (32.0)
Chronic lung disease, No. (%)	16 691 (30.9)	223 065 (30.4)
Cardiovascular disease, No. (%)	39 013 (72.3)	525 406 (71.6)

Figure 2. Estimated Vaccine Effectiveness Among Immunocompromised Individuals and Subgroups Against Respiratory Syncytial Virus-Associated Medically Attended Respiratory Illness, Emergency Department or Urgent Care Visits, or Hospitalizations, October 1, 2023, to April 30, 2024

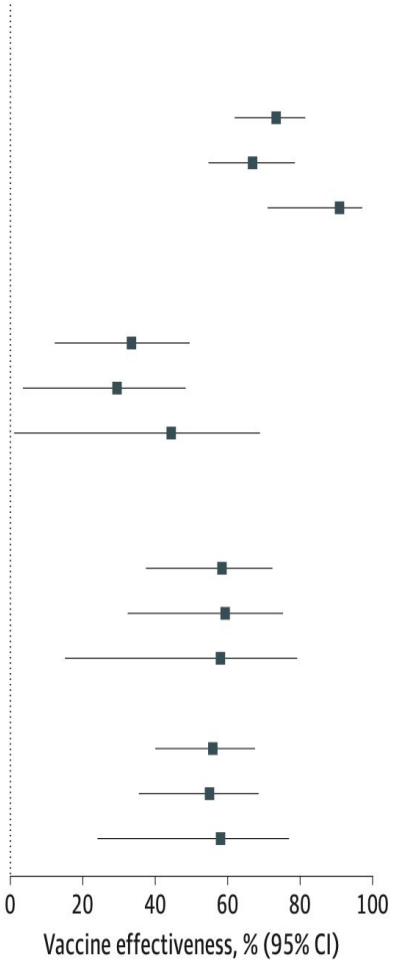
A Immunocompromised individuals

Age group, y	No. of vaccinated cases/total No. (%)	No. of vaccinated controls/total No. (%)	Vaccine effectiveness, % (95% CI)
ARI			
≥60	579/16 744 (3.5)	25 315/234 799 (10.8)	70.4 (67.8-72.7)
60-74	263/8039 (3.3)	10 978/118 038 (9.3)	67.0 (62.6-70.9)
≥75	316/8705 (3.6)	14 337/116 761 (12.3)	73.1 (69.8-76.0)
ED/UC			
≥60	155/5284 (2.9)	6461/62 343 (10.4)	73.9 (69.3-77.8)
60-74	63/2603 (2.4)	2807/32 974 (8.5)	73.3 (65.7-79.3)
≥75	92/2681 (3.4)	3654/29 369 (12.4)	75.0 (69.1-79.8)
Hospitalization			
≥60	248/8313 (3.0)	11 807/129 045 (9.1)	69.5 (65.3-73.1)
60-74	99/3518 (2.8)	4532/59 084 (7.7)	65.2 (57.3-71.5)
≥75	149/4795 (3.1)	7275/69 961 (10.4)	72.4 (67.4-76.6)



B Transplant recipients

Age group, y	No. of vaccinated cases/total No. (%)	No. of vaccinated controls/total No. (%)	Vaccine effectiveness, % (95% CI)
Solid organ transplant recipients			
ARI			
≥60	32/847 (3.8)	1492/11 614 (12.8)	73.4 (61.9-81.4)
60-74	29/634 (4.6)	1068/8449 (12.6)	66.9 (54.6-78.4)
≥75	3/213 (1.4)	424/3165 (13.4)	90.8 (71.0-97.1)
Hematopoietic stem cell transplant recipients			
ARI			
≥60	62/626 (9.9)	650/4587 (14.2)	33.4 (12.3-49.4)
60-74	48/492 (9.8)	476/3584 (13.3)	29.4 (3.5-48.4)
≥75	14/134 (10.4)	174/1003 (17.3)	44.4 (1.0-68.8)
Transplant recipients			
ED/UC			
≥60	26/450 (5.8)	453/3528 (12.8)	58.4 (37.4-72.3)
60-74	17/328 (5.2)	309/2623 (11.8)	59.1 (32.4-75.2)
≥75	9/122 (7.4)	144/905 (15.9)	57.9 (15.1-79.1)
Hospitalization			
≥60	45/798 (5.6)	1186/9943 (11.9)	55.9 (40.0-67.5)
60-74	33/592 (5.6)	835/7213 (11.6)	54.9 (35.4-68.5)
≥75	12/206 (5.8)	351/2730 (12.9)	58.1 (24.1-76.8)



Original Investigation | Infectious Diseases

Estimated Vaccine Effectiveness for Respiratory Syncytial Virus–Related Lower Respiratory Tract Disease

Sara Y. Tartof, PhD, MPH; Negar Aliabadi, MD, MS; Gabriella Goodwin, MS; Jeff Slezak, MS; Vennis Hong, MPH; Bradley Ackerson, MD; Qing Liu, MS; Sally Shaw, DrPH, MPH; Sabrina Welsh, MPH; Julie A. Stern, MPH; Banshri Kapadia, MS; Brigitte C. Spence, MPH; Joseph A. Lewnard, PhD; Gregg S. Davis, PhD, MPH; Michael Aragones, MD; Michael Dutro, PharmD; Erica Chilson, PharmD; Elisa Gonzalez, MS; Robin Hubler, MS; Brandon Chia, BA; Luis Jodar, PhD; Bradford D. Gessner, MD; Elizabeth Begier, MD, MPH

JAMA Network Open. 2024;7(12):e2450832

- Retrospective chart review
- Adults > 60years or older with hospitalizations or ED vists at a US hospital with LRTD November 24,2023,to April 9 ,2024,
- Swabbed for RSV
- 7047 LRTD related admissions/ ED visits
- Mean age: 76.8
- 54% females
- 14% immunocompromised
- 93% CCI $\geq$1

Table 2. RSVpreF Vaccine Effectiveness (VE) Against Respiratory Syncytial Virus (RSV)-Related Lower Respiratory Tract Disease Hospitalizations and Emergency Department Visits

Lower respiratory tract disease hospitalizations and emergency department visits	Patients, No. (%)				VE (95% CI)	
	Test negative controls (strict n = 804; broad n = 6424)		Test positive cases (n = 623)			
	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Crude	Adjusted[a]
Strict definition/primary analysis (n = 1427)[b]	775 (96.4)	29 (3.6)	621 (99.7)	2 (0.3)[c]	91 (64-98)	91 (59-98)
Broad definition/sensitivity analysis (n = 7047)[d]	6203 (96.6)	221 (3.4)	621 (99.7)	2 (0.3)[c]	91 (64-98)	90 (59-97)

UKHSA study showed RSV vaccination programme resulted in 30% reduction in hospitalization in personsn75 to 79 year olds, at a vaccination rate of 40% of eligible individuals.1

.Mensah et al. The lancet 2025; 405:1139

Real-world effectiveness of RSVpreF vaccination during pregnancy against RSV-associated lower respiratory tract disease leading to hospitalisation in infants during the 2024 RSV season in Argentina (BERNI study): a multicentre, retrospective, test-negative, case–control study

*Gonzalo Pérez Marc, Carla Vizzotti, Deshayne B Fell, Lucila Di Nunzio, Santiago Olszevicki, Shauna Wolf Mankiewicz, Virginia Braem, Ramiro Rearte, Jessica E Atwell, Alejandra Bianchi, Nora Fuentes, Romina Zadoff, Gabriela Vecchio, María Gabriela Abalos, Rong Fan, Graciela del Carmen Morales, Bradford D Gessner, Luis Jodar, Romina Libster, Analía Rearte, on behalf of the BERNI study working group**

- A multicentre, retrospective, test-negative, case-control study during 2024 RSV season

  12 hospitals across Argentina (BERNI study).
- Cases were infants ≤ 6 months old with any positive RSV test and controls were PCR-confirmed negative for RSV.

- Primary outcome: VE against hospitalsation from RSV LRTD
  - 78.6% (0-3 months)
  - 71.3 % (0 -6 months)
- Secondary outcome: VE against severe RSV LRTD : 76.9%

Published online May 5, 2025 https://doi.org/10.1016/S1473-3099(25)00156-2

Early Safety Findings Among Persons Aged ≥60 Years Who Received a Respiratory Syncytial Virus Vaccine — United States, May 3, 2023–April 14, 2024

TABLE 1. Symptoms and health impacts reported to V-safe for persons aged ≥60 years who received a respiratory syncytial virus vaccine, by manufacturer — United States, May 3, 2023–April 14, 2024

Event	% Reporting symptoms or health impact after vaccination* (no.)			
	GSK	Pfizer	Do not know/Cannot recall	Total
No. of participants	6,402	3,882	5,936	**16,220**
Symptoms reported as related to vaccination	48.6 (3,113)	27.3 (1,058)	36.3 (2,157)	**39.0 (6,328)**
Injection site symptoms	43.9 (2,808)	20.3 (787)	31.1 (1,846)	**33.5 (5,441)**
Pain	41.3 (2,641)	17.7 (688)	28.6 (1,697)	**31.0 (5,026)**
Swelling	11.5 (737)	5.6 (217)	8.4 (497)	**8.9 (1,451)**
Redness	10.5 (671)	5.0 (195)	8.1 (478)	**8.3 (1,344)**
Itching	6.4 (412)	4.2 (162)	5.6 (330)	**5.6 (904)**
Underarm swelling or tenderness	2.6 (165)	1.8 (69)	1.4 (84)	**2.0 (318)**
Rash	1.6 (101)	1.0 (38)	1.4 (86)	**1.4 (225)**
Systemic symptoms	36.6 (2,344)	21.6 (839)	27.9 (1,656)	**29.8 (4,839)**
Fatigue or tiredness	25.6 (1,640)	13.3 (515)	19.7 (1,172)	**20.5 (3,327)**
Muscle or body aches	22.0 (1,407)	12.5 (484)	16.0 (952)	**17.5 (2,843)**
Headache	19.2 (1,227)	10.6 (413)	13.8 (820)	**15.2 (2,460)**
Fever†	13.1 (836)	7.5 (293)	10.7 (636)	**10.9 (1,765)**
Chills	12.1 (772)	5.8 (226)	8.3 (493)	**9.2 (1,491)**
Joint pain	11.8 (756)	6.6 (255)	8.0 (477)	**9.2 (1,488)**
Nausea	5.0 (317)	3.2 (123)	4.2 (249)	**4.2 (689)**
Diarrhea	3.1 (201)	2.1 (80)	2.9 (172)	**2.8 (453)**
Rash	0.5 (32)	0.5 (20)	0.5 (30)	**0.5 (82)**
Vomiting	0.4 (25)	0.3 (13)	0.6 (36)	**0.5 (74)**
Other§	3.9 (248)	2.5 (98)	2.8 (168)	**3.2 (514)**
Health impact	10.2 (654)	6.2 (239)	8.8 (524)	**8.7 (1,417)**
Unable to complete normal daily activities	9.1 (580)	5.3 (205)	8.1 (479)	**7.8 (1,264)**
Unable to work or attend school	1.9 (119)	1.3 (51)	1.7 (99)	**1.7 (269)**
Care from health care professional¶	0.5 (29)	0.5 (19)	0.3 (20)	**0.4 (68)**
Office visit or urgent care	0.2 (14)	0.3 (12)	0.2 (11)	**0.2 (37)**
Telehealth	0.2 (10)	0.1 (2)	0.1 (3)	**0.1 (15)**
Emergency department	0.03 (2)	0.1 (3)	0.1 (7)	**0.1 (12)**
Hospitalization	0.02 (1)	0.03 (1)	0.03 (2)	**0.02 (4)**
Other	0.1 (8)	0.1 (2)	0 (—)	**0.1 (10)**

Hause et al. MMWR May 2024

TABLE 3. Events reported to the Vaccine Adverse Event Reporting System for persons aged ≥60 years after receipt of a respiratory syncytial virus vaccine — United States, May 3, 2023–April 14, 2024

Event	Vaccine, no. reporting (%)			
	GSK	Pfizer	Do not know/Cannot recall	Total
Total participants	**2,193**	**919**	**88**	**3,200**
Events among nonserious reports*,†	2,026 (92.5)	821 (89.1)	72 (81.8)	**2,919 (91.2)**
Arthralgia	183 (9.0)	85 (10.4)	7 (9.7)	**240 (8.2)**
Erythema	186 (9.2)	57 (6.9)	4 (5.6)	**384 (13.2)**
Fatigue	235 (11.6)	102 (12.4)	18 (25.0)	**355 (12.2)**
Fever	215 (10.6)	83 (10.1)	9 (12.5)	**247 (8.5)**
Headache	261 (12.9)	105 (12.8)	10 (13.9)	**376 (12.9)**
Injection site erythema	261 (12.9)	66 (8.0)	2 (2.8)	**275 (9.4)**
Injection site pain	291 (14.4)	72 (8.8)	7 (9.7)	**370 (12.7)**
Injection site swelling	187 (9.2)	51 (6.2)	2 (2.8)	**376 (12.9)**
Pain	276 (13.6)	85 (10.4)	12 (16.7)	**373 (12.8)**
Pain in extremity	282 (13.9)	94 (11.4)	8 (11.1)	**384 (13.2)**
Events among serious reports§,¶	**167 (7.6)**	**98 (10.7)**	16 (18.2)	**281 (8.8)**
Allergic reaction**	3	4	0	**7**
Anaphylaxis	1	1	0	**2**
Arrhythmia, other	4	1	1	**6**
Atrial fibrillation††	8	3	3	**14**
Congestive heart failure	2	2	0	**4**
Dyspnea or cough	3	2	0	**5**
Encephalitis or aseptic meningitis	5	5	1	**11**
Guillain-Barré syndrome§§	**18**	**19**	0	**37**
Injection site pain or reaction¶¶	4	0	0	**4**
Immune thrombocytopenia***	5	6	0	**11**
Myocardial infarction	3	1	0	**4**
Pneumonia	5	3	1	**9**
Rash	1	2	1	**4**
RSV infection	3	2	0	**5**
Sepsis, bacteremia, or both	6	5	0	**11**
Shoulder pain	7	1	3	**11**
Stroke or transient ischemic attack	13	10	1	**24**
Syncope	6	1	0	**7**
Thromboembolic event, other†††	7	4	2	**13**
Transverse myelitis	2	1	0	**3**
Unevaluable	2	2	0	**4**
Death§§§	22	11	2	**35**

Reporting rates of GBS :

4.4 per million doses of Abrysvo vaccine administered, were higher than estimated expected background yet to be verified with chart review

Hause et al. MMWR May 2024; Britton et al. MMWR Aug 2024

RSV Vaccine Post-Market Analyses

- Post-market analyses* to assess the safety of RSV vaccines among Medicare Fee-for-Service (FFS) beneficiaries ages 65 and older

Analyses	Includes Vaccines Administered Through	Data Through Date	Number of Doses		Number GBS Cases
			RSV PreF3+AS01	RSVPreF	
Early-Season SCCS	October 22, 2023	April 6, 2024	872,068	456,107	28
End-of-Season SCCS	January 28, 2024	July 13, 2024	2,202,247	1,024,442	95

SCCS: Self-controlled case series

End-of-Season SCCS Results: GBS and RSV Vaccination

IRR and Attributable Risk (AR)

Seasonality, Farrington Analysis, and PPV-Based Multiple Imputation – Chart Confirmed + Not Returned Cases

Inferential Analysis Results	RSVPreF3+AS01	RSVPreF
Eligible Vaccines	2,202,247	1,024,442
*Cases in the Risk Interval	24	18
*Cases in the Control Interval	11	<11
IRR (95% CI)	2.46 (1.19, 5.08)	2.02 (0.93, 4.40)
AR per 100,000 Doses (95% CI)	0.65 (0.18, 1.12)	0.90 (-0.02, 1.81)
AR Per 100,000 PY (95% CI)	5.71 (1.61, 9.80)	7.82 (-0.17, 15.81)

IRR : Incidence relative risk, AR: attributable risk, PY: Person years

Table 3. Risk of Guillain-Barré Syndrome and ITP After Respiratory Syncytial Virus Vaccination for Older Adults From July 1, 2023, to June 31, 2024

Risk	Cases during risk period, No.	Vaccines Administered, No.	IRR (95% CI)	Excess cases per 1 000 000 doses (95% CI)
Guillain-Barré syndrome				
Overall	102	4 746 518	2.1 (1.5 to 2.9)	11.2 (7.2 to 14.1)
RSVPreF3	51	3 070 888	1.5 (0.9 to 2.2)	5.2 (-0.9 to 9.2)
RSVPreF	51	1 643 827	2.4 (1.5 to 4.0)	18.2 (9.8 to 23.3)
ITP				
Overall	257	4 740 401	1.0 (0.9 to 1.2)	1.9 (-7.7 to 10.1)
RSVPreF3	171	3 067 030	1.1 (8.7 to 1.3)	3.7 (-8.4 to 13.5)
RSVPreF	84	1 641 602	0.9 (0.7 to 1.2)	-4.1 (-22.5 to 9.7)

JAMA Network Open. 2025;8(5):e258322. doi:10.1001/jamanetworkopen.2025.8322

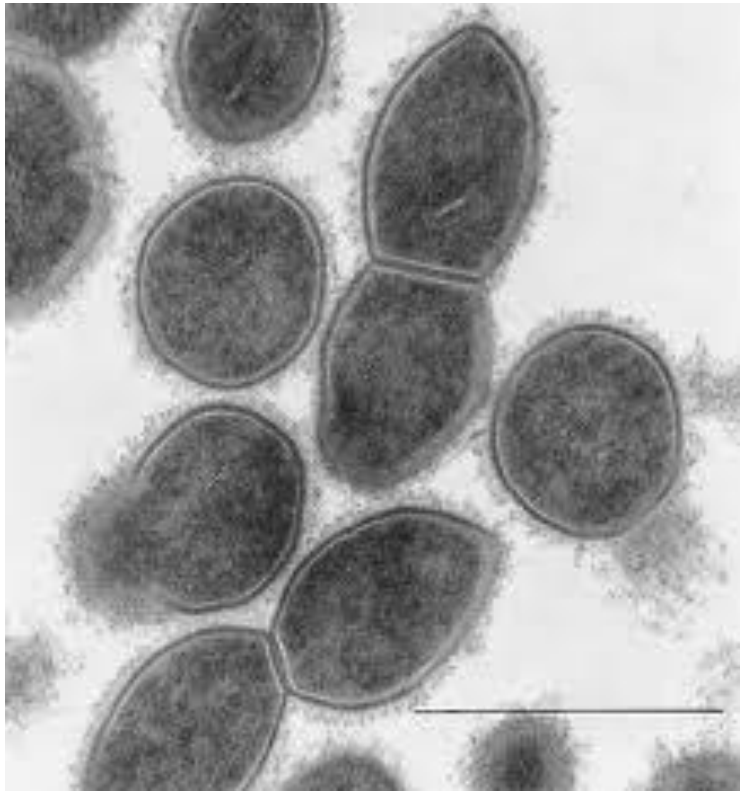
To wrap up about RSV vaccines

- A single dose of either protein-based RSV vaccine for adults prevented RSV infections associated with the lower respiratory tract in about 70-90 of 100 vaccine recipients.
- This is a vaccine important for the seniors, immunocompromised host and pregnant women.

Prevention of invasive pneumococcal Disease: PCV 20

Streptococcus pneumoniae

- Nasophargynx commensal
- > 90 serotypes
- Polysaccharide capsule – VIRULENCE factor
- Antibiotics resistance
- Can get it more than once



Centers for Disease Control and Prevention. Pneumococcal disease. In: Hamborsky J, Kroger A, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 13th ed. Washington, DC: Public Health Foundation; 2015:279-296.

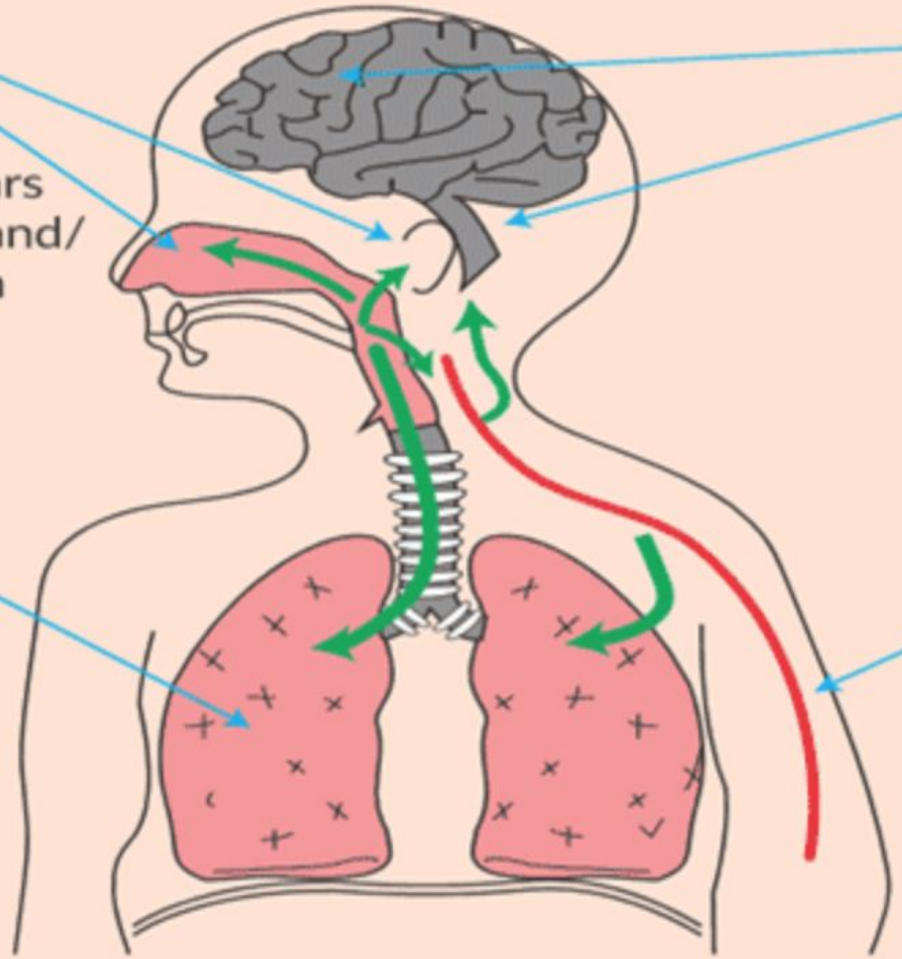
What Diseases does Pneumococcus Cause?

Otitis & Sinusitis

- Fever
- Pain and discharge from ears
- Tenderness over sinusesa and/ or peristent discharge from the nose.

Pneumonia

- Fever with or without shaking or chills
- Cough
- Rapid breathing
- Chest wall indrawing



Meningitis

- Fever
- Headaches
- Sensitivity to light
- Neck stiffness
- Convulsions
- Sometimes, confusion or altered consciousness

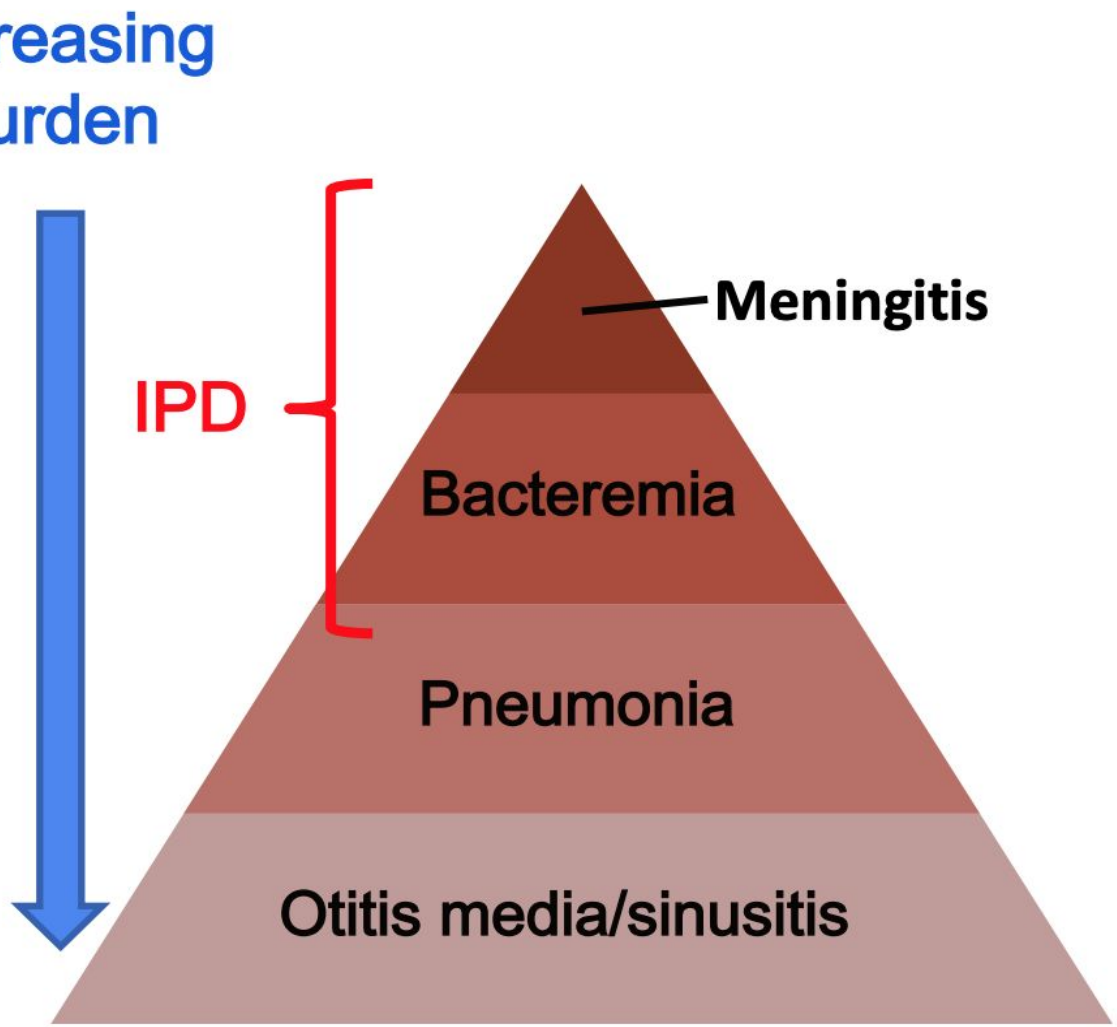
Bacteraemia, sepsis

- Fever
- Chills
- Altered consciousness
- Septic shock

Journal of Global Health 2022

Pneumococcal disease

- Invasive pneumococcal disease (IPD)
  - e.g., meningitis, bacteremia, bacteremic pneumonia
- Non-invasive disease
  - e.g., non-bacteremic pneumonia



- **Incubation Period**

Not well defined as colonization usually precedes invasive disease; may be as short as 1 to 3 days.

- **Infectious Period**

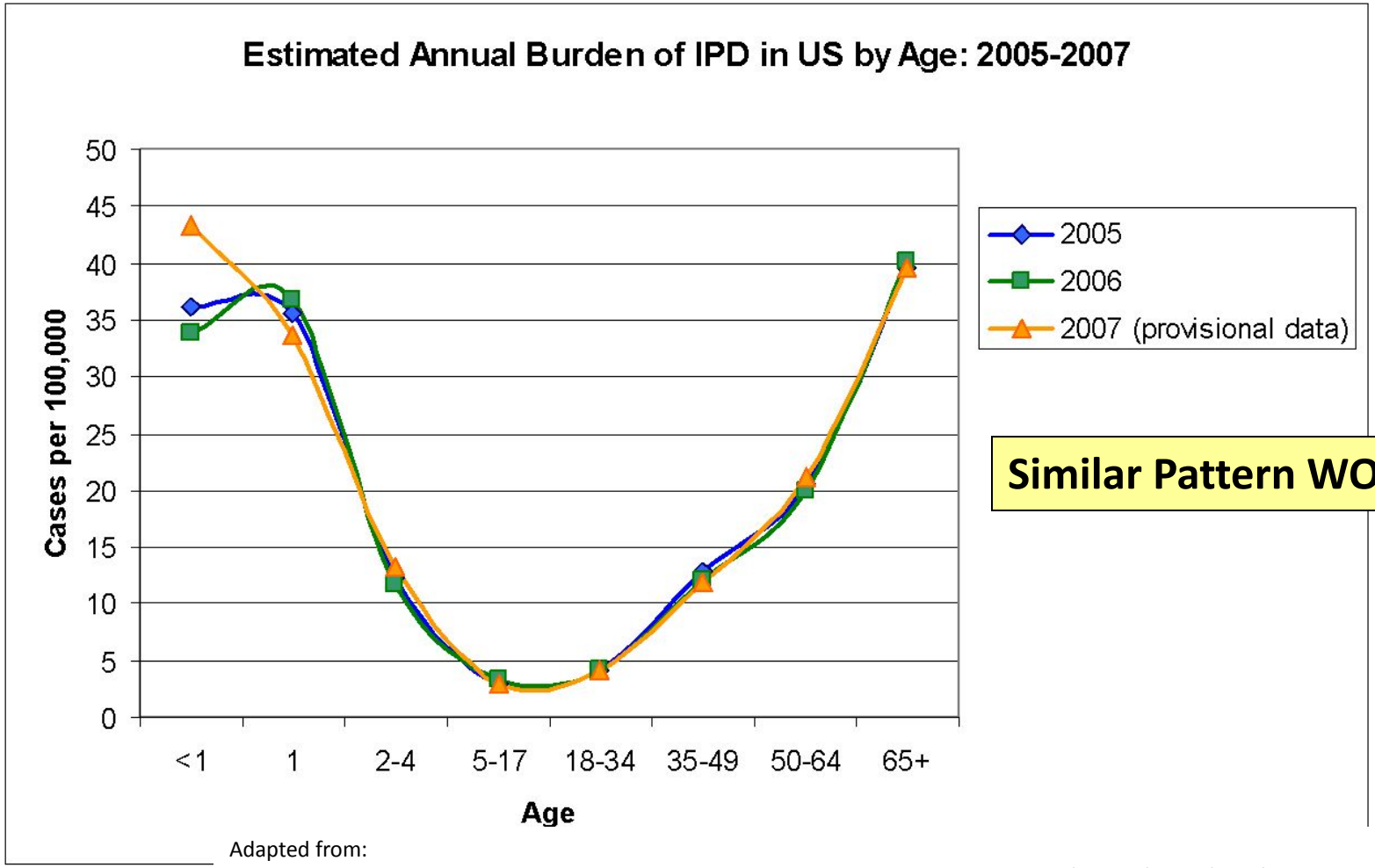
Presumably as long as pneumococci are carried in oro-nasal secretions in asymptomatic individuals (colonization usually lasts weeks to months);

with penicillin treatment, persons infected with susceptible strains are rendered non-infectious within 24-48 hours.

- **Transmission**

Respiratory droplets and direct contact with respiratory secretions of an infected person (usually requires frequent or prolonged close contact).

Invasive Pneumococcal Disease: Estimated Annual Burden of IPD in US by Age



Similar Pattern WORLDWIDE

Adapted from:

1. CDC 2005. Active Bacterial Core Surveillance Report, EIP Network, 2005 www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu05.pdf.
2. CDC 2006. Active Bacterial Core Surveillance Report, EIP Network, 2006 www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu06.pdf.
3. CDC 2007. Active Bacterial Core Surveillance Report, EIP Network, 2007 www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu07.pdf.

Pneumococcal Disease: Risk Factors

Extremes of age

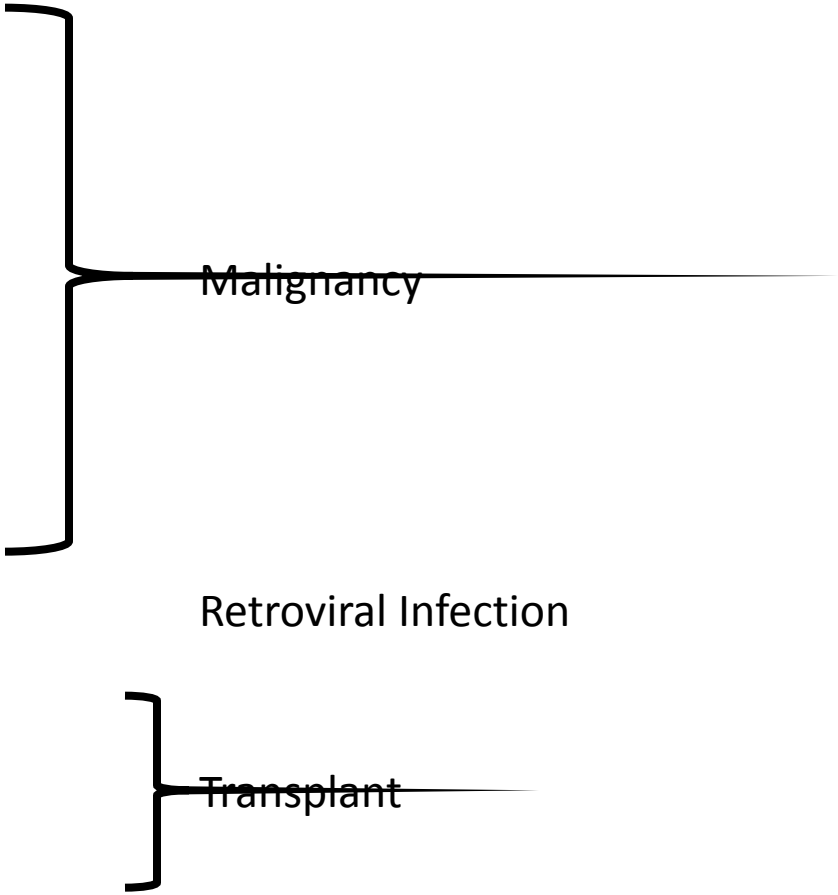
MODIFIABLE RISK FACTOR
CIGARETTE SMOKING
ALCOHOLISM

- **Chronic cardiovascular disease**
- **Chronic pulmonary disease**
- **Asthma**
- **Diabetes mellitus**
- **Chronic liver disease**
- **Cerebrospinal fluid leaks**
- **Chronic renal failure**
- **Nephrotic syndrome**
- **Functional or anatomic asplenia**

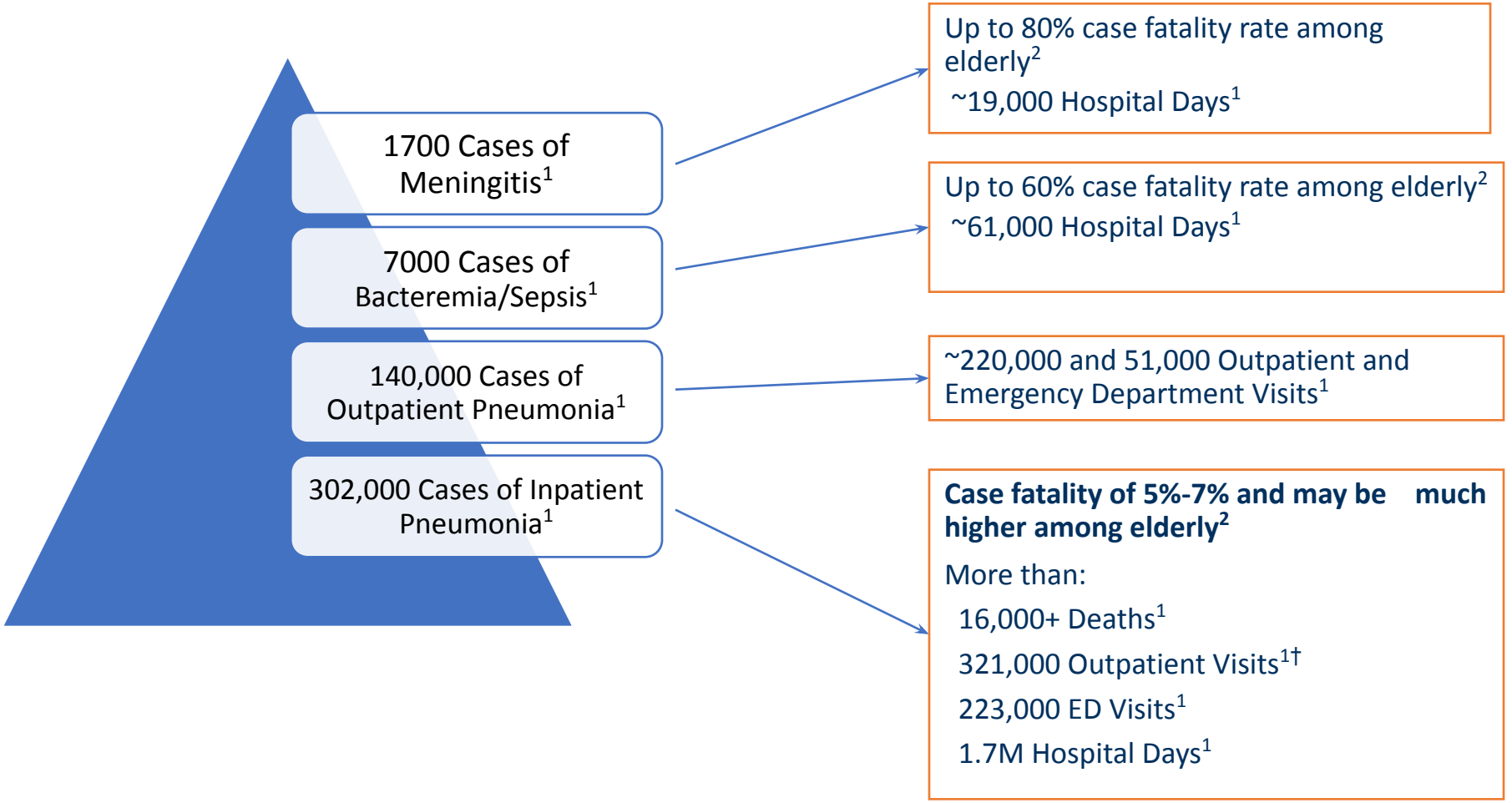
Adapted from ACIP. Pneumococcal polysaccharide vaccine. *MMWR* 1997;46(RR-8):1–24.
ACIP. Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). *MMWR* 2010;59:1102-6.
ACIP. Prevention of pneumococcal disease among infants and children—Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine. *MMWR* 2010;59(RR-11):1-19.

Immune Suppression

Leukemia
Hodgkin's disease
Lymphoma
Multiple myeloma
Generalized malignancy
HIV infection
Organ or bone marrow transplant
Immunosuppressive chemotherapy



Major Clinical Syndromes of Pneumococcal Disease and their Estimated Impact[1]* on US Adults 50+



1. Huang SS, et al. *Vaccine.* 2011;29:3398-3412.
2. CDC. The Pink Book. *Epidemiology and Prevention of Vaccine Preventable Diseases,* 12th ed. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf. Accessed May 30, 2011.

Overall Case Fatality Rates (IPD) in some Asian countries

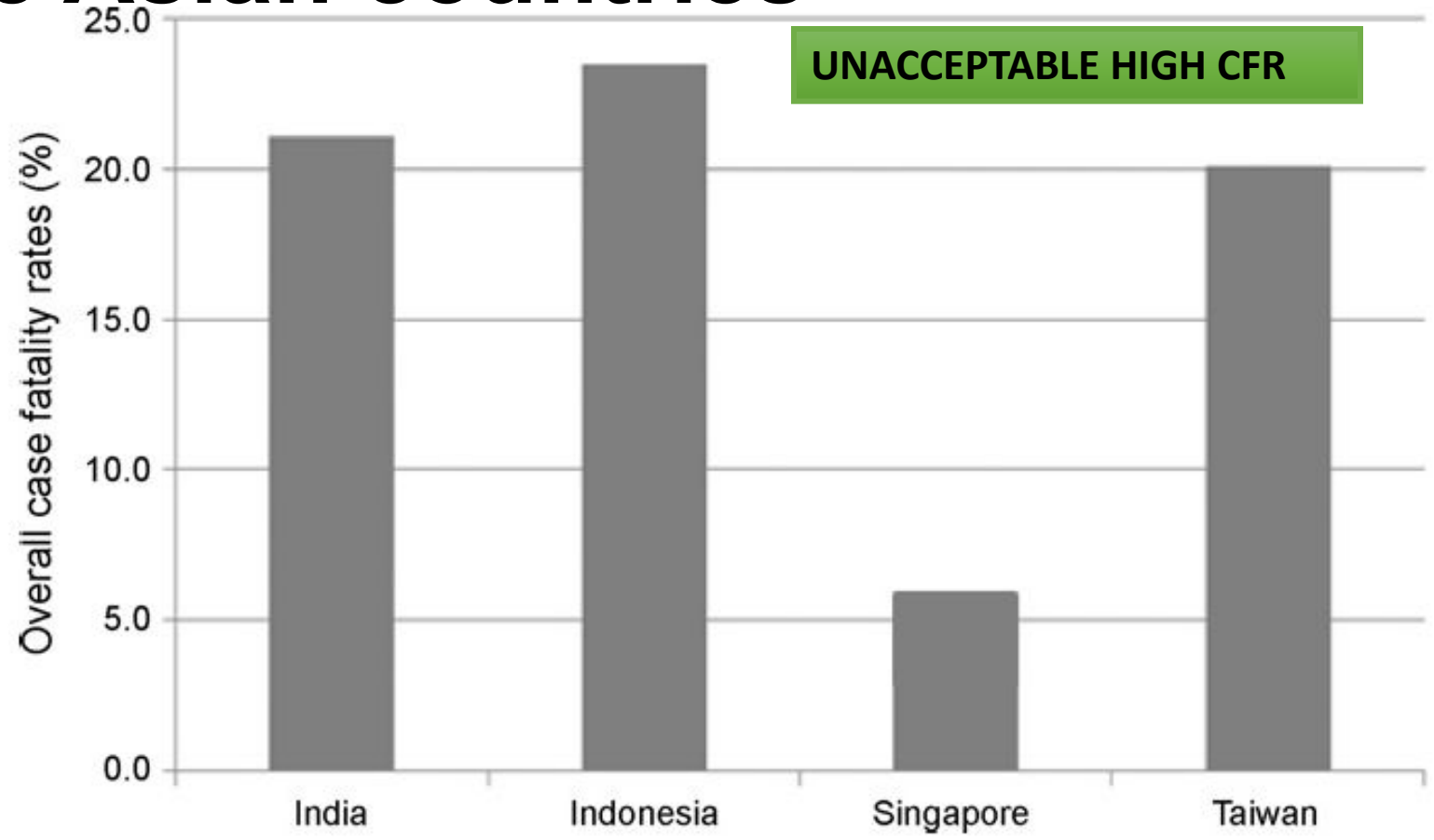


Fig. 3. Overall case fatality rates due to IPD as reported by studies from different ASAP member countries (Hadinegoro, in press) [18,23,24,51].

LC Bravo et al. Vaccine 27(2009) 7282-7291

Pneumococcal Disease in SG

Age group	Number of notifications				Incidence rate per 100,000 resident population*
	Male	Female	Total	%	
0-4	2	7	9	6.9	4.3
5-14	5	1	6	4.6	1.2
15-24	3	0	3	2.3	0.4
25-34	4	1	5	3.8	0.3
35-44	6	4	10	7.7	1.3
45-54	9	3	12	9.2	1.8
55-64	15	8	23	17.7	3.8
65+	43	19	62	47.7	11.1
Total	**87**	**43**	**130**	**100**	

Communicable Diseases Surveillance Report Singapore 2018

Serotypes

Children

Pneumococcal Type/ Group	Number of isolates (n = 8) (%)
Type 3 §	2 (25.0)
Type 19A §	1 (12.5)
Type 19F §	1 (12.5)
Non-groupable	4 (50.0)

§ Serotype included in PCV13.

Communicable Diseases Surveillance Report Singapore 2018

Pneumococcal Type/ Group	Number of isolates (n = 94) (%)
Type 1 §	0 (0)
Type 3 §	12 (12.8)
Type 4 *§	3 (3.2)
Type 6A §	3 (3.2)
Type 6B *§	2 (2.1)
Type 6C	2 (2.1)
Type 7C	0 (0)
Type 7F §	5 (5.3)
Type 8	1 (1.1)
Type 9V *§	1 (1.1)
Group 9 (not 9N or 9V)	1 (1.1)
Group 10	0 (0)
Group 11	0 (0)
Group 12	5 (5.3)
Type 14 *§	5 (5.3)
Type 15A	5 (5.3)
Type 15B	4 (4.3)
Type 15C	3 (3.2)
Type 15F	0 (0)
Group 17	1 (1.1)
Type 18C *§	1 (1.1)
Group 18 (not 18C and 18F)	1 (1.1)
Type 19A §	9 (9.6)
Type 19F *§	3 (3.2)
Group 20	1 (1.1)
Type 22F	1 (1.1)
Type 23A	7 (7.4)
Type 23B	2 (2.1)
Type 23F *§	5 (5.3)
Group 33	0 (0)
Non-groupable	11 (11.7)

* Serotype included in PCV7
§ Serotype included in PCV13

hot

ADULTS

serotype 3: thicker capsule

higher invasion capacity

Epidemiology, vaccine effectiveness, and risk factors for mortality for pneumococcal disease among hospitalised adults in Singapore: a case-control study

Tyson Chan[1,2†], Min Zhi Tay[1,2†], Win Mar Kyaw[1], Angela Chow[1] and Hanley J. Ho[1*]

Chan et al. BMC Infectious Diseases 2020: 20;423

Case control study 2015 to 2017

1600-bed hospital (adult)

496 pneumococcal disease cases, of whom 92 (18.5%) had IPD.

controls (N = 9181)

	IPD(n = 92)	Controls(n = 9181)	
Median Age	61.5 ± 16.3 years	72.2 ± 16.1 years	p < 0.001
Charlson score	1	3	p < 0.001
ICU admission	20.7%	8.7	p < 0.001
Inpatient mortality	26.1%	9.1	p < 0.001
Median LOS	9	8	0.003

Risk factors for mortality among pneumococcal disease patients were

- ICU admission,
- diagnosis of IPD,
- age ≥ 85 years
- Charlson’s score > 3.

- **IPD was negatively associated with prior pneumococcal vaccination (adjusted relative risk ratio = 0.20, 95%CI 0.06–0.69; p = 0.011).**

History of PCV vaccination

1977 The first PPSV (14 serotypes)

1983, an improved PPSV 23 (Pneumovax, Merck)

- adults ≥65 years
- Between 2 to 64 years, risk factors

2000, The first PCV7 (Prevnar 7, Pfizer)

2010, an improved PCV13 (Prevnar13, Pfizer)

PCV 15

Adults (2021)

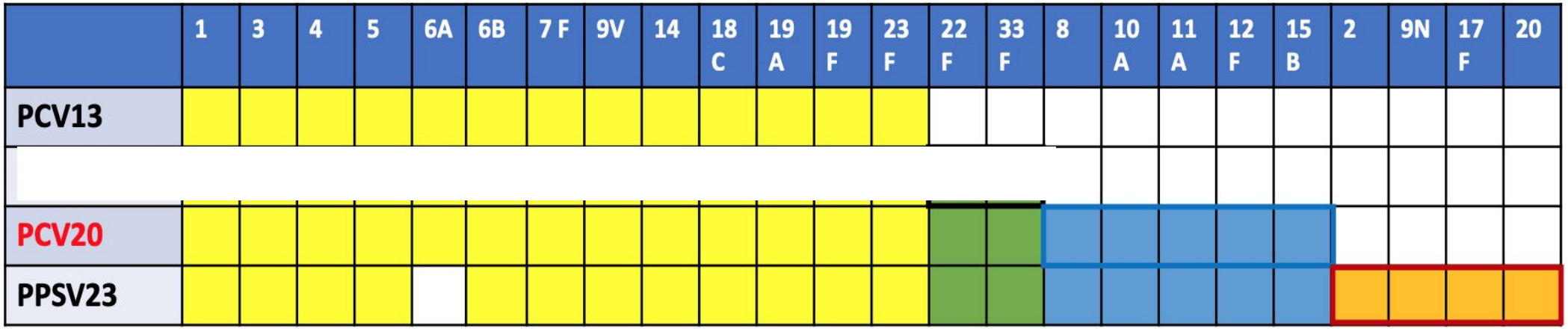
Children(2022)

PCV 20

Adults (2021)

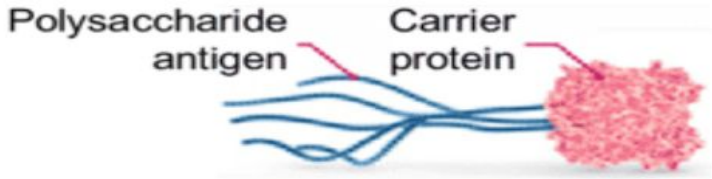
Children (2023)

Serotypes Contained in Current and New Pneumococcal Vaccines

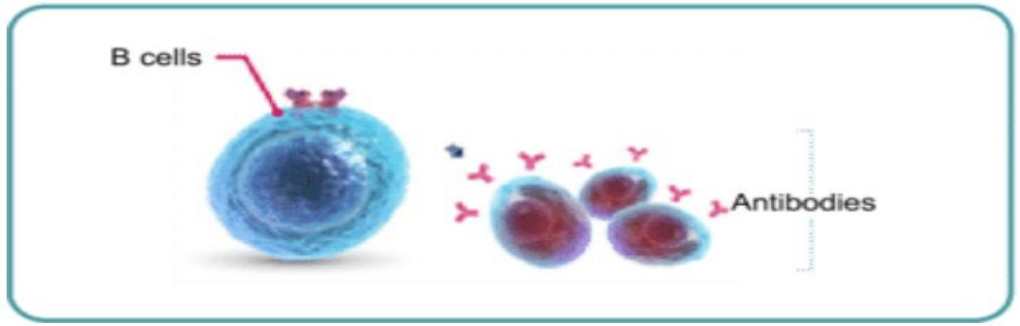


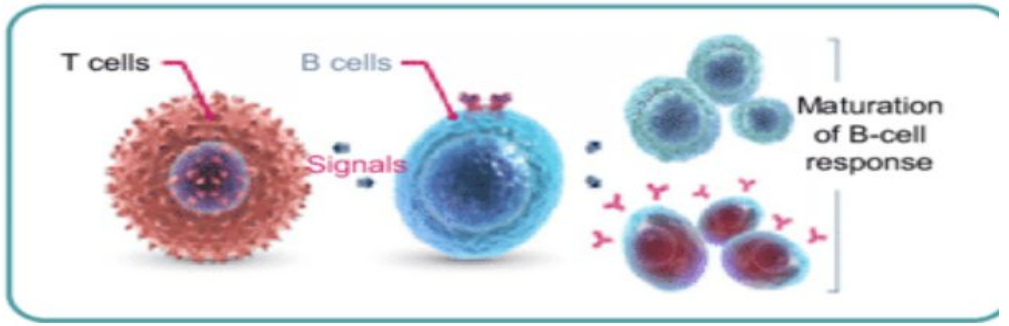
- **PCV15 non-PCV13**: includes serotypes **22F and 33F**
- **PCV20 non-PCV13**: includes serotypes **22F, 33F, 8, 10A, 11A, 12F, and 15B**
- **PPSV23 non-PCV20**: includes serotypes **2, 9N, 17F, and 20**

Polysaccharide vs Conjugate vaccine



Polysaccharide vaccines	Conjugate vaccines
Contain polysaccharide antigens	Contain polysaccharide antigens covalently linked to a carrier protein
T-cell-independent immunoresponse	T-cell-dependent immunoresponse
Stimulate B cells to produce antibodies	Stimulate T cells to help B cells produce antibodies and generate immune memory Provide improved immunological responses Prevent nasopharyngeal carriage





Immunity wanes with time

Immunity long lasting

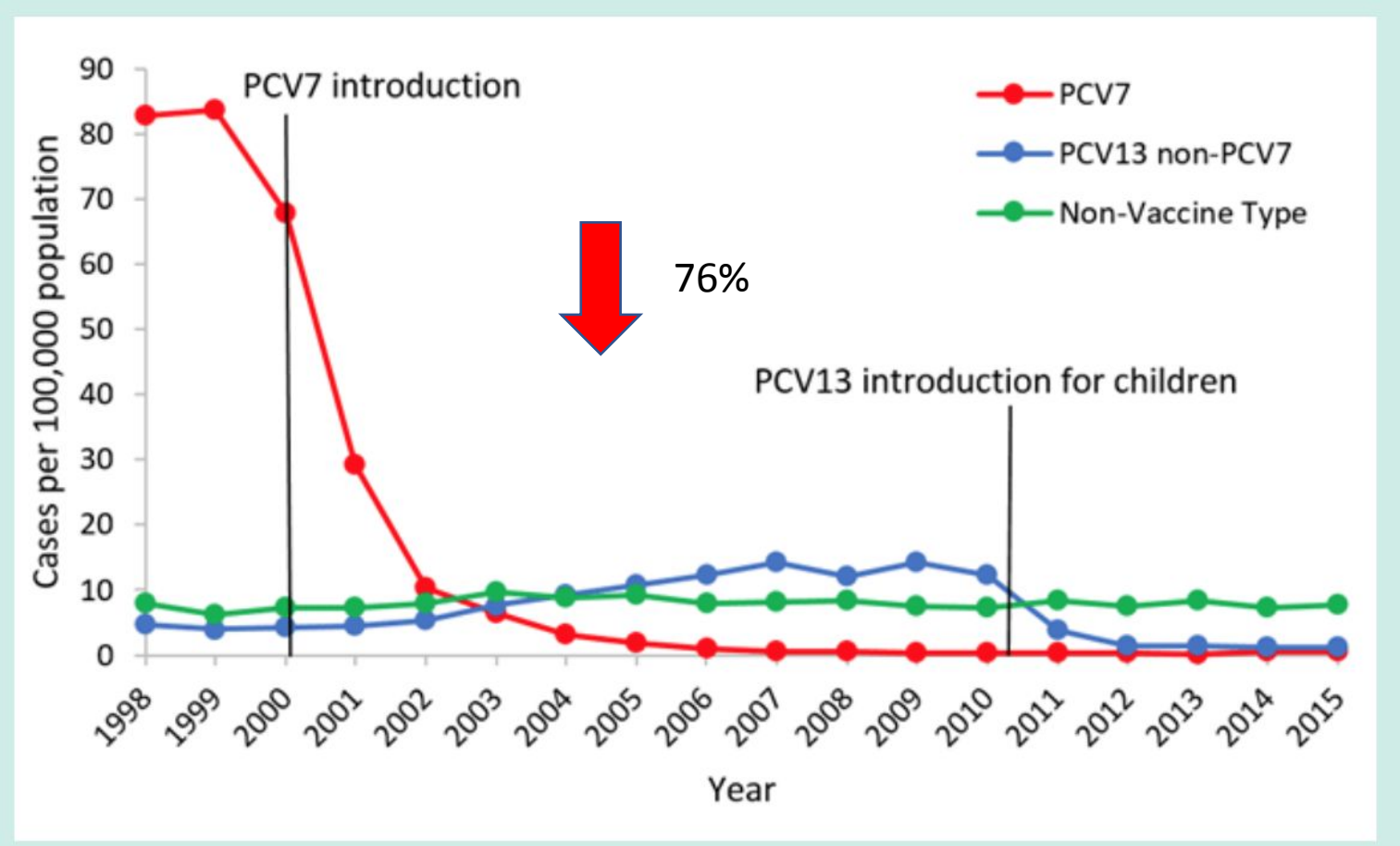
WHAT IS EXPECTED FOR POLYSACCHARIDE AND CONJUGATE VACCINES

Property	Polysaccharide	Conjugate
Effective in infants <2 years	NO	YES
Immune memory	NO	YES
Prolonged duration of protection	NO	YES
Booster effect	NO	YES
Reduction of carriage	NO	YES
Contributes to herd effect	NO	YES
Hyporesponsiveness	YES	NO

Harrison LH. Clin Microbiol Rev. 2006;19:142-164.

Examples of conjugate vaccines Haemophilus influenza B, Pneumococcus, Meningococcus

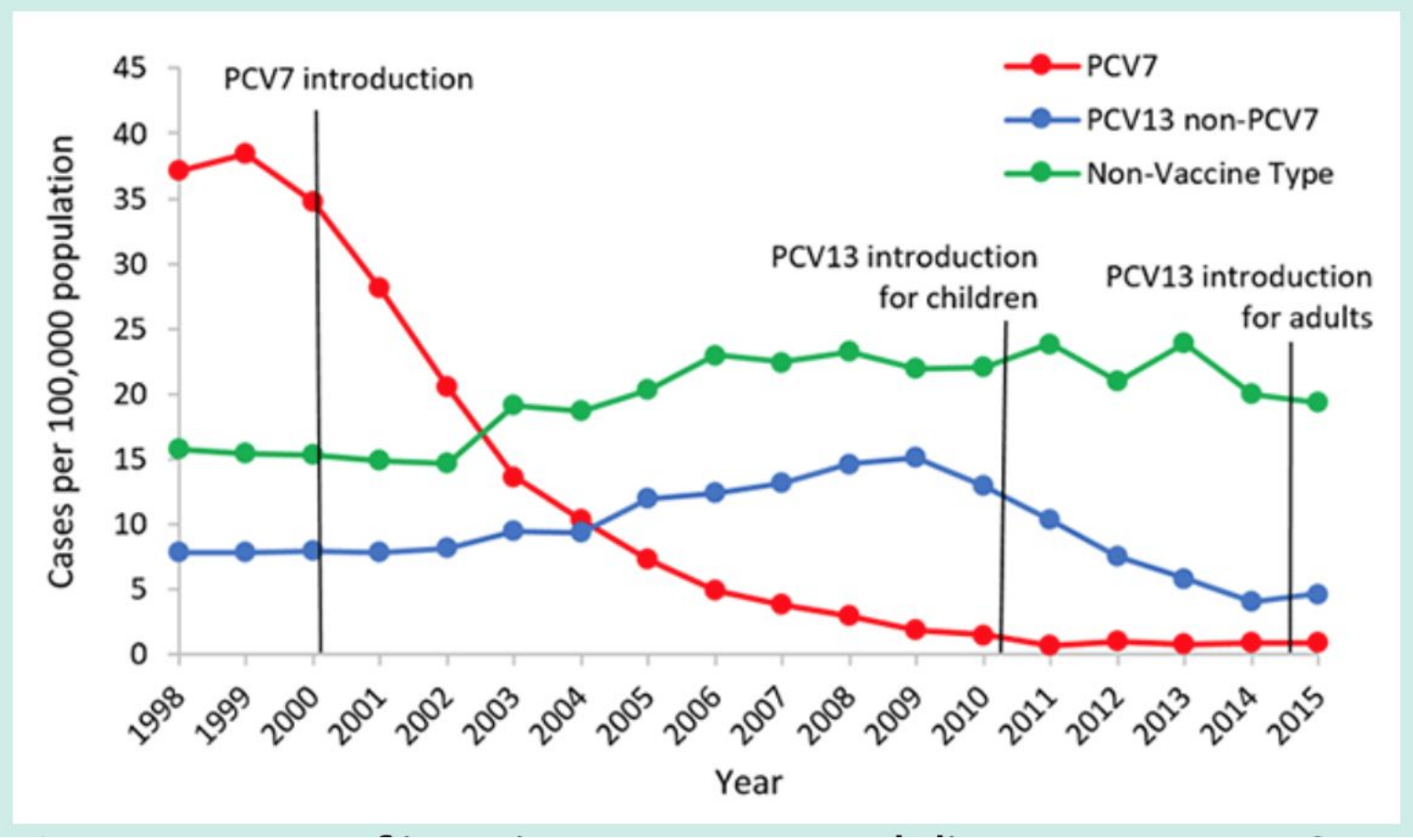
Rates of invasive pneumococcal disease among children <5 years of age, 1998–2015



US CDC Manual for surveillance of vaccine preventable diseases Chapter 11 Accessed 9 March 2024

Rates of invasive pneumococcal disease among U.S. adults >65 years of age, 1998–2015

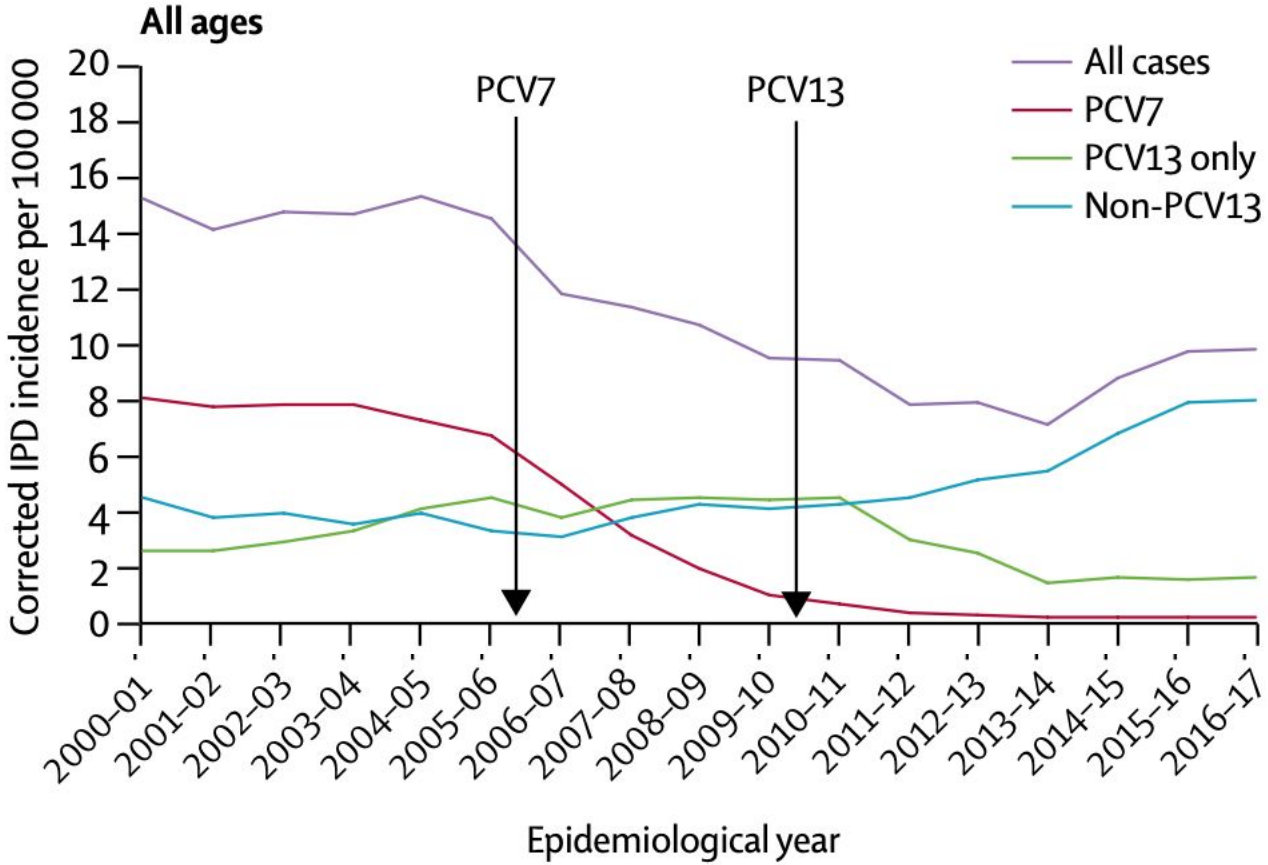
46% for all ages



US CDC Manual for surveillance of vaccine preventable diseases Chapter 11 Accessed 9 March 2024

Rapid increase in non-vaccine serotypes causing invasive pneumococcal disease in England and Wales, 2000–17: a prospective national observational cohort study

Shamez N Ladhani, Sarah Collins, Abdelmajid Djennad, Carmen L Sheppard, Ray Borrow, Norman K Fry, Nicholas J Andrews, Elizabeth Miller, Mary E Ramsay



Lancet Infect Dis 2018 18: 441–51

PCV 20 in adults

- Phase 1 and 2 trials published in 2019 and 2021
- Well tolerated in healthy adults(18 to 49 years) and (60 to 64 years)
- Good immunogenicity
- US FDA designated as breakhrough therapy

Thompson et al. Vaccine 2019;37(42):6201
Hurley et al. Clin Infect Dis 2021;73(7)

PCV 20 clinical trials

- Phase 3 adult clinical program for 20vPnC includes 3 studies, which combined, have enrolled more than 6,000 adult subjects, including populations of vaccine-naïve adults and adults with prior pneumococcal vaccination.

- **NCT03760146**

- **NCT03828617**: Phase 3 randomized, double-blind trial, designed to provide additional safety data and evaluate three different lots of 20vPnC in adults 18 to 49 years of age with no history of pneumococcal vaccination..

- **NCT03835975**: Phase 3 randomized, open-label trial, designed to describe the safety and immune response of 20vPnC in an estimated 875 adults aged ≥65 years with prior pneumococcal vaccination.

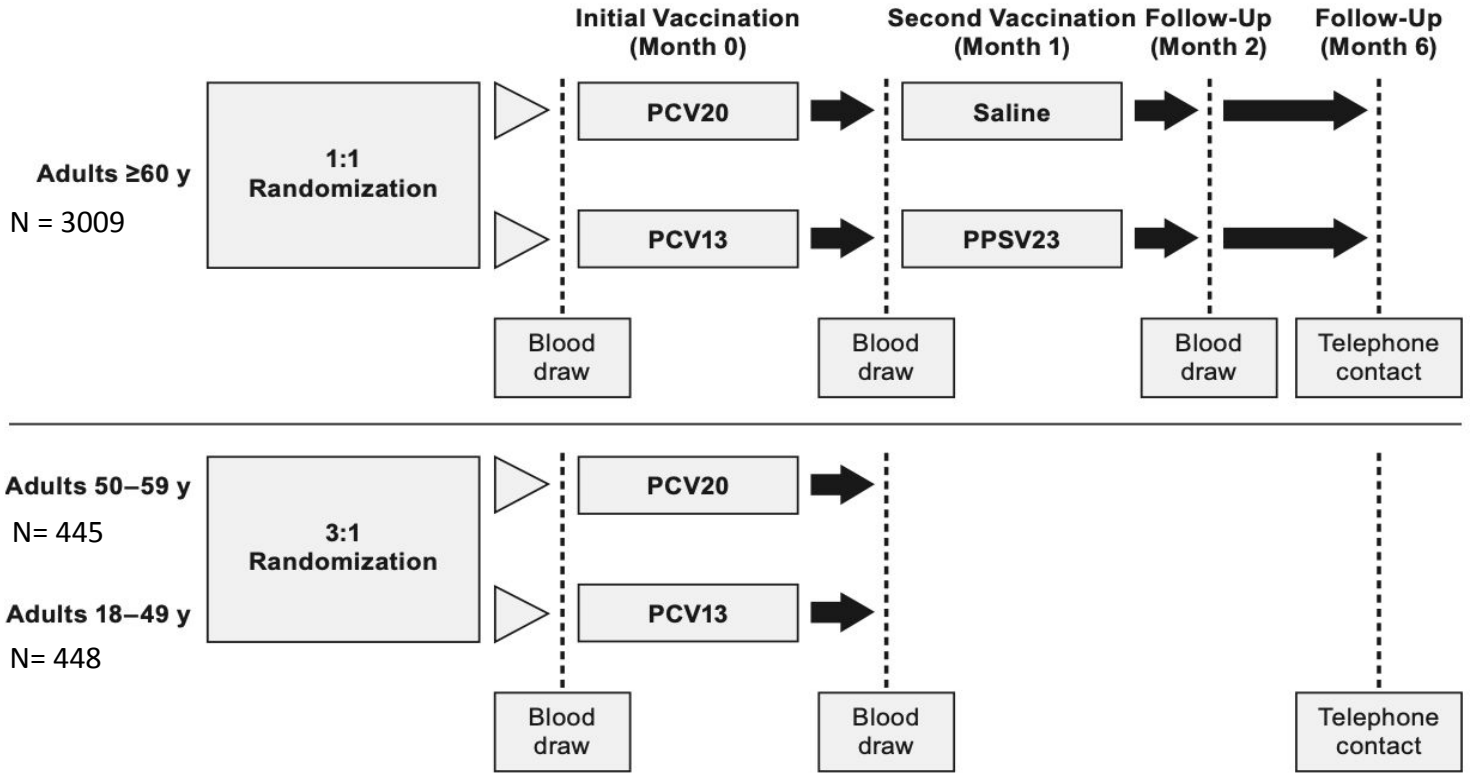
Data From Pfizer's Adult and Pediatric Clinical Trial Programs for 20-Valent Pneumococcal Conjugate Vaccine Presented at IDWeek 2020

Pivotal Phase 3 Randomized Clinical Trial of the Safety, Tolerability, and Immunogenicity of 20-Valent Pneumococcal Conjugate Vaccine in Adults Aged ≥18 Years NCT0376014

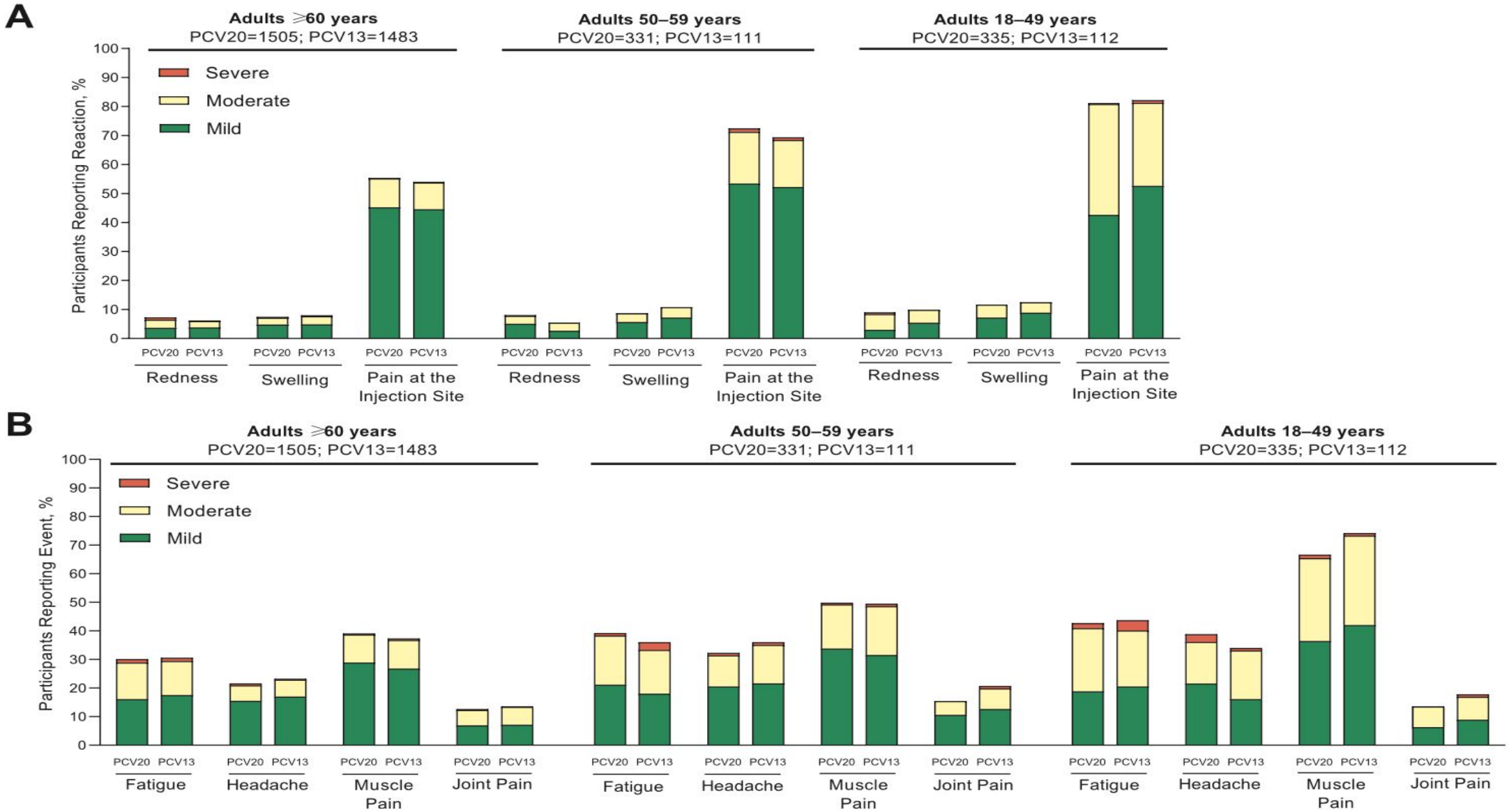
Brandon Essink,[1] Charu Sabharwal,[2] Kevin Cannon,[3] Robert Frenck,[4] Himal Lal,[5] Xia Xu,[5] Vani Sundaraiyer,[6] Yahong Peng,[5] Lisa Moyer,[5] Michael W. Pride,[2] Ingrid L. Scully,[2] Kathrin U. Jansen,[2] William C. Gruber,[2] Daniel A. Scott,[5] and Wendy Watson[5]

6

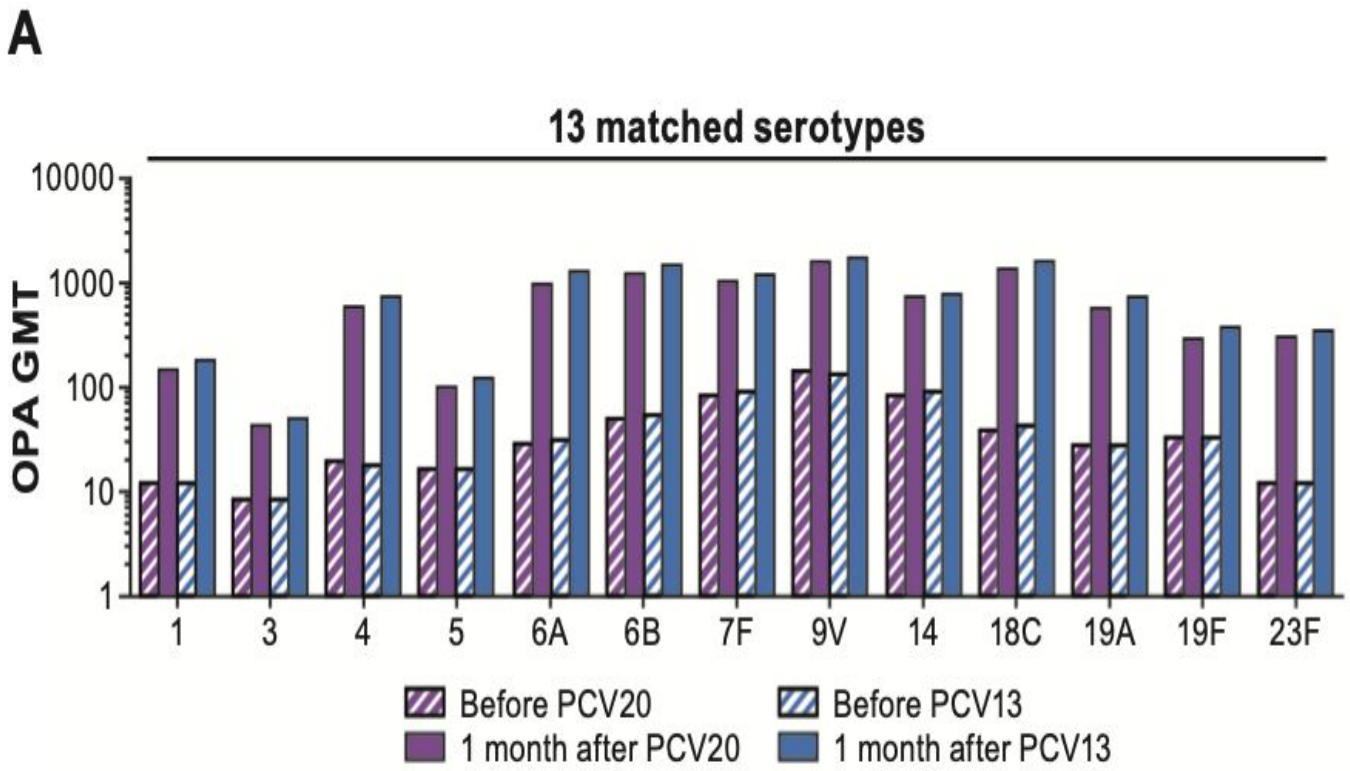
- Excludes: previous vaccination with any pneumococcal vaccine, diagnosis of a serious unstable chronic disorder or immunocompromising condition, or treatment with immunosuppressive therapies

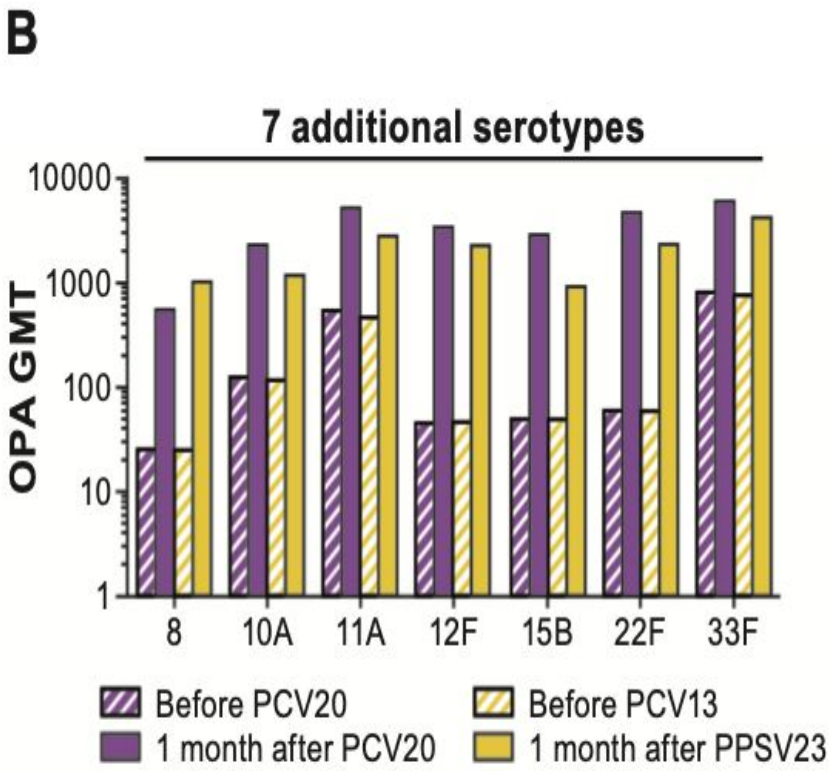


Clinical Infectious Diseases 2022;75(3):390–8


A
Adults ⩾60 years
PCV20=1505; PCV13=1483
Adults 50–59 years
PCV20=331; PCV13=111
Adults 18–49 years
PCV20=335; PCV13=112
Severe
Moderate
Mild
Participants Reporting Reaction, %
100
90
80
70
60
50
40
30
20
10
0
PCV20 PCV13
Redness
Swelling
Pain at the Injection Site
B
Adults ⩾60 years
PCV20=1505; PCV13=1483
Adults 50–59 years
PCV20=331; PCV13=111
Adults 18–49 years
PCV20=335; PCV13=112
Severe
Moderate
Mild
Participants Reporting Event, %
Fatigue
Headache
Muscle Pain
Joint Pain

SEROTYPE 8 MISSED THE STATISTICAL NON-INFERIORITY CRITERION





GMFRs From Baseline to 1 Month After Vaccination														
Serotype		1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
PCV20	GMFR	12.6	4.8	31.2	6.1	34.3	23.8	12.2	11.0	9.3	33.8	21.0	8.6	24.9
PCV13	GMFR	15.4	5.8	39.3	7.2	42.6	26.5	13.5	12.5	8.3	37.7	25.9	10.8	30.7

GMFRs From Baseline to 1 Month After Vaccination								
Serotype		8	10A	11A	12F	15B	22F	33F
PCV20	GMFR	22.1	18.5	9.3	72.4	55.4	78.5	7.5
PPSV23	GMFR	40.4	10.1	6.0	47.3	18.2	37.9	5.7

ACIP guidance for PCV 20

At-Risk Group	Prior Pneumococcal Vaccine	When to give PCV-20
Adults age ≥65 years	None	Now
	PPSV-23	At least 1 year after last pneumococcal vaccine
	PCV-13	At least 1 year after last pneumococcal vaccine
	PCV-13 + PPSV-23 at age **<65** years	At least 5 years after last pneumococcal vaccine
	PCV-13 + PPSV 23 at age **≥65** years	At least 5 years after last pneumococcal vaccine *(shared decision)*
Immunocompromised* adults age 19 – 64 years	None	Now
	PPSV-23	At least 1 year after last pneumococcal vaccine
	PCV-13	At least 1 year after last pneumococcal vaccine
	PCV-13 + x1 dose PPSV-23	At least 5 years after last pneumococcal vaccine
	PCV-13 + x2 doses PPSV-23	At least 5 years after last pneumococcal vaccine
Adults age 19 – 64 with cochlear implant or cerebrospinal fluid leak	None	Now
	PPSV-23	At least 1 year later
	PCV-13	At least 1 year after last pneumococcal vaccine
	PCV-13 + x1 dose PPSV-23	At least 5 years after last pneumococcal vaccine
*Chronic renal failure, nephrotic syndrome, asplenia, immunodeficiency, generalised malignancy, HIV, Hodgkin's disease, iatrogenic immunosuppression, sickle cell disease/hemoglobinopathies, solid organ transplant		

Table from Zheng S Pneumoccocal vaccine efficacy and real world evidence The Singapore Family Physician 2023

Vaccination rates In Asia

- Korea : **< 15 %**
- Thailand : **< 20%** in patients with Type II Diabetes (2010 to 2018)
- Singapore: The self-reported pneumococcal vaccination coverage among seniors aged 65 to 74 years also increased from **10.3% in 2019 to 22.4% in 2021.**

The Journal of Infectious Diseases 2022;225:836–45
Yotsapon Thewjitcharoen,et al. Journal of Clinical and Translational Endocrinology Volume 20, June 2020, 100227
https://www.moh.gov.sg/news-highlights/details/national-population-health-survey-2021-highlights-need-to-focus-on-preventive-health
accessed 9 March 2024

Starting the conversation of vaccination

Shared clinical decision making

Know your patient

Understand their condition, needs

Prioritising vaccinations

Make them understand

Subsidy

PCV 20

- will be in the NAIS and subsidized Vaccine list from Sept 2025
- Medisave can be tapped to pay for cost of vaccine after subsidies

Abrysvo

No subsidy

https://ask.gov.sg/has/questions/cli1fvtyz0003l508qxuinhnr


Thank
you