Pneumococcal Vaccines

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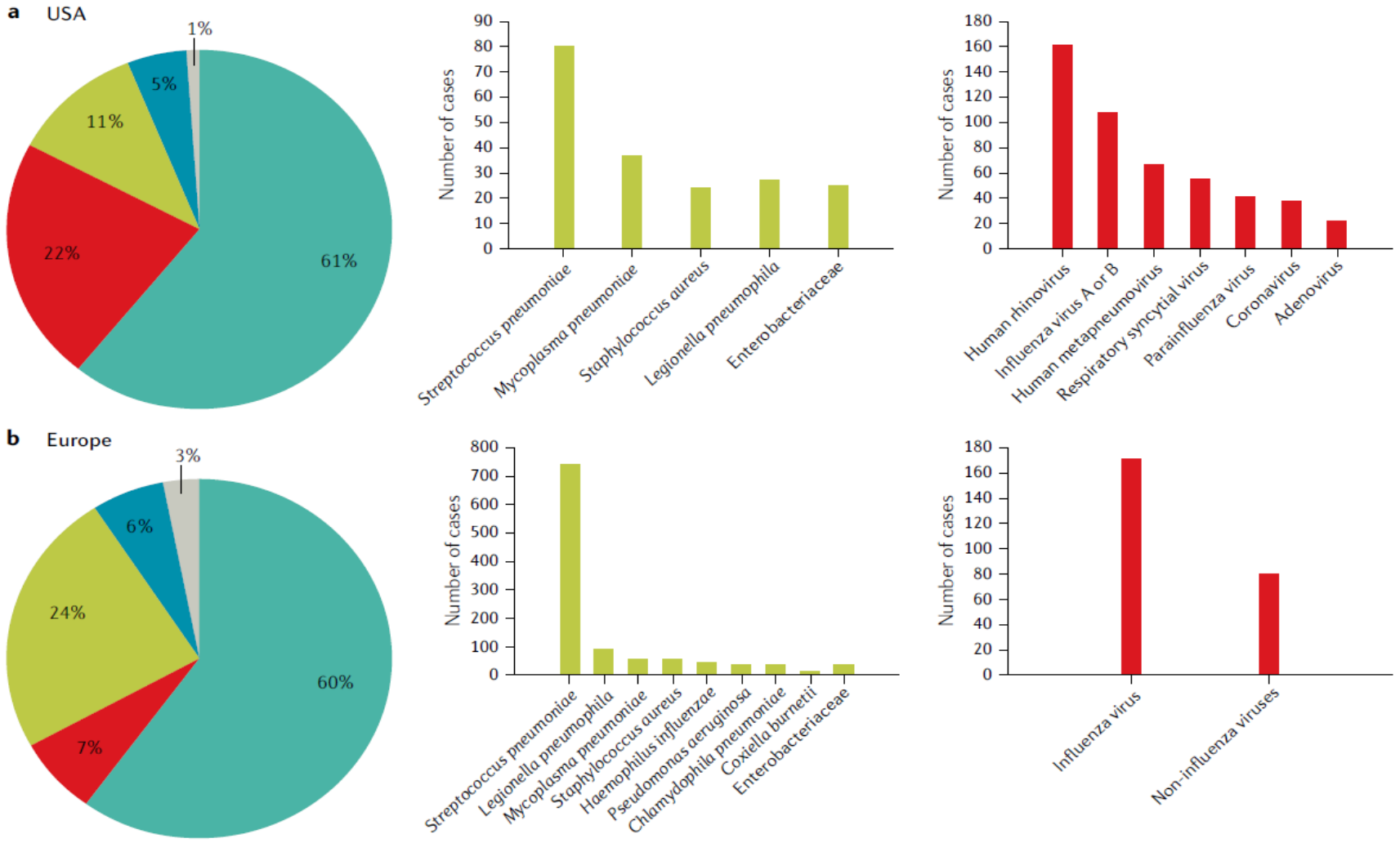
Overview slide

Vaccine information	Information
Which vaccines on the market	PPV23, PCV13,PCV20, PCV21
Vaccine immunogenicity in older adults	Confirmed
Vaccine efficacy / effectiveness in older adults	Confirmed
Vaccine safety in older adults	Confirmed
Long lasting protection in older adults	4 years for PCV13.To be confirmed in PCV20 and 21
Vaccine co-administration in older adults	Confirmed for PCV13,PCV20 and PCV21
Other relevant information in context of older adults?	What is elderly? See October 2024 ACIP recommendations

Microorganisms causing community-acquired pneumonia



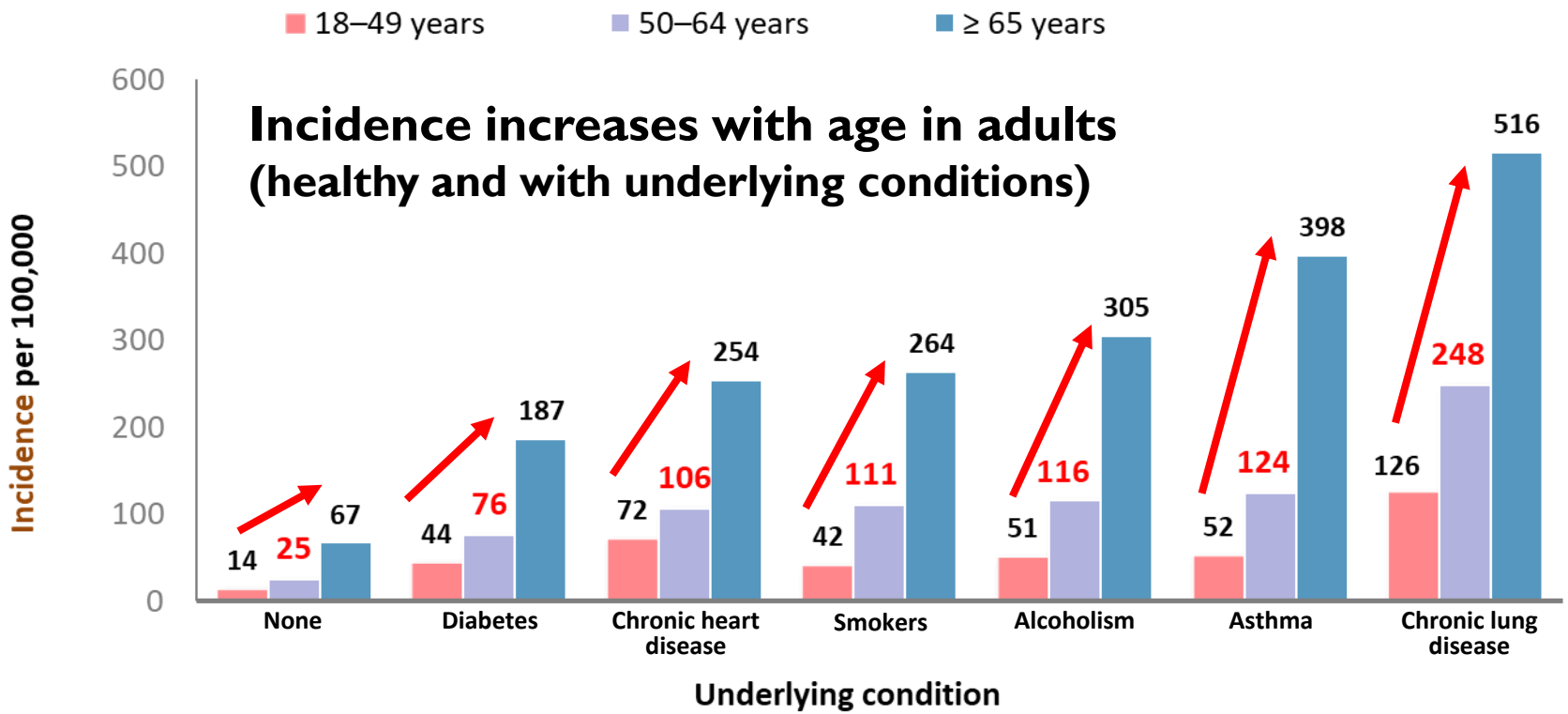
Torres A, et al Nature Prime Disease 2022

The risk of IPD and pneumococcal pneumonia

Age and Ageing

Pneumococcal pneumonia incidence in adults with underlying conditions

Incidence of pneumococcal pneumonia, 2007–2010, US*

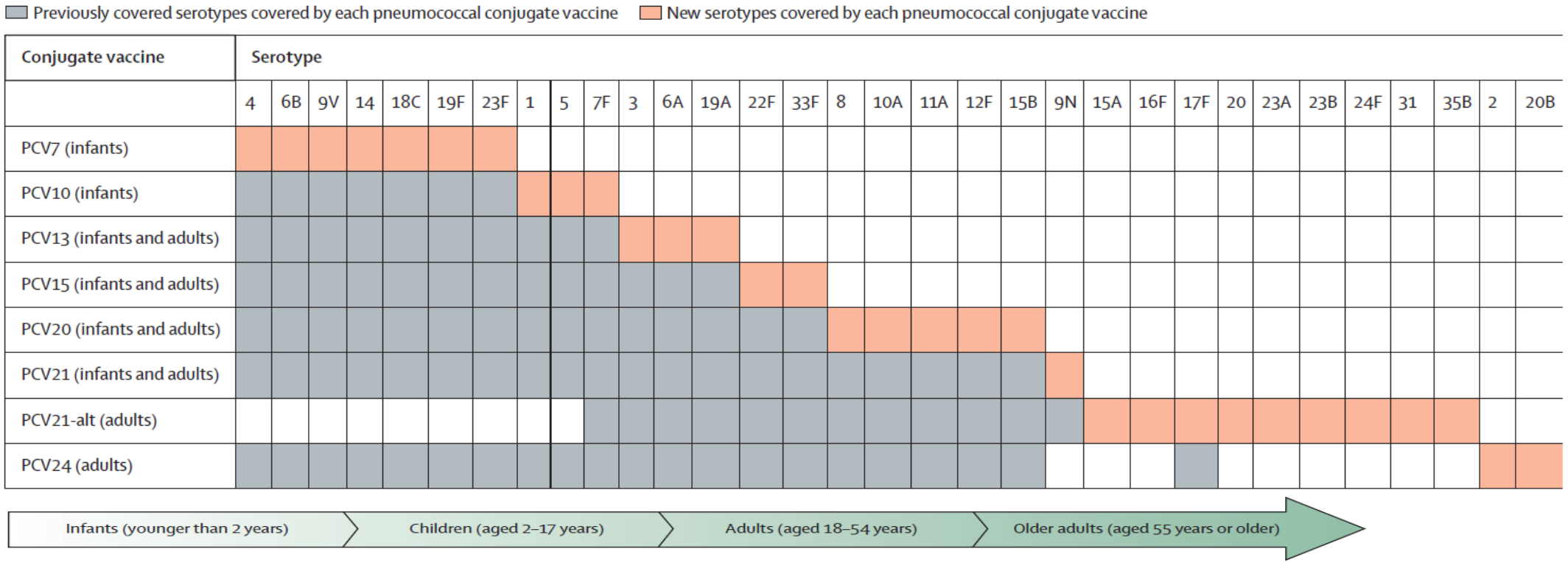


Study details: Retrospective cohort analysis utilising healthcare claims data from 2007 through 2010 comparing rates of pneumococcal disease among persons with certain chronic conditions versus their age-matched healthy counterparts. The databases included medical (ie, facility and professional service) claims and outpatient pharmacy claims from private US health plans. Note: At-risk—immunocompetent with ≥1 selected chronic condition, including chronic lung disease, alcoholism, asthma, chronic heart disease, chronic liver disease, diabetes, neuromuscular/ seizure disorders, and smoking.

*Persons aged 18–49 years, 50–64 years, and ≥ 65 years contributed a total of 49.3 million, 30.6 million and 11.7 million person-years of observation, respectively

Shea KM, et al. Open Forum Infect Dis. 2014;1(1):ofu024.

A



Lancet Infect Dis 2025
Published Online
March 17, 2025
https://doi.org/10.1016/
S1473-3099(24)00740-0

01 PCV20 is an extension of PCV13 plus 7 additional serotypes

02 Indirect effect does not eliminate the need for direct protection of adults with PCV20

03 PCV20 maintains direct protection against serotypes relevant to public health

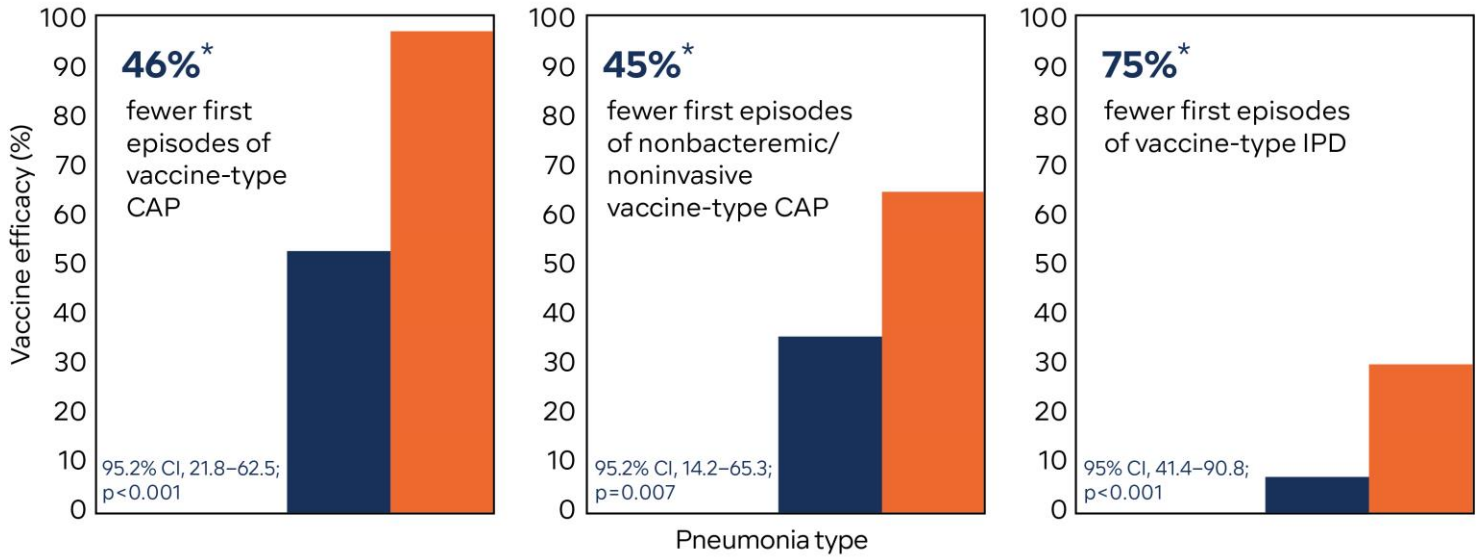
Adult Immunization Board

PCV13 Was Effective in Preventing Vaccine-type CAP in Adults Aged ≥65 Years: The CAPITA Trial

PCV-13 prevented:

- First episodes of vaccine-type strains of pneumococcal CAP
- Nonbacteremic and noninvasive pneumococcal CAP
- Invasive pneumococcal disease

Efficacy of PCV-13 in the CAPITA trial



*per protocol analysis
Adapted from Bonten MJ, *et al*. *N Engl J Med.* 2015;372(12):1114–1125.

CAP: Community-acquired pneumonia; ; CAPITA: Community-acquired pneumonia immunization trial in adults; CI: Confidence interval; IPD: Invasive pneumococcal disease; PCV-13: 13 valent pneumococcal vaccine.

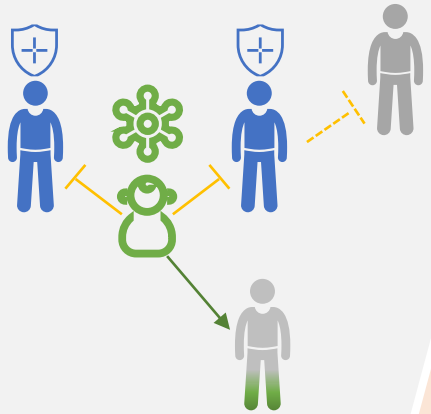
Bonten MJ, *et al*. *N Engl J Med.* 2015;372(12):1114–1125.

Patterson, S.; Webber, C.; Patton, M.; Drews, W.; Huijts, S.M.; Bolkenbaas, M.; Gruber, W.C.; Scott, D.A.; Bonten, M.J. A post hoc assessment of duration of protection in CAPiTA (Community Acquired Pneumonia immunization Trial in Adults). *Trials Vaccinol.* 2016, 5, 92–96. [CrossRef]

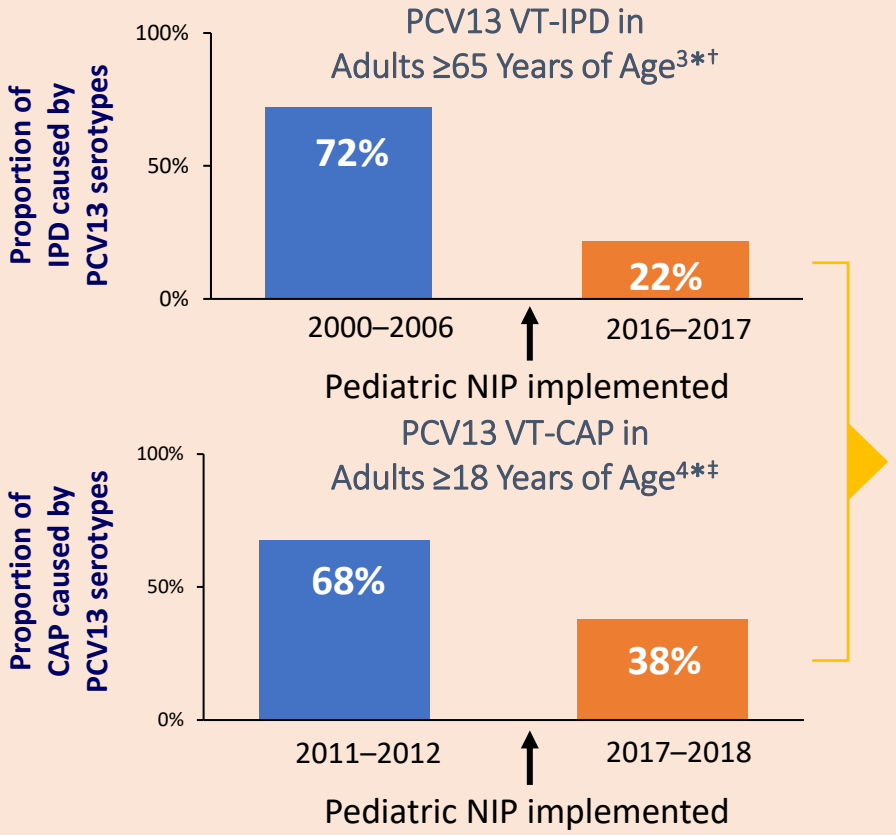
Herd Effect Reduces Pneumococcal Disease Among Adults, But Does Not Eliminate It

Indirect protection from pediatric NIPs can help **reduce encounters** with vaccine serotypes[1]

- Unvaccinated individual
- Vaccinated individual
- Transmitting individual



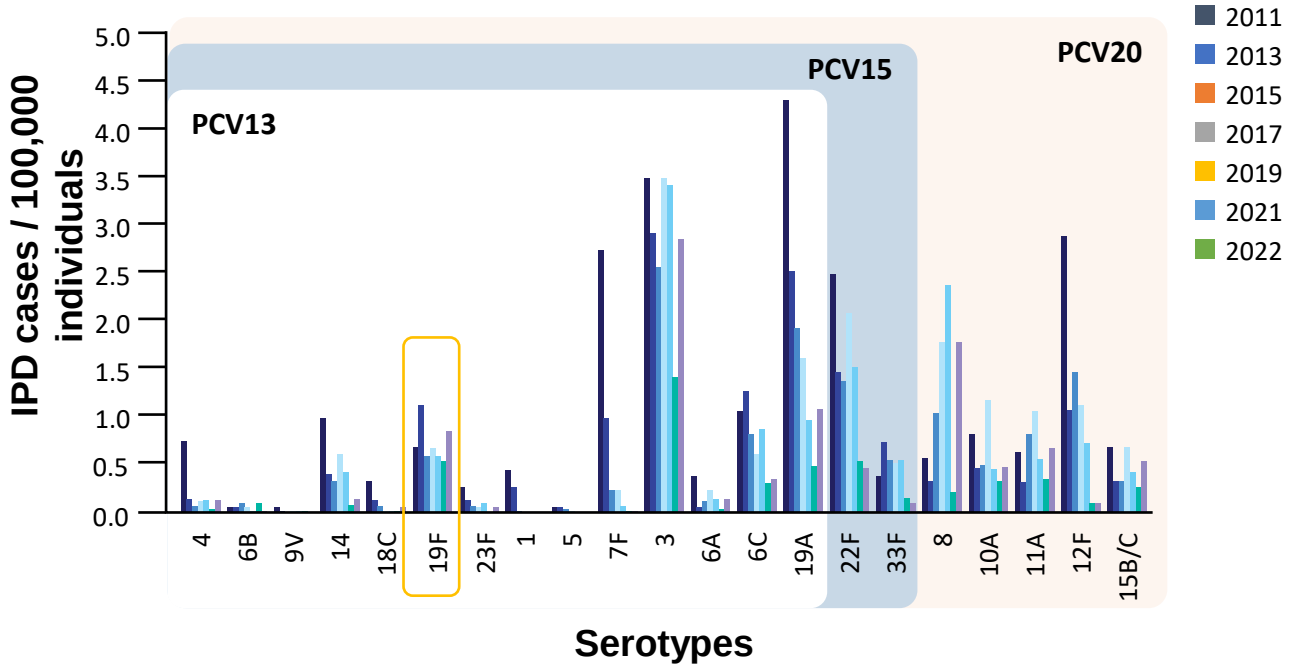
but **unvaccinated adults are not protected** against these serotypes if they are exposed[2]



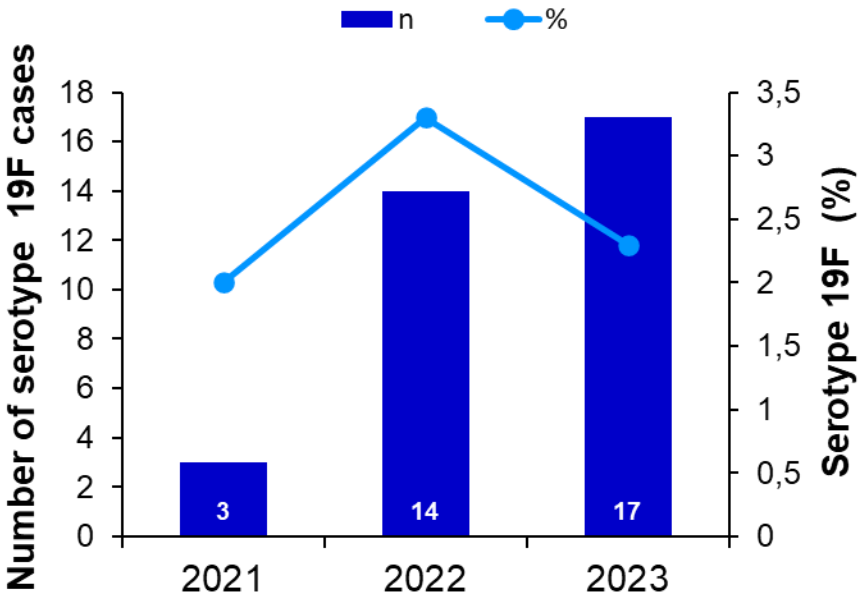
Following implementation of PCV13 in pediatric NIPs, VT disease in adults was substantially reduced, but **a notable amount of VT disease remained**

Serotype 19F Remains Significant in Italy and France

IPD Incidence by Serotype
Among Adults >64 Years of Age in France, 2011 -2022[1]



Number and Proportion of Serotype 19F IPD Among Adults
>64 Years of Age in Italy, 2021-2023[2]



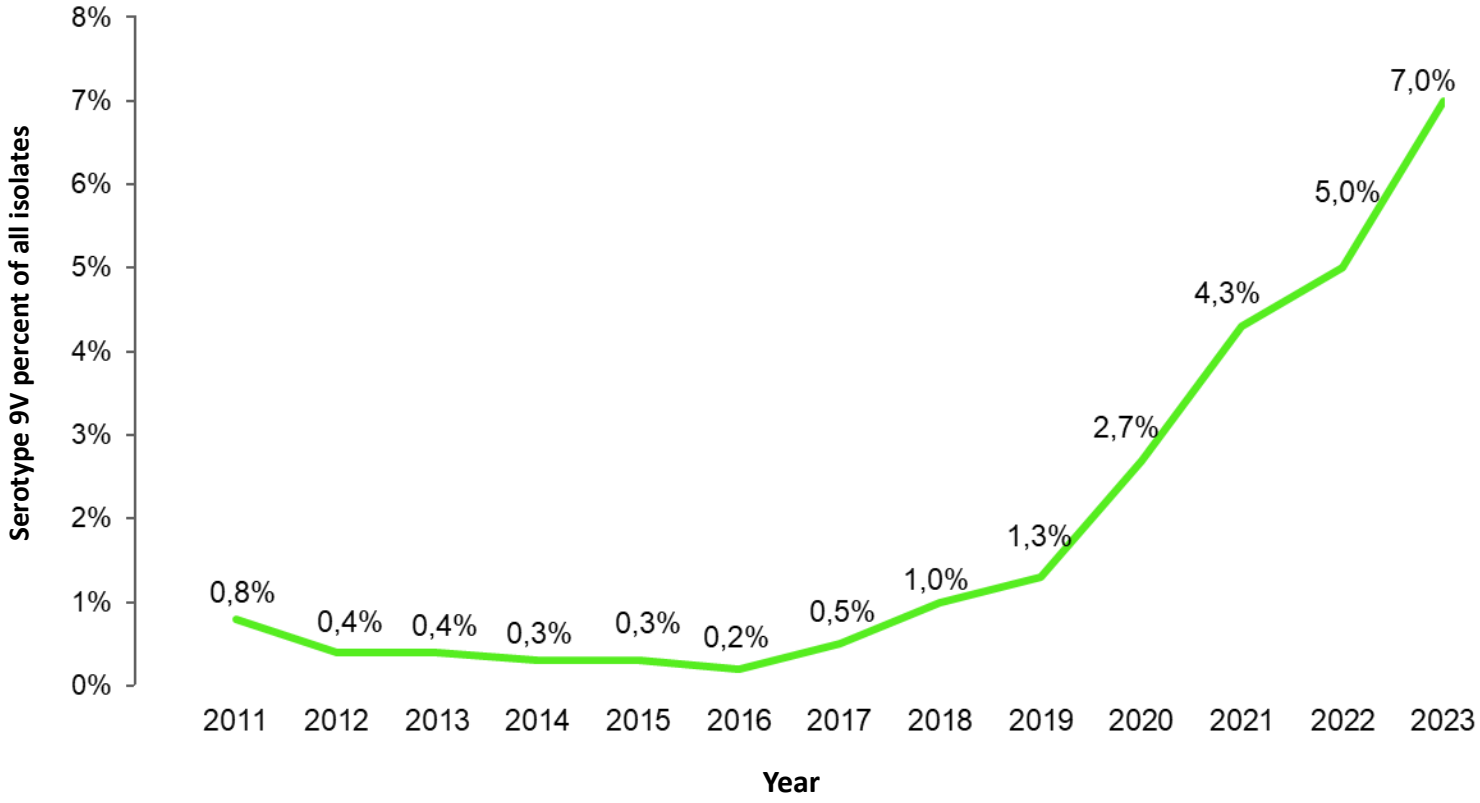
Despite the use of PCV13 in infants, serotype 19F persists in causing invasive disease, particularly in older adults

IPD = invasive pneumococcal disease; PCV = pneumococcal conjugate vaccine
1. Sante' Publique. Centre National de Référence Pneumocoques Rapport Annuel D'activite 2024. Accessed Nov 2024. https://cnr-pneumo.com/docman/rapports/92-2023-epidemiologie-2022/file; 2. Instituto Superi
Sorveglianza nazionale delle malattie batteriche invasive. 2024. Accessed Oct 2024. https://www.iss.it/documents/20126/6703853/RIS+2-2024.pdf/67f460ad-111b-9fd9-24bd-4e23160ad864?t=1727273034488

Increases in Serotype 9V Have Been Observed in Canada and in the IRIS Consortium Surveillance System

- In Canadian adults, the prevalence of serotype 9V IPD increased by 14-fold in 2023 compared with 2017, despite the amount of overall disease remaining stable during the study period. This increase was noted across all adult age groups, and was driven by a multi-drug-resistant clone[1]
- A study utilizing the IRIS Consortium of pooled surveillance data from 27 countries found a 124% increase in the prevalence of 9V among adults 45–64 years of age in 2022, compared with pre-pandemic years (2018–2019)[2]

Proportion of Serotype 9V IPD Cases Among Canadian Adults, 2011-2023[1]



IPD = invasive pneumococcal disease; IRIS = Invasive Respiratory Infection Surveillance

1. Golden A, et al. Poster presented at ISPPD-13, Cape Town, South Africa, March 17-20, 2024; 2. Brueggemann AB, et al. Poster presented at ISPPD-13, Cape Town, South Africa, March 17-20, 2024

Serotype 4 Has Recently Re-Emerged as One of the Leading Causes of IPD[1,2]

- From 2018 to 2022, **serotype 4 increased from the 15th to the 5th most isolated serotype causing IPD**[2]
- This increase was predominantly observed in the adult population[2]
  - Percent increase of serotype 4 incidence rates in 2022 compared with 2018 / 2019[2]
    - **15–24 years of age:** 108.6%
    - **25–44 years of age**: 102.7%
    - **45–64 years of age**: 60.2%
    - **≥65 years of age:** 42.1%

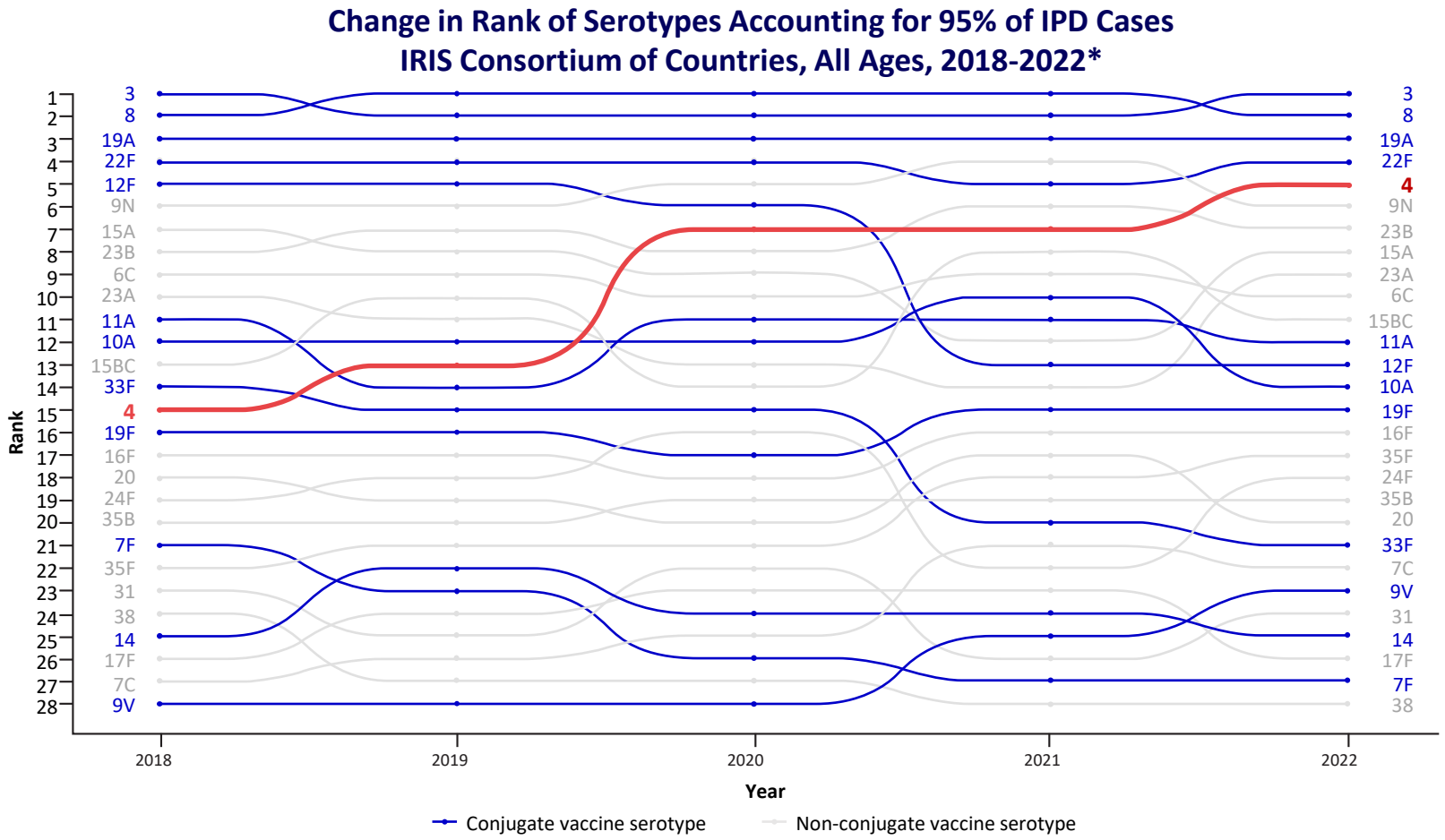


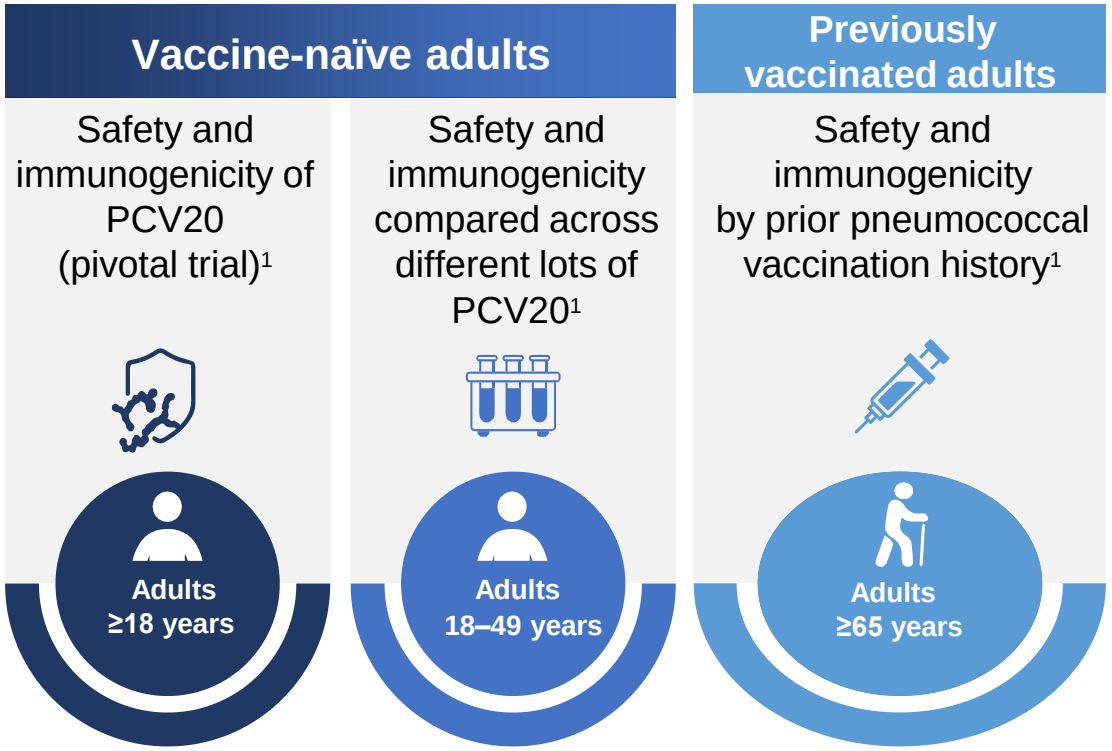
Figure adapted from Brueggemann AB, et al. 2024. Figure 1A
*Data are from the IRIS Consortium, a prospective surveillance program comprised of >50 reference or regional laboratories in 30 countries across 6 continents.
The chart displays 140,537 pooled IPD cases from 27 counties across all age ranges. All results have been adjusted for population size and population surveillance coverage
IPD = invasive pneumococcal disease; IRIS = Invasive Respiratory Infection Surveillance
1. Shaw D, et al. *Lancet Digit Health*. 2023; 5(9):e582-e593; 2. Brueggemann AB, et al. Poster presented at ISPPD-13, Cape Town, South Africa, March 17-20, 2024

Clinical Characteristics of the 7 Additional Serotypes Selected for PCV20

	8	10A	11A	12F	15B	22F	33F
Global cause of IPD[1]	●	●	●	●	●	●	●
Antibiotic resistance[1]	●	●	●	●	●	●	●
Meningitis[1]	●	●	●	●	●	●	●
Mortality / higher CFR[1]	●	●	●	●	●	●	●
Outbreaks[2,3]	●			●			

PCV20 was evaluated for safety and immunogenicity in ~6000 adults across three Phase 3 clinical trials

Key immunogenicity studies of PCV20*†



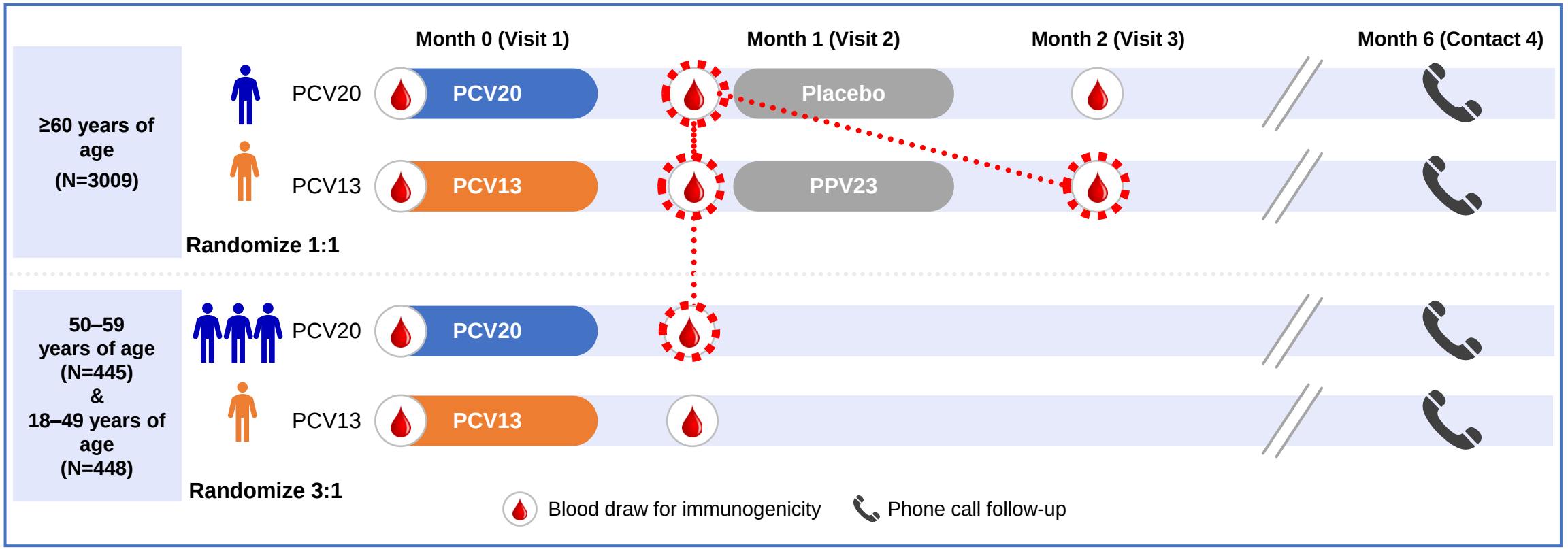
~6000 participants included:

Vaccine-naive
Previously vaccinated
Healthy, aged 18–64 years
Healthy, aged 65 years and older
Those with comorbid conditions

*Participants in this study included those with risk factors that placed them at increased risk for serious pneumococcal disease; †Not all participants received PCV20.

Prevenar 20 [summary of product characteristics]. Gulf & Levant 2024

B7471007 study: Design



Primary immunogenicity objective: Noninferior serotype-specific OPA GMTs in adults ≥60 years of age (vs PCV13 for the 13 serotypes in common, vs PPV23 for the 7 additional serotypes)

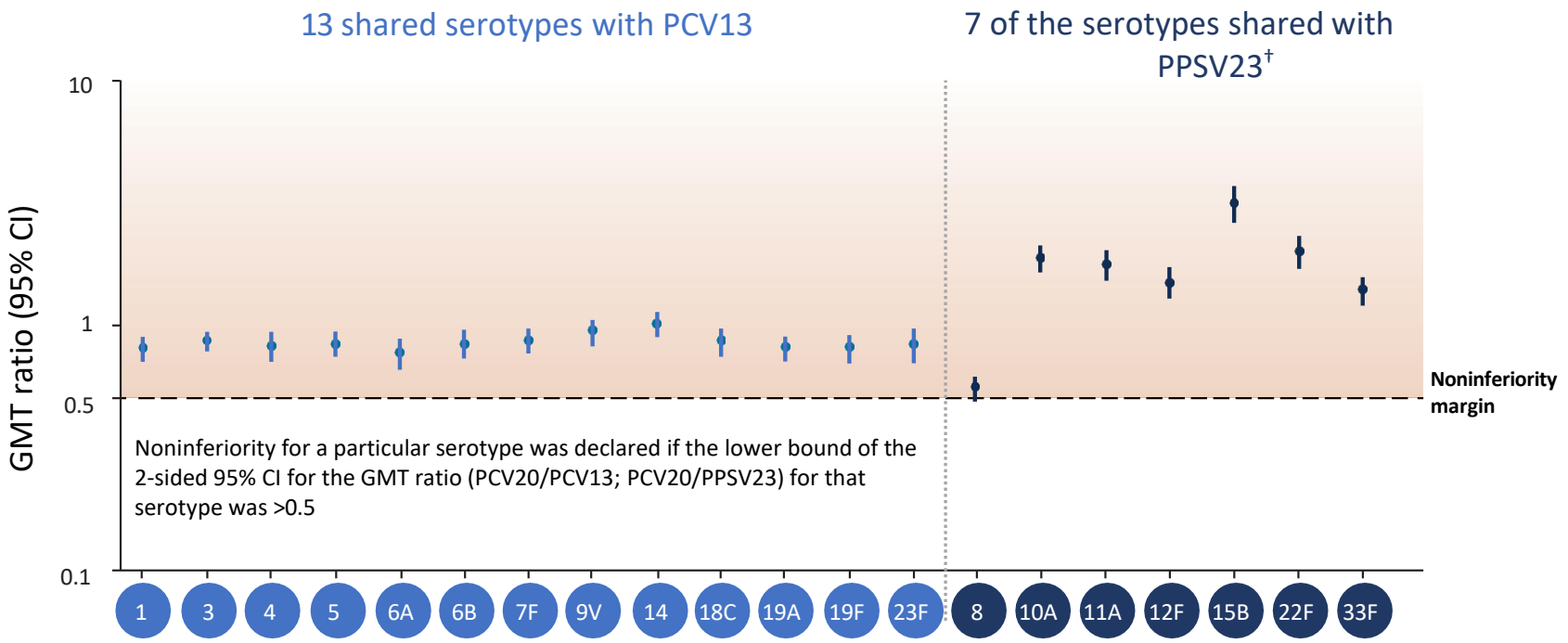
Secondary objective: Serotype-specific OPA GMT in 18-to-49- and 50-to-59-year-olds noninferior to those 60–64 years of age

GMT=geometric mean titer; OPA=opsonophagocytic activity.

Essink B et al. Clin Infect Dis 2022;75:390–398.

PCV20 demonstrated a noninferior immune response to all PCV13 shared serotypes and 6 of 7 PPV23 shared serotypes[1–3]

Immunogenicity for 20 serotypes in PCV20 measured in vaccine-naïve adults aged ≥60 years*



*OPA GMTs 1 month after vaccination with PCV20 versus control vaccine; †PPV23 and PCV20 have 19 shared serotypes. The 7 shared serotypes evaluated are unique to PPV23 and PCV20 and are not contained in PCV13.[1,2]

- Immune responses elicited by PCV20 (n=1157–1430) met noninferiority criteria for all shared serotypes with PCV13 (n=1390–1419) and 6 of 7 shared serotypes with PPV23 (n=1201–1319)
- The response to serotype 8 missed the prespecified statistical noninferiority criterion (the lower bound of the 2-sided 95% CI for the GMT ratio being 0.49 versus >0.50)
- In supportive analyses, 77.8% of participants in the PCV20 group achieved a ≥4-fold rise in serotype 8 OPA titers from before vaccination to 1 month post-vaccination, in line with other serotype responses

CI=confidence interval; GMT=geometric mean titer; OPA=opsonophagocytic activity; PPV23=23-valent polysaccharide vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine.

1. Prevenar 20 [summary of product characteristics]. Gulf & Levant 2024. 2. PNEUMOVAX 23 Summary of Product Characteristics. Available at: https://conecta.msd.com.ar/wp-content/uploads/sites/11/2021/06/pneumovax_23.pdf (accessed July 2024); 3. Prevenar 13 [summary of product characteristics]. Gulf & Levant 2021.

Coadministration of PCV20 with Influenza or COVID-19 Vaccines

Estudio / Población (N)	Cohortes, grupos y aleatorización	Resumen de los resultados
B7471004[1,2] **PCV20 + QIV** **Ensayo Fase 3, multicéntrico, doble ciego y aleatorizado; EE.UU.** N=1796	**Adultos ≥65 años** Aleatorización 1:1 • Coadministración (n=898) • Administración separada (n=898)	• Se demostró la seguridad e inmunogenicidad de **PCV20** cuando se coadministra con QIV en adultos de edad ≥65 años.[2] • Se cumplieron los criterios de no inferioridad para la respuesta inmunitaria en el esquema de administración concomitante *frente al* de administración separada para los 20 serotipos de neumococo y para las 4 cepas de gripe[2]
B7471026 [3,4] **Vacuna PCV20 + ARNm COVID-19** **Ensayo Fase 3, multicéntrico, doble ciego y aleatorizado; EE.UU.** N=570	**Adultos ≥65 años** Aleatorización 1:1:1 • Coadministración (n=184) • PCV20 (n=182) • Vacuna COVID-19 ARNm (n=183)	• Se demostró la seguridad e inmunogenicidad de **PCV20** cuando se coadministra con una dosis de refuerzo de la vacuna fente a la COVID-19 de Pfizer-BioNTech en adultos de ≥65 años.[4] • La inmunogenicidad de la administración conjunta de PCV20 y BNT162b2 fue similar a la de PCV20 o BNT162b2 administradas por separado.[4]

PCV20 = vacuna antineumocócica conjugada 20-valente; QIV = vacuna antigripal tetravalente;
Referencias en la página de notas

PCV21, 21-valent Pneumococcal Conjugate Vaccine Formulation

Formulated in a 0.5 mL dose for intramuscular (IM) injection

21

Contains 21 pneumococcal capsular polysaccharides of the following serotypes:
4 µg each of serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B

Uses CRM197 as a carrier protein
CRM197 is a non-toxic variant of diphtheria toxin originating from *Corynebacterium diphtheriae*

Does not contain an adjuvant

1. Platt H, Omole T, et al. Safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine, V116, in healthy adults: phase 1/2, randomised, double-blind, active comparator-controlled, multicentre, US-based trial. Lancet Infect Dis. 2023 Feb;23(2):233-246. https://pubmed.ncbi.nlm.nih.gov/36116461/
2. Safety and Immunogenicity of V116 in Pneumococcal Vaccine-naïve Adults (V116-003, STRIDE-3) https://clinicaltrials.gov/ct2/show/NCT05425732?term=V116&draw=1&rank=2

Rationale for the Development of PCV21

Adult and Pediatric Serotype Variation

The top serotypes that cause pneumococcal disease vary between adults and children.[1]

Widespread use of PCVs in infants has led to **different IPD trends between children <5 years and adults**, as indicated by differences in serotype prevalence and higher disease incidence in adults.[1,2,3]

IPD due to non-vaccine serotypes has increased in adults.[6,7]

Residual/Persistent PD Burden in Adults

Although adults have indirectly benefited from pediatric PCV use, **PD continues to cause significant mortality and morbidity among adults globally**.[4]

In countries with a robust pediatric PCV immunization program, V116 has the potential to address the unmet medical need in adults.[5]

Complementary Strategy

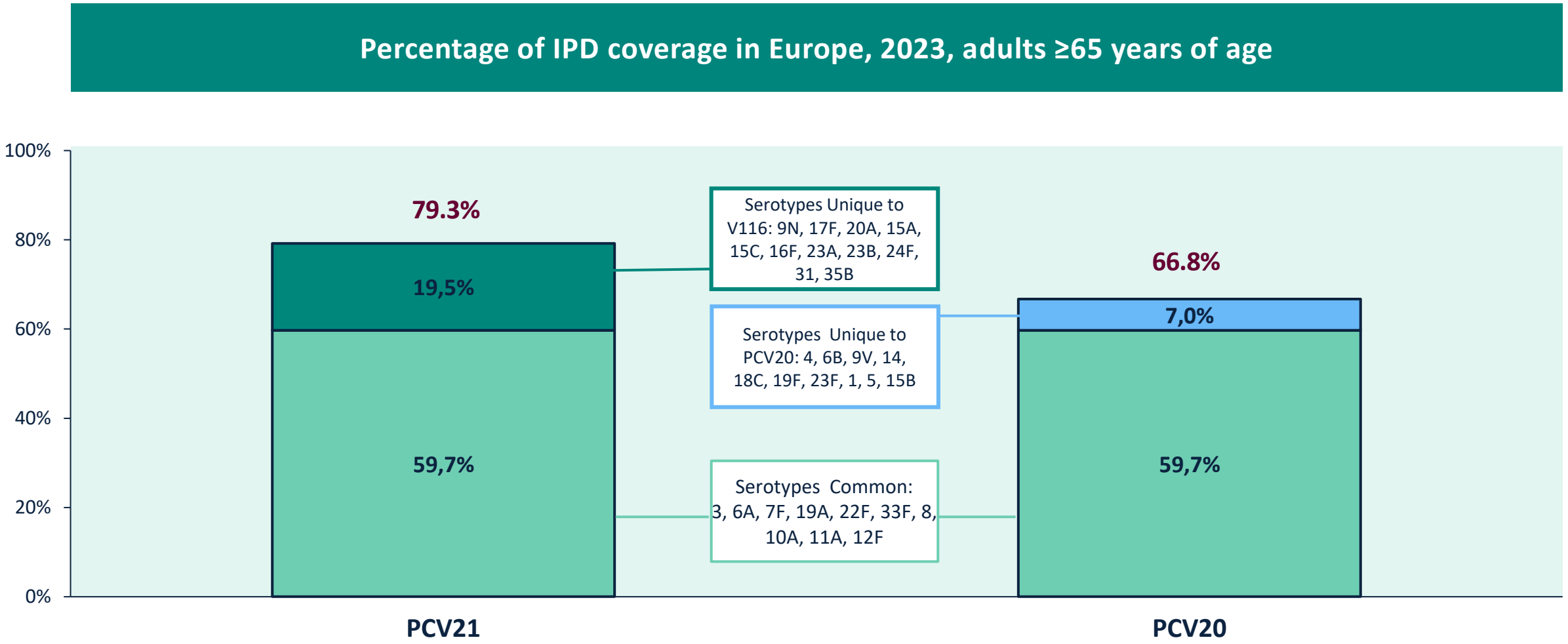
Complementary approach of pairing pediatric and adult vaccines could be a more effective and cost-saving strategy.[8,9]

An **adult population-specific vaccine** has the potential to reduce pneumococcal disease burden in older adults over the current indirect protection from the infant PCV vaccine programs.[5]

IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine; V116, pneumococcal conjugate vaccine, 21-valent; PD, pneumococcal disease

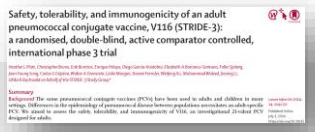
1. Cui YA, et al. Hum Vaccin Immunother 2017;13: 1–13. https://pubmed.ncbi.nlm.nih.gov/28125317/ 2. Pilishvili T, et al. *J Infect Dis* 2010; 201: 32–41. https://pubmed.ncbi.nlm.nih.gov/19947881/ 3. Feikin DR, et al. *PLoS Med* 2013; 10: e1001517. https://pubmed.ncbi.nlm.nih.gov/24086113/ 4. Weinberger DM, Shapiro ED. Clin Infect Dis. 2020;70(12):2493-2495. https://pubmed.ncbi.nlm.nih.gov/31402388/ 5. Platt H, Omole T, et al. Safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine, V116, in healthy adults: phase 1/2, randomised, double-blind, active comparator-controlled, multicentre, US-based trial. Lancet Infect Dis. 2023 Feb;23(2):233-246. https://pubmed.ncbi.nlm.nih.gov/36116461/ 6. Pick H, et al. *Thorax* 2020; 75: 38–49. https://pubmed.ncbi.nlm.nih.gov/31594801/ 7. Naucler P, et al. *Clin Infect Dis* 2017; 65: 1780–89. https://pubmed.ncbi.nlm.nih.gov/29020171/ 8. Colijn C, et al. *Nat Microbiol* 2020; 5: 473–85. https://pubmed.ncbi.nlm.nih.gov/32015499/. 9. Kremer PHC, et al. *eLife*. 2022;11:e69244. https://pubmed.ncbi.nlm.nih.gov/35881438/.

Serotypes in PCV21 are Responsible for the Majority of Residual Invasive Pneumoc Disease (IPD) in Adults



ECDC Atlas Infectious diseases, https://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=40

PCV21 Clinical Development Program—Overview of Phase 3 Studies


Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial

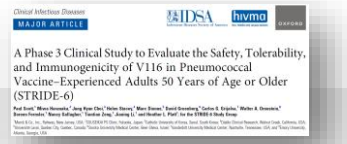
Key Studies

V116-P003[a] (STRIDE-3)
Pivotal
(n=2600)
NCT05425732

≥18 years old

V116-P004 (STRIDE-4)
Clinical Lot Consistency
(n=2040)
NCT05464420

18–49 years old


MAJOR ARTICLE

A Phase 3 Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine–Experienced Adults 50 Years of Age or Older (STRIDE-6)

Supportive

V116-P005 (STRIDE-5)
Concomitant Flu
(n=1000)
NCT05526716

V116-P006 (STRIDE-6)
Vaccine Experienced
(n=700)
NCT05420961

≥50 years old

Special Populations

V116-007 (STRIDE-7)
High Risk (HIV)
(n=300)
NCT05393037

≥18 years old

V116-008 (STRIDE-8)
At-Risk Adults
(n=500)
NCT05696080

18–64 years old

V116-013 (STRIDE-13)
Pediatric with Increased Risk
(n=820)
NCT06177912

≥2–<18 years old

Ex-US

V116-009 (STRIDE-9)
Japan Local
(n=440)
NCT05633992

≥65 years old

V116-010 (STRIDE-10)
PPSV23 Comparator
(n=1400)
NCT05569954

≥50 years old

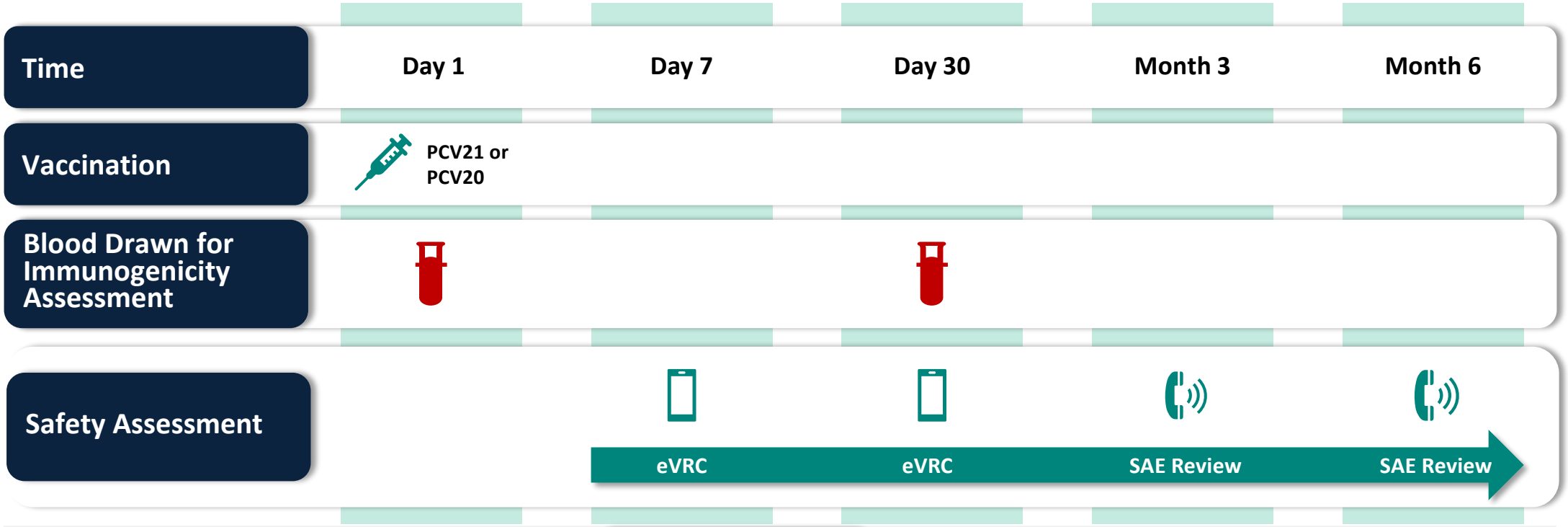

vaccines

A Phase 3 Randomized Trial Investigating the Safety, Tolerability, and Immunogenicity of V116, an Adult-Specific Pneumococcal Vaccine, Compared with PPSV23, in Adults ≥50 Years of Age (STRIDE-10)

[a]Comparator to PCV20.; V116, pneumococcal conjugate vaccine, 21-valent; PPSV23, pneumococcal polysaccharide vaccine, 23-valent; HIV, human immunodeficiency virus

1. (V116-004, STRIDE-4) https://clinicaltrials.gov/ct2/show/NCT05464420?term=V116&draw=2&rank=3 2. (V116-003, STRIDE-3) https://clinicaltrials.gov/ct2/show/NCT05425732?term=V116&draw=1&rank=2
3.(V116-005, STRIDE-5) https://clinicaltrials.gov/ct2/show/NCT05526716?term=05526716&draw=2&rank=1 4. (V116-006, STRIDE-6) https://clinicaltrials.gov/ct2/show/NCT05420961?cond=V116-006&draw=2&rank=1 5. (V116-007, STRIDE-7) https://clinicaltrials.gov/ct2/show/NCT05393037?cond=V116-007&draw=2&rank=1 6. (V116-008, STRIDE-8) https://clinicaltrials.gov/ct2/show/NCT05696080?term=V116&draw=2&rank=1 7. (V116-009, STRIDE-9) https://clinicaltrials.gov/ct2/show/NCT05633992?term=V116&draw=1&rank=4 8. (V116-010, STRIDE-10) https://clinicaltrials.gov/ct2/show/NCT05569954?term=V116&draw=1&rank=6 9. (V116-013, STRIDE-13) https://clinicaltrials.gov/study/NCT06177912?term=V116&checkSpell=false&rank=5

Phase III Study V116-003 (STRIDE-3): Study Design



Study Groups

N=2600 Total Enrollment Target

≥50 Years (Cohort 1)
1:1 Randomization[a]
N=2300 Enrollment Target

→ PCV21 (n=1150 participants)
PCV20 (n=1150 participants)

18-49 Years (Cohort 2)
2:1 Randomization
N=300 Enrollment Target

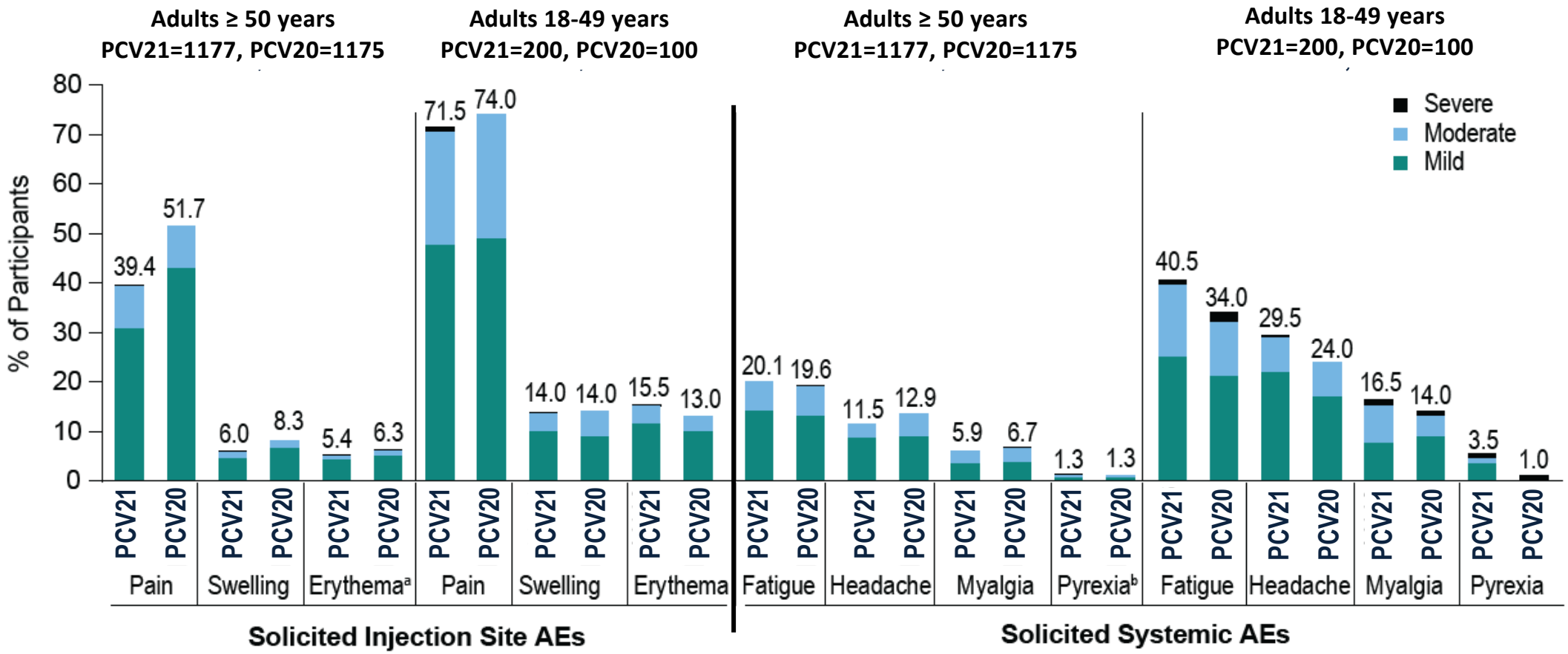
→ PCV21 (n=200 participants)
PCV20 (n=100 participants)

Both cohorts included pneumococcal vaccine-naïve individuals, with or without chronic pre-existing conditions

[a]Stratified by age (50-64 years, 65-74 years, 75-84 years, and ≥85 years) with at least 50% of patients ≥65 years.
eVRC, electronic vaccination report card; PCV20, pneumococcal conjugate vaccine, 20-valent; SAE, serious adverse event; PCV21, pneumococcal conjugate vaccine, 21-valent.
https://classic.clinicaltrials.gov/ct2/show/NCT05425732?term=V116&draw=1&rank=2

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext

Phase III Study V116-003 (STRIDE-3): Safety Summary



The proportion of participants with AEs were generally comparable between the PCV21 and PCV20 intervention groups

[a]One report of erythema each in the PCV20 and PCV21 groups, cohort 1, were of unknown intensity [b]One report of pyrexia in the PCV21 group, cohort 2, was reported as grade 4 (life-threatening), but the investigator considered the value to be erroneous based on the clinical assessment of the participant. Body temperature was collected days 1-5; temperature of ≥100.4°F was classified as pyrexia.

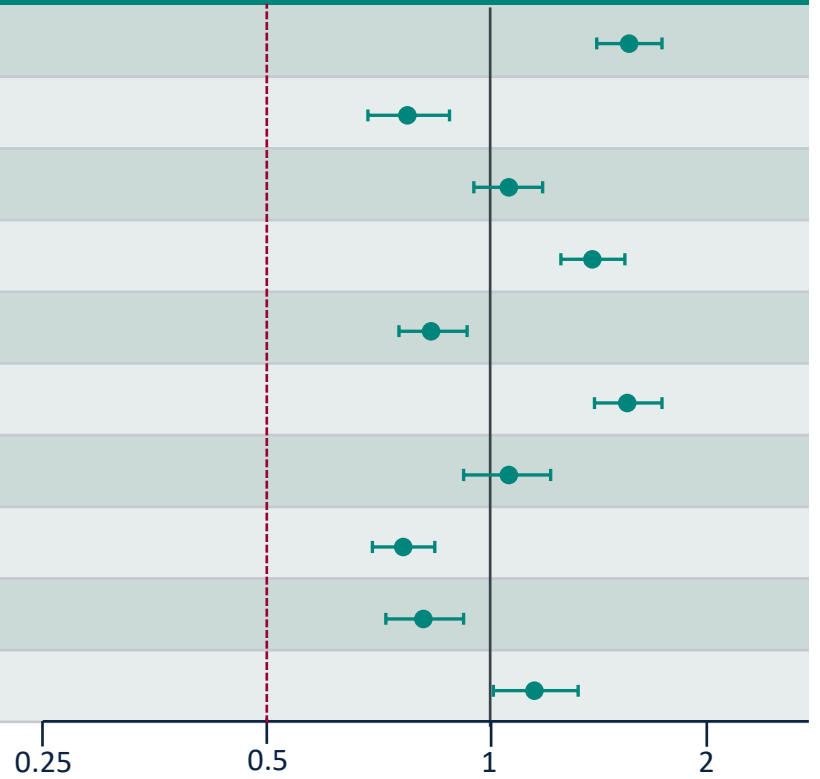
AE, adverse event; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext

Phase III Study V116-003 (STRIDE-3): Immunogenicity Results

OPA GMTs and GMT Ratios; 10 Common Serotypes; Adults ≥50 Years

Serotipo	PCV21 OPA GMT (n=1145-1161)	PCV20 OPA GMT (n=1150-1162)	OPA GMT Ratios (PCV21/PCV20)[a]
3	274.0	176.7	1.55 (1.40, 1.72)
6A	2302.0	2972.5	0.77 (0.68, 0.88)
7F	3637.4	3429.9	1.06 (0.95, 1.18)
8	2501.3	1811.1	1.38 (1.25, 1.53)
10A	3893.4	4678.0	0.83 (0.75, 0.93)
11A	3232.6	2092.8	1.54 (1.39, 1.72)
12F	2641.2	2499.6	1.06 (0.92, 1.21)
19A	2136.1	2817.8	0.76 (0.69, 0.84)
22F	3874.5	4770.1	0.81 (0.72, 0.92)
33F	13,558.9	11,742.1	1.15 (1.01, 1.32)



PCV21 met non-inferiority criteria[b] for each of the 10 common serotypes in OPA GMT ratio at 30 days postvaccination

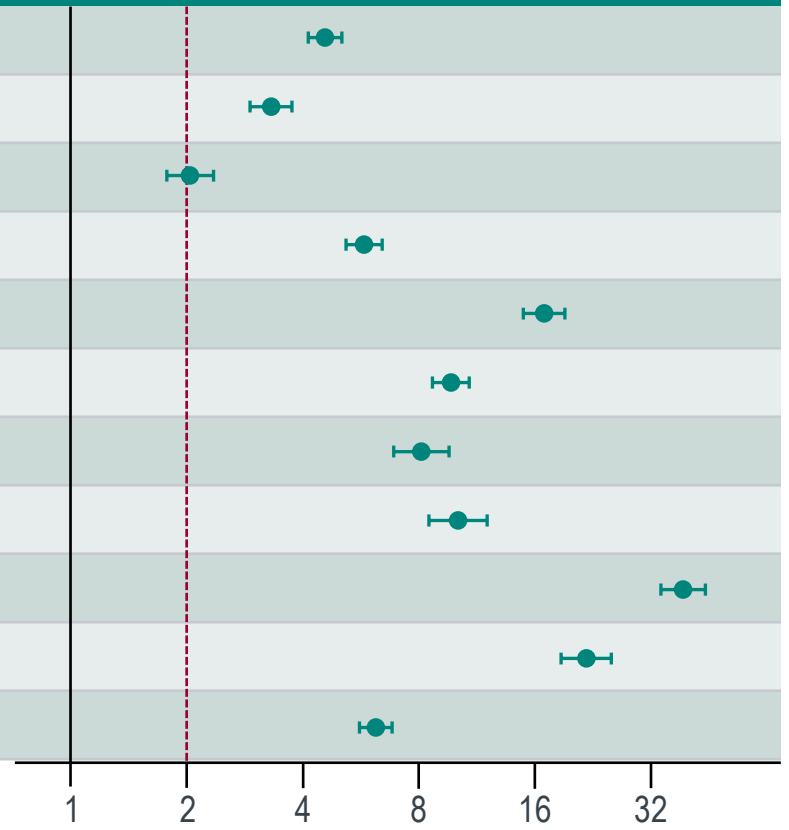
[a]Reported as V116/PCV20 (95% CI); OPA GMT Ratio plotted on $\log_{10}$ scale. [b]Lower bound of 95% CI of the V116/PCV20 OPA GMT ratio is >0.5.
CI, confidence interval; GMT, geometric mean titer; OPA, opsonophagocytic activity; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.

Phase III Study V116-003 (STRIDE-3): Immunogenicity Results

OPA GMTs and GMT Ratios; 11 PCV21 Unique Serotypes; Adults ≥50 Years

Serotype	PCV21 OPA GMT (n=1107-1161)	PCV20 OPA GMT (n=1102-1160)	OPA GMT Ratios (PCV21/PCV20)[a]
9N	7470.7	1640.4	4.55 (4.12, 5.04)
15A	5237.2	1589.0	3.30 (2.91, 3.74)
15C	4216.2	2072.3	2.03 (1.77, 2.34)
16F	4868.2	846.3	5.75 (5.16, 6.41)
17F	7764.9	460.4	16.86 (14.90, 19.09)
20A	6099.2	631.1	9.66 (8.66, 10.79)
23A	3737.2	461.5	8.10 (6.86, 9.55)
23B	1082.5	107.3	10.09 (8.48, 12.00)
24F	2728.6	70.5	38.71 (33.87, 44.25)
31	3132.5	144.4	21.69 (18.68, 25.18)
35B	8527.8	1383.0	6.17 (5.59, 6.80)



PCV21 met superiority criteria[b] for 10 of the 11 PCV21 unique serotypes in OPA GMT ratio at 30 days postvaccination

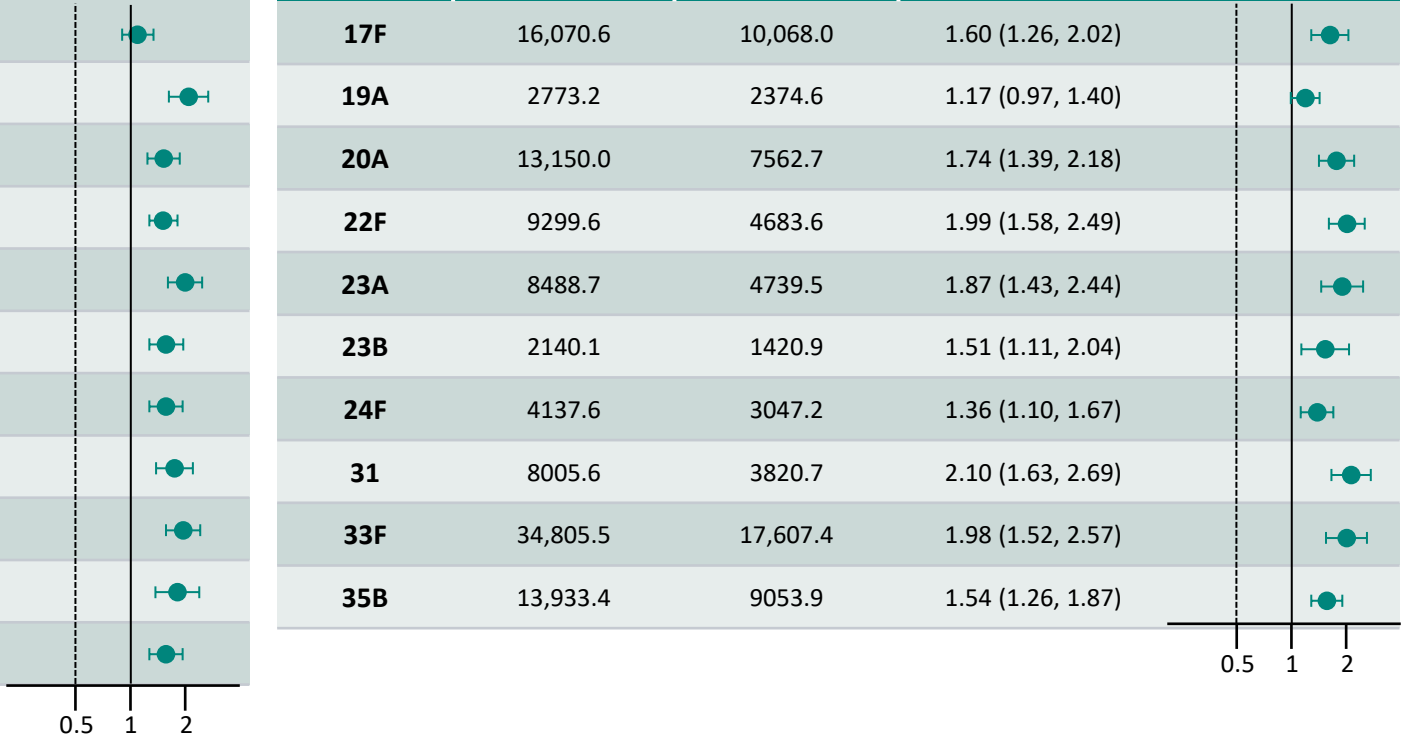
[a]Reported as PCV21/PCV20 (95% CI); OPA GMT Ratio plotted on $\log_{10}$ scale. [b]Lower bound of 95% CI of the PCV21/PCV20 OPA GMT ratio is >2.0.
CI, confidence interval; GMT, geometric mean titer; OPA, opsonophagocytic activity; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.

Phase III Study V116-003 (STRIDE-3): Immunogenicity Results

OPA GMTs and GMT Ratios; V116 Serotypes; Adults 18–49 and 50–64 Years

Serotype	PCV21 18-49 Years (n=184-198)	PCV21 50-64 Years (n=550-575)	OPA GMT Ratio (18-49 Years/50-64 Years)[a]
3	308.6	282.7	1.09 (0.90, 1.33)
6A	5289.6	2572.9	2.06 (1.61, 2.62)
7F	6447.2	4278.8	1.51 (1.23, 1.84)
8	4516.0	3004.7	1.50 (1.26, 1.79)
9N	17,283.2	8791.4	1.97 (1.59, 2.43)
10A	6808.1	4382.6	1.55 (1.26, 1.92)
11A	5871.6	3785.8	1.55 (1.26, 1.91)
12F	6150.4	3561.2	1.73 (1.37, 2.17)
15A	11,319.2	5901.2	1.92 (1.55, 2.37)
15C	10,194.0	5708.0	1.79 (1.36, 2.35)
16F	8877.0	5720.0	1.55 (1.26, 1.91)
17F	16,070.6	10,068.0	1.60 (1.26, 2.02)
19A	2773.2	2374.6	1.17 (0.97, 1.40)
20A	13,150.0	7562.7	1.74 (1.39, 2.18)
22F	9299.6	4683.6	1.99 (1.58, 2.49)
23A	8488.7	4739.5	1.87 (1.43, 2.44)
23B	2140.1	1420.9	1.51 (1.11, 2.04)
24F	4137.6	3047.2	1.36 (1.10, 1.67)
31	8005.6	3820.7	2.10 (1.63, 2.69)
33F	34,805.5	17,607.4	1.98 (1.52, 2.57)
35B	13,933.4	9053.9	1.54 (1.26, 1.87)



PCV21 met non-inferiority[b] for immunobridging in participants 18–49 years compared to participants 50–64 years for all 21 serotypes as assessed by serotype-specific OPA GMTs at 30 days postvaccination

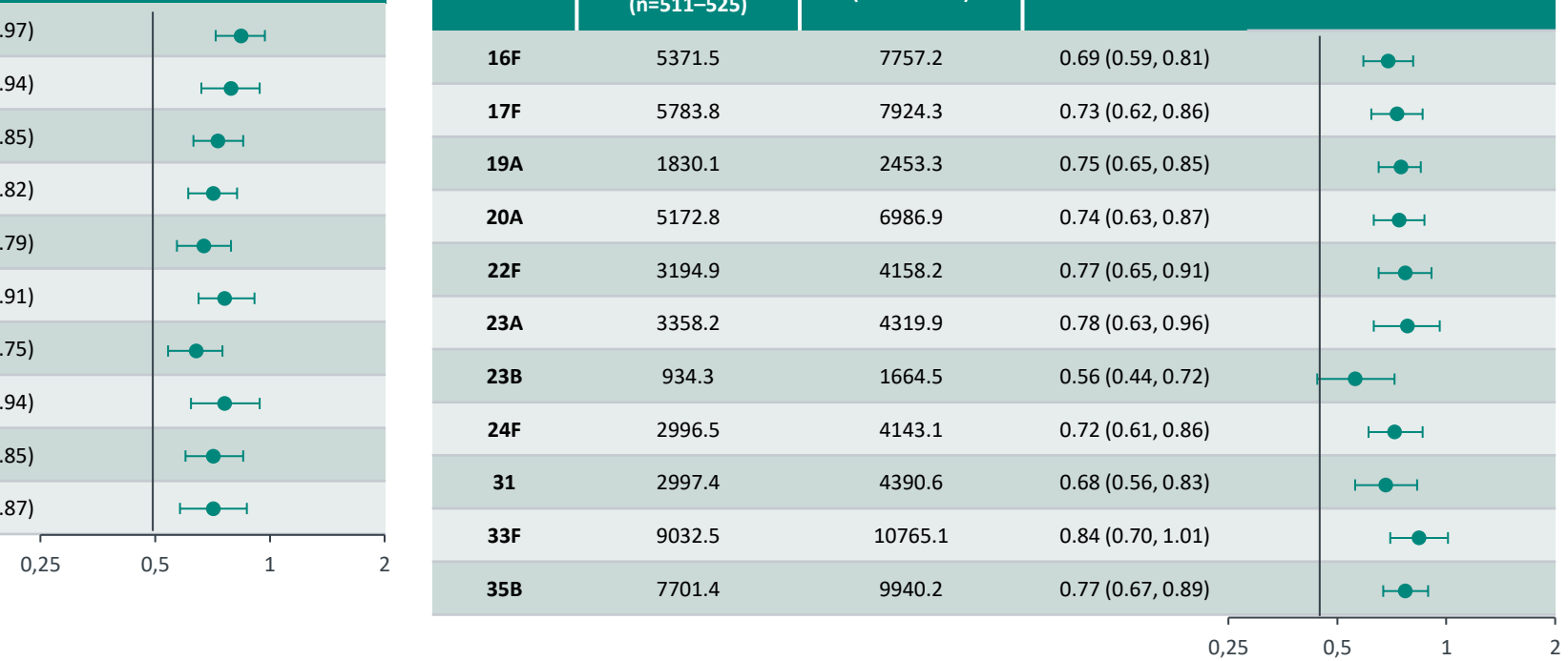
[a]Plotted on $\log_{10}$ scale. [b]Lower bound of 95% CI of the PCV21 (18-49 years)/PCV21 (50-64 years) ratio is >0.5.
CI, confidence interval; GMT, geometric mean titer; OPA, opsonophagocytic activity; PCV21, pneumococcal conjugate vaccine, 21-valent.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.

Phase III Study V116-005 (STRIDE-5): Immunogenicity Results

OPA GMTs and GMT Ratios

Serotype	Concomitant Group OPA GMT (n=511–525)	Sequential Group OPA GMT (n=458–499)	OPA GMT Ratios (Concomitant Group/Sequential Group)[a]
3	209.2	250.1	0.84 (0.72, 0.97)
6A	2056.4	2608.2	0.79 (0.66, 0.94)
7F	2399.2	3275.4	0.73 (0.63, 0.85)
8	1508.9	2135.7	0.71 (0.61, 0.82)
9N	5075.6	7566.6	0.67 (0.57, 0.79)
10A	3033.6	3966.2	0.76 (0.65, 0.91)
11A	2576.3	4051.1	0.64 (0.54, 0.75)
12F	1869.9	2449.5	0.76 (0.62, 0.94)
15A	4670.6	6559.7	0.71 (0.60, 0.85)
15C	3426.0	4832.6	0.71 (0.58, 0.87)
16F	5371.5	7757.2	0.69 (0.59, 0.81)
17F	5783.8	7924.3	0.73 (0.62, 0.86)
19A	1830.1	2453.3	0.75 (0.65, 0.85)
20A	5172.8	6986.9	0.74 (0.63, 0.87)
22F	3194.9	4158.2	0.77 (0.65, 0.91)
23A	3358.2	4319.9	0.78 (0.63, 0.96)
23B	934.3	1664.5	0.56 (0.44, 0.72)
24F	2996.5	4143.1	0.72 (0.61, 0.86)
31	2997.4	4390.6	0.68 (0.56, 0.83)
33F	9032.5	10765.1	0.84 (0.70, 1.01)
35B	7701.4	9940.2	0.77 (0.67, 0.89)



PCV21 administered concomitantly with QIV is noninferior to PCV21 administered sequentially for 20 of 21 PCV21 serotypes (except for serotype 23B) as assessed by OPA GMTs at 30 days postvaccination

Serotype 15C represents the immune response to the deOAc15B polysaccharide as the molecular structure for deOAc15B and 15C are similar; anti-15C immune responses are assessed in this study.

[a]Reported as Concomitant Group/Sequential Group (95% CI); OPA GMT Ratio plotted on $\log_{10}$ scale.

CI, confidence interval; GMT, geometric mean titer; OPA, opsonophagocytic activity; QIV, Quadrivalent Influenza Vaccine; V116, pneumococcal conjugate vaccine, 21-valent.

Omole T, et al. A Phase 3 Randomized Study to Evaluate Safety, Tolerability, and Immunogenicity of V116, an Investigational Adult-Specific Pneumococcal Conjugate Vaccine, Administered Concomitantly with Influenza Vaccine in Adults ≥50 Years (STRIDE-5). Poster Presented at: ISPPD, March 17-20,2024; Cape Town, South Africa.

PCV21 Take-Home Messages

- 21-valent pneumococcal vaccine has been developed as a **population-specific** vaccine to prevent invasive disease and pneumonia in **adults**, as part of a complementary vaccination approach to PCV pediatric immunization programs.
- Pneumococcal serotypes contained in PCV21 (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) account for **79,3% of IPD in adults aged ≥65 years in Europe**.
- PCV21 demonstrated a **safety profile** comparable to PCV20.
- Clinical studies have demonstrated **immunogenicity** to all PCV21 vaccine serotypes.
- PCV21 met **non-inferiority** criteria for **all 21 serotypes**.
- PCV21 met **superiority** criteria for 10 of the 11 PCV21 unique serotypes in OPA GMT, as well the proportion of patients with a 4-fold rise in OPA responses at 30 days postvaccination.
- PCV21 was **approved by the EMA** on March 24th, 2025.

U.S. Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 74 / No. 1
January 9, 2025

Expanded Recommendations for Use of Pneumococcal Conjugate Vaccines Among Adults Aged ≥50 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024

Miwako Kobayashi, MD[1]; Andrew J. Leidner, PhD[2]; Ryan Gierke, MPH[1]; Wei Xing, MSTAT[1]; Emma Accorsi, PhD[1]; Pedro Moro, MD[3]; Mini Kamboj, MD[4]; George A. Kuchel, MD[5]; Robert Schechter, MD[6]; Jamie Loehr, MD[7]; Adam L. Cohen, MD[1]

Summary

What is already known about this topic?

Before October 2024, a single dose of 15-valent, 20-valent, or 21-valent pneumococcal conjugate vaccine (PCV), was recommended for adults aged 19–64 years with risk conditions for pneumococcal disease and for all adults aged ≥65 years.

What is added by this report?

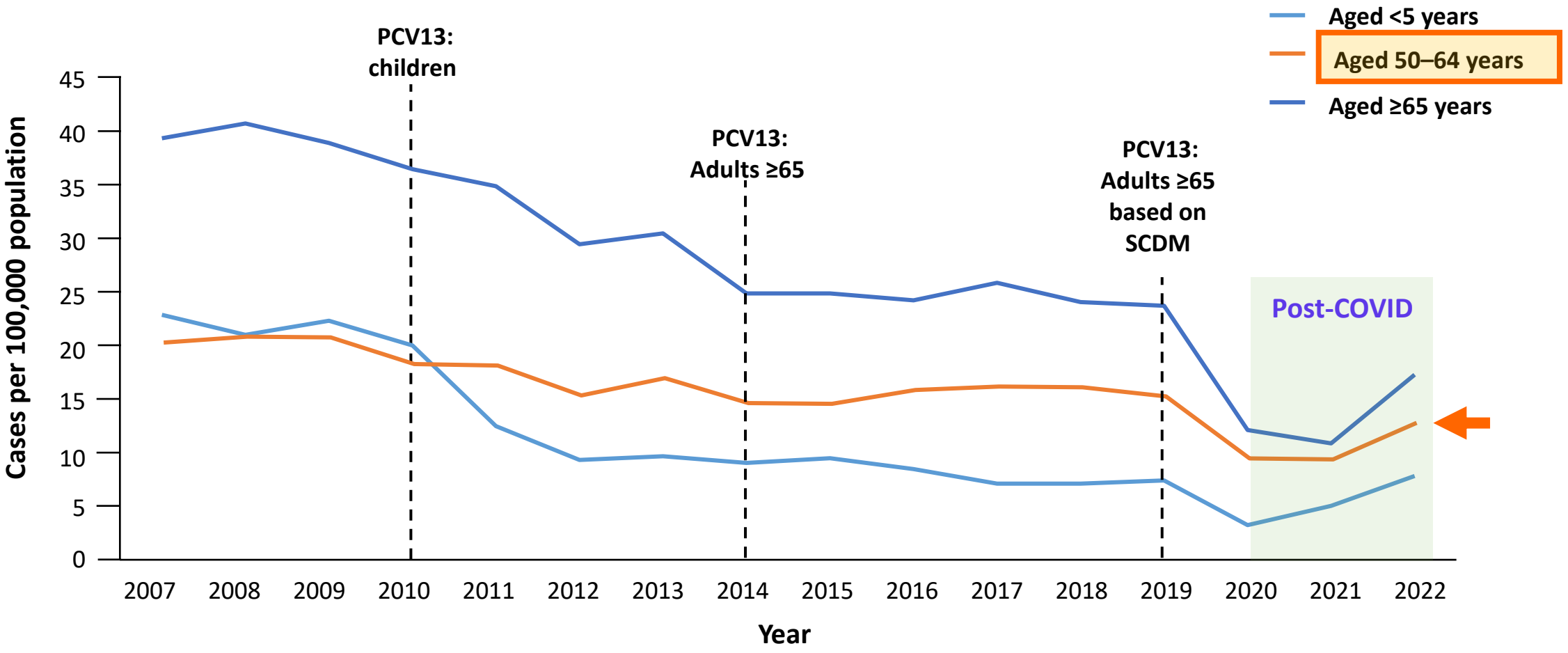
On October 23, 2024, the Advisory Committee on Immunization Practices recommended a single dose of PCV for all adults aged ≥50 years who are PCV-naïve or who have unknown vaccination history. The risk-based recommendation for adults aged 19–49 years is unchanged.

What are the implications for public health practice?

The updated, expanded age-based recommendation is expected to improve pneumococcal disease prevention in adults aged 50–64 years, particularly among demographic groups experiencing higher disease rates.

Adults aged 19–49 years with an immunocompromising condition,† a CSF leak, or a cochlear implant	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is used, administer a single dose of PPSV23* ≥8 weeks after the PCV15 dose.
	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.
	PCV13 only	A single dose of PCV21 or PCV20 administered ≥1 year after the PCV13 dose.
	PCV13 and 1 dose of PPSV23	A single dose of PCV21 or PCV20 ≥5 years after the last pneumococcal vaccine dose. The pneumococcal vaccination series is complete, and it need not be followed by additional pneumococcal vaccine doses.
	PCV13 and 2 doses of PPSV23	The pneumococcal vaccination recommendations should be reviewed again when the person turns age 50 years. Alternatively, a single dose of either PCV21 or PCV20 should be administered ≥5 years after the last pneumococcal vaccine dose. If PCV21 or PCV20 is used, the series is complete, and it need not be followed by additional pneumococcal vaccine doses.

IPD Incidence Rates in the US by Age Group, 2007–2022



Data from CDC Active Bacterial Core surveillance
CDC = Centers for Disease Control and Prevention; IPD = invasive pneumococcal disease; PCV = pneumococcal conjugate vaccine; SCDM = shared clinical decision-making
Adapted from Kobayashi M. Summary of Work Group interpretation of EtR and policy options. Presentation at the October 2024, ACIP Meeting. October 23, 2024. https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/04-Kobayashi-Pneumococcal-508.pdf [accessed Oct 23, 2024]

FUTURE PNEUMOCOCCAL VACCINES

Lancet Infect Dis 2025

Published Online
March 17, 2025
https://doi.org/10.1016/
S1473-3099(24)00740-0

- **Monovalent protein vaccines**

  Pneumococcal histidine protein D (PhtD)

  Pneumolysin (Ply D1)

- **Multivalent protein vaccines**

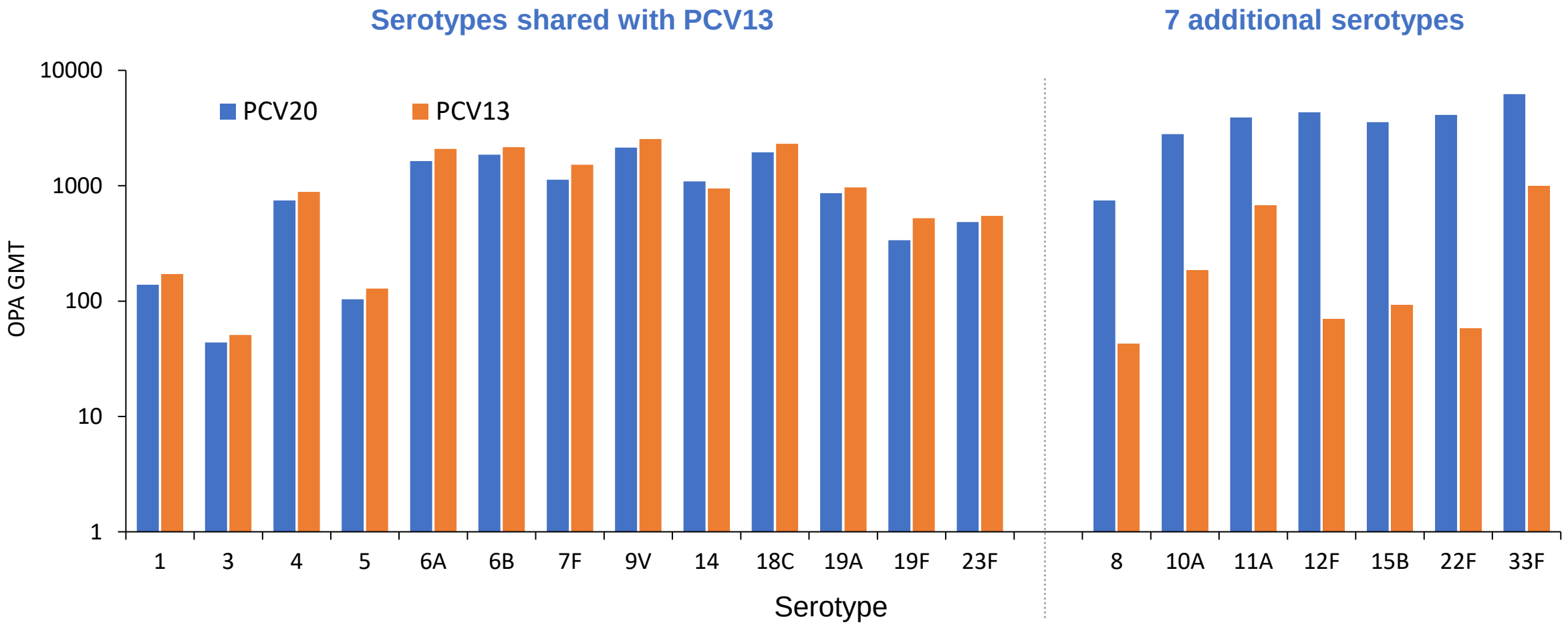
  Recombinant trivalent: PhtD +Ply+PcpA

  PhtD+Ply+H.influenza non typeable protein D

- **Conjugate/protein combinations**.

  Ply + PhtD vaccine + PCV1o

B7471007 Study: PCV20 elicited a similar immune response to PCV13 in adults 18–64 years of age with at least 1 risk condition*



*Chronic cardiovascular disease, chronic liver disease, chronic pulmonary disease, or diabetes mellitus. Smoking was not considered a risk factor for serious pneumococcal disease in this analysis.
GMT=geometric mean titer; OPA=opsonophagocytic activity.

Sabharwal C et al. Hum Vaccin Immunother 2022;18:e2126253.

Phase III Study V116-003 (STRIDE-3): Baseline Characteristics

Cohort 1 (≥50 Years of Age)

	PCV21 N=1179	PCV20 N=1177
Sex	n (%)	n (%)
Male	492 (41.7)	507 (43.1)
Female	687 (58.3)	670 (56.9)
Age (Years)		
Median (min to max)	65 (50 to 91)	65 (50 to 97)
Race		
American Indian or Alaska Native	4 (0.3)	4 (0.3)
Asian	148 (12.6)	168 (14.3)
Black or African American	116 (9.8)	115 (9.8)
Multiple	26 (2.2)	30 (2.5)
Native Hawaiian or Other Pacific Islander	17 (1.4)	16 (1.4)
White	867 (73.5)	844 (71.7)
Missing	1 (0.1)	0 (0.0)
Risk Factors[a]		
0	732 (62.1)	768 (65.3)
1	347 (29.4)	328 (27.9)
≥2	100 (8.5)	81 (6.9)

Cohort 2 (18 to 49 Years of Age)

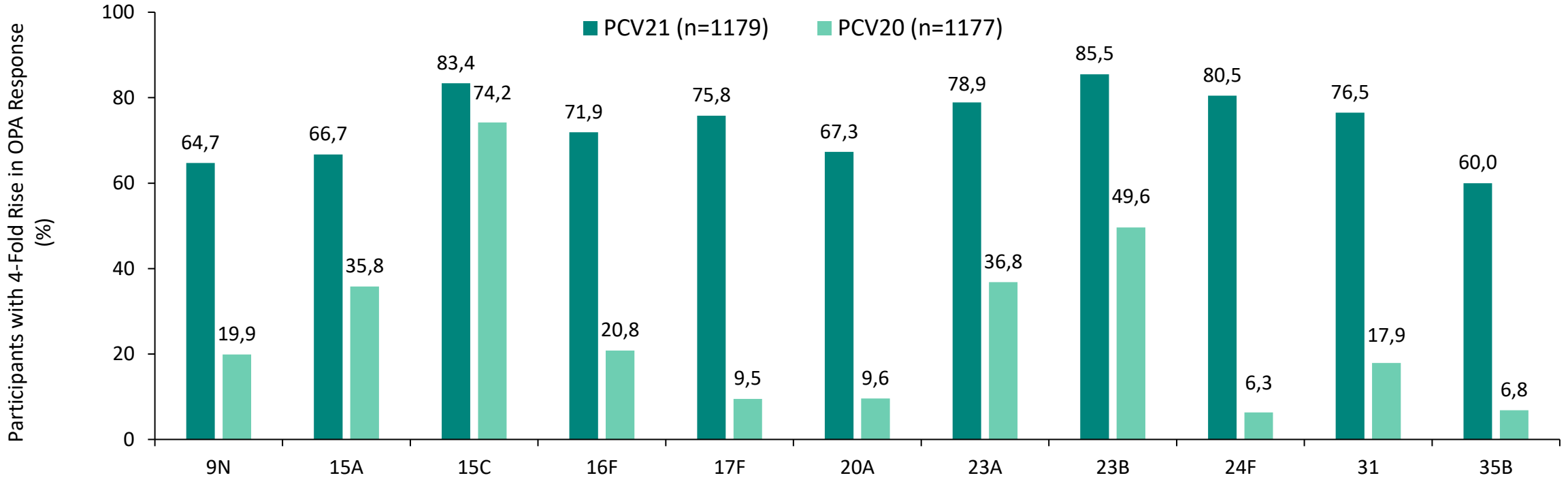
	PCV21 N=200	PCV20 N=100
Sex	n (%)	n (%)
Male	63 (31.5)	36 (36.0)
Female	137 (68.5)	64 (64.0)
Age (Years)		
Median (min to max)	36 (18 to 49)	34 (18 to 49)
Race		
American Indian or Alaska Native	0 (0.0)	1 (1.0)
Asian	38 (19.0)	15 (15.0)
Black or African American	13 (6.5)	14 (14.0)
Multiple	9 (4.5)	6 (6.0)
Native Hawaiian or Other Pacific Islander	1 (0.5)	2 (2.0)
White	139 (69.5)	62 (62.0)
Risk Factors[a]		
0	152 (76.0)	81 (81.0)
1	45 (22.5)	18 (18.0)
≥2	3 (1.5)	1 (1.0)

PCV20, pneumococcal conjugate vaccine, 20-valent; SD, standard deviation; PCV21, pneumococcal conjugate vaccine, 21-valent.
[a]Risk factors include: alcoholism, chronic heart disease, chronic kidney disease, chronic liver disease, chronic lung disease, diabetes, and smoking.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024.
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext

Phase III Study V116-003 (STRIDE-3): Immunogenicity Results

Proportion of Participants with ≥4-fold Rise in OPA Responses; 11 PCV21 Unique Serotypes; Adults ≥50 Years



	9N	15A	15C	16F	17F	20A	23A	23B	24F	31	35B
Difference (%)[a]	44.7 (40.7, 48.6)	30.9 (25.8, 35.8)	9.2 (5.6, 12.9)	51.1 (47.1, 54.9)	66.3 (62.8, 69.6)	57.7 (54.2, 61.1)	42.2 (37.6, 46.6)	35.9 (32.1, 39.6)	74.2 (71.1, 77.1)	58.6 (54.8, 62.1)	53.2 (49.6, 56.6)

PCV21 met superiority criteria[b] for 10 of the 11 PCV21 unique serotypes for the proportion of patients with a 4-fold rise in OPA responses at 30 days postvaccination

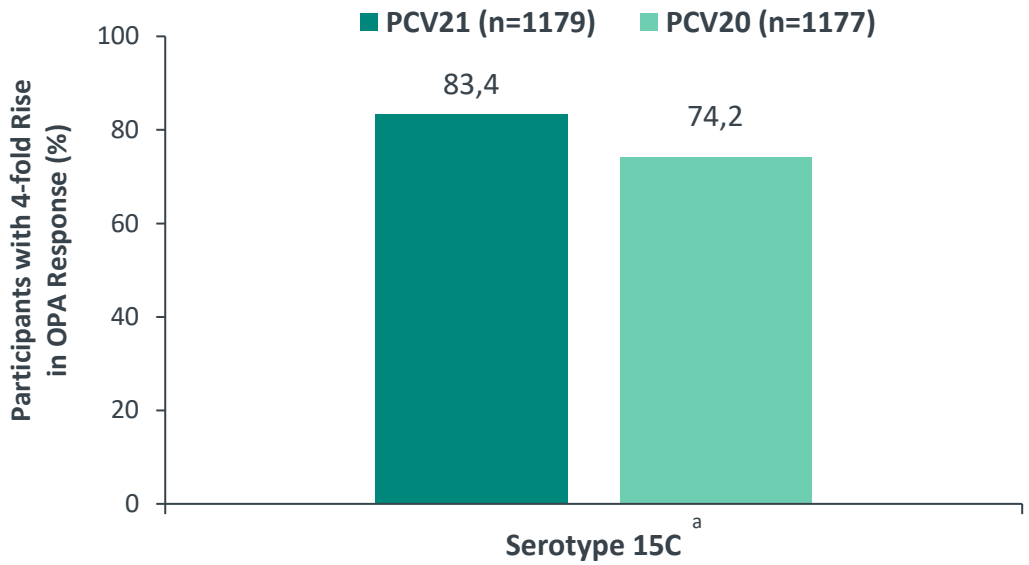
[a]Reported as the percentage point difference of V116-PCV20 (95% CI). [b]Lower bound of 95% CI of the percentage point difference of V116-PCV20 >10 percentage points.

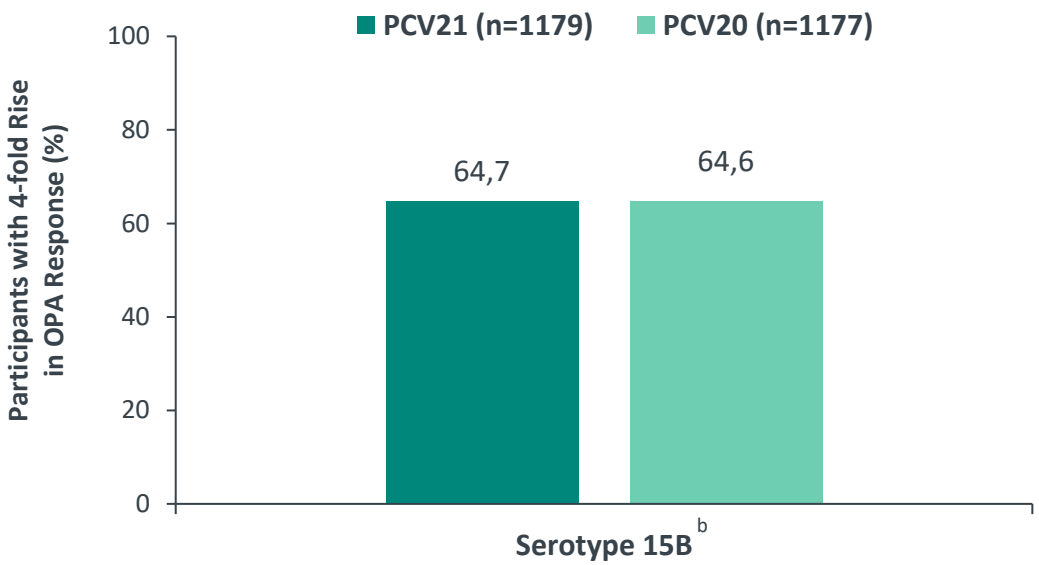
CI, confidence interval; OPA, opsonophagocytic activity; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.

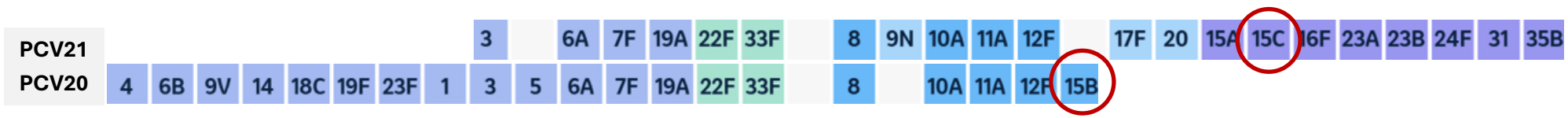
Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.

Phase III Study V116-003 (STRIDE-3): Immunogenicity Results

Proportion of Participants with ≥4-fold Rise in OPA Responses
Serotypes 15C (included in PCV21) and 15B (cross-reactive to 15C); Adults ≥50 Years







For serotype 15C, 83.4% of participants in the PCV21 group achieved a ≥4-fold rise in OPA titers

For serotype 15B, 64.7% of participants in the PCV21 group achieved a ≥4-fold rise in OPA titers

[a]Serotype 15C is included in V116 and immune responses to serotype 15B are cross-reactive. [b]Serotype 15B is included in PCV20 and immune responses to serotype 15C are cross-reactive.
CI, confidence interval; OPA, opsonophagocytic activity; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.
Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial.
Lancet Infect Dis 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.

Real-World Effectiveness of PCV13 Against Vaccine-Type CAP in Adults Aged ≥65 Years: Louisville Trial (2/2)

73%

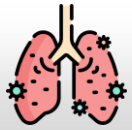
Vaccine effectiveness against hospitalized vaccine type-CAP

[95% CI, 12.8%–91.5%]

70%

Vaccine effectiveness against nonbacteremic vaccine-type CAP

[95% CI, 4.1%–90.7%]



PCV 13 reduces the risk of hospitalized VT-CAP by 73%.

CAP: Community-acquired pneumonia; CI: Confidence interval; PCV13: 13-valent pneumococcal conjugate vaccine.

McLaughlin JM, *et al. Clin Infect Dis*. 2018;67(10):1498–1506.

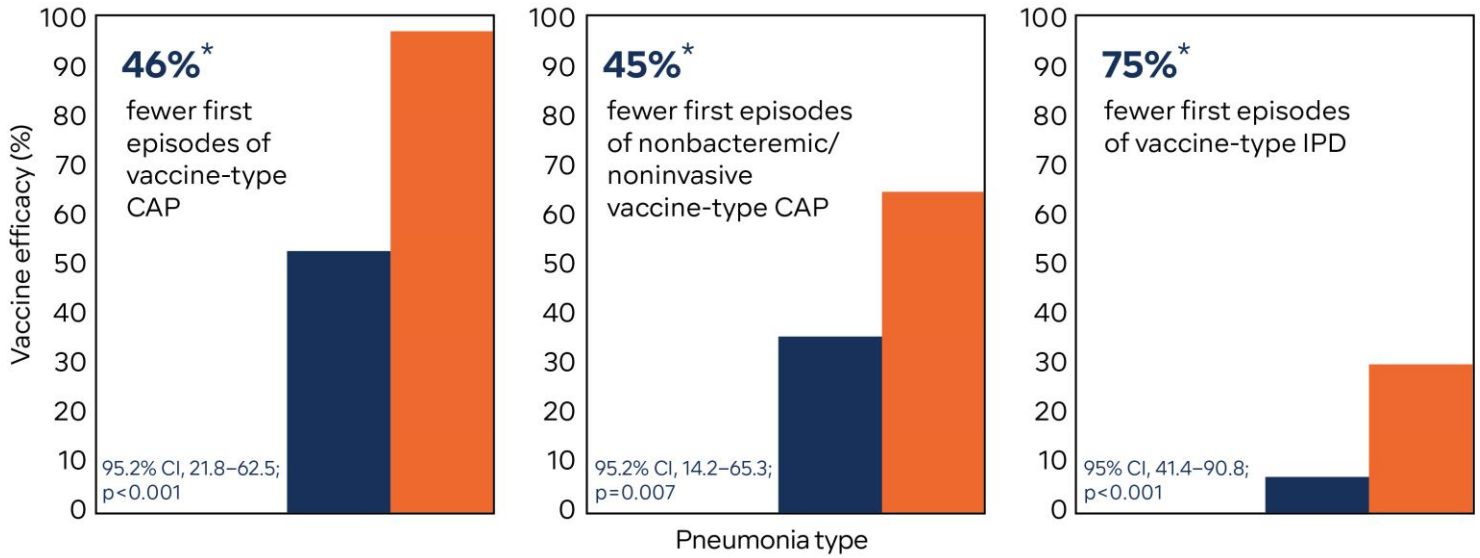
Images for representation purpose only

PCV13 Was Effective in Preventing Vaccine-type CAP in Adults Aged ≥65 Years: The CAPITA Trial

PCV-13 prevented:

- First episodes of vaccine-type strains of pneumococcal CAP
- Nonbacteremic and noninvasive pneumococcal CAP
- Invasive pneumococcal disease

Efficacy of PCV-13 in the CAPITA trial



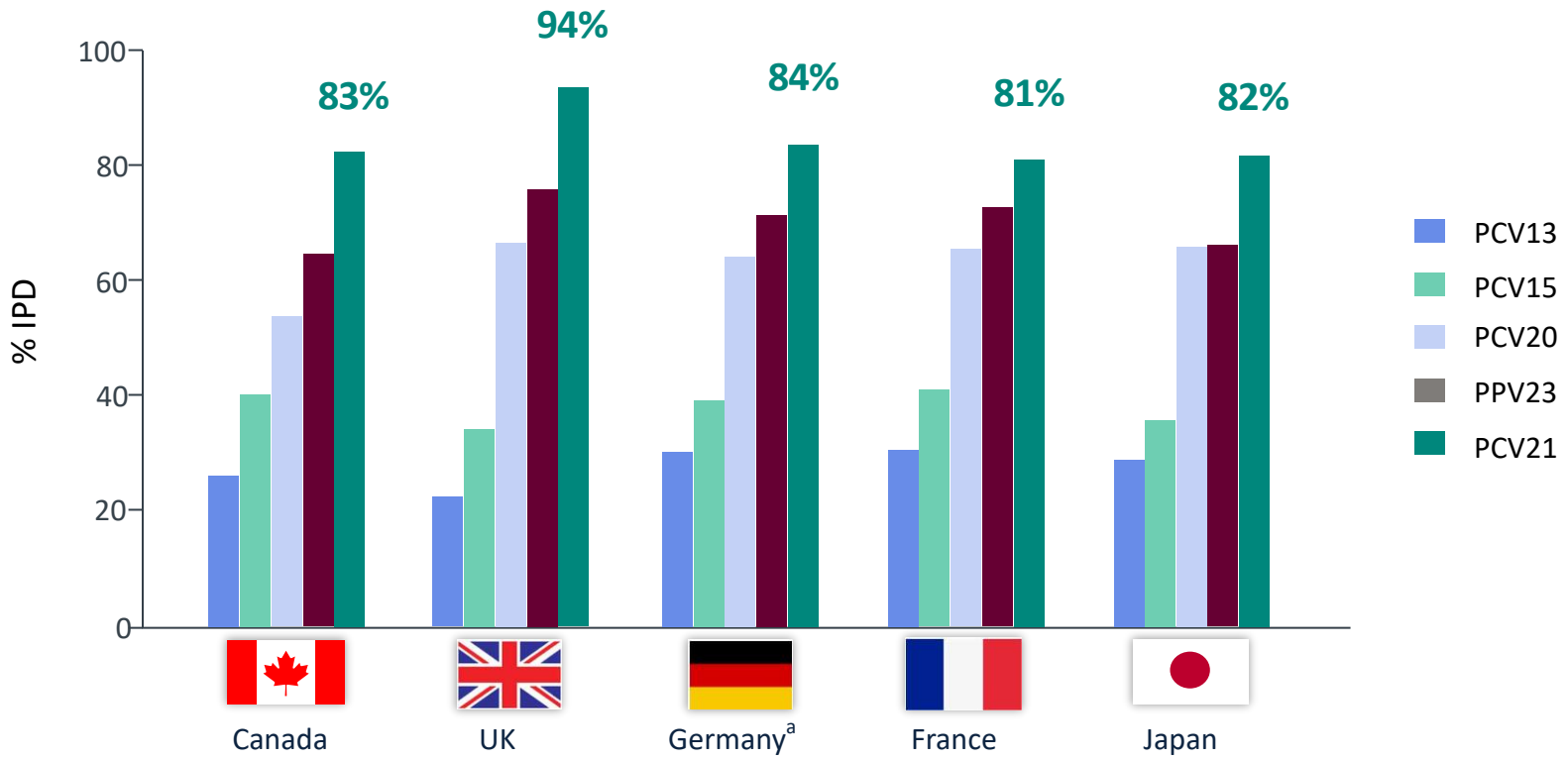
*per protocol analysis
Adapted from Bonten MJ, *et al*. *N Engl J Med.* 2015;372(12):1114–1125.

CAP: Community-acquired pneumonia; ; CAPITA: Community-acquired pneumonia immunization trial in adults; CI: Confidence interval; IPD: Invasive pneumococcal disease; PCV-13: 13 valent pneumococcal vaccine.

Bonten MJ, *et al*. *N Engl J Med.* 2015;372(12):1114–1125.

Percent of IPD Cases Covered by the Serotype Composition of Pneumococcal Vaccines

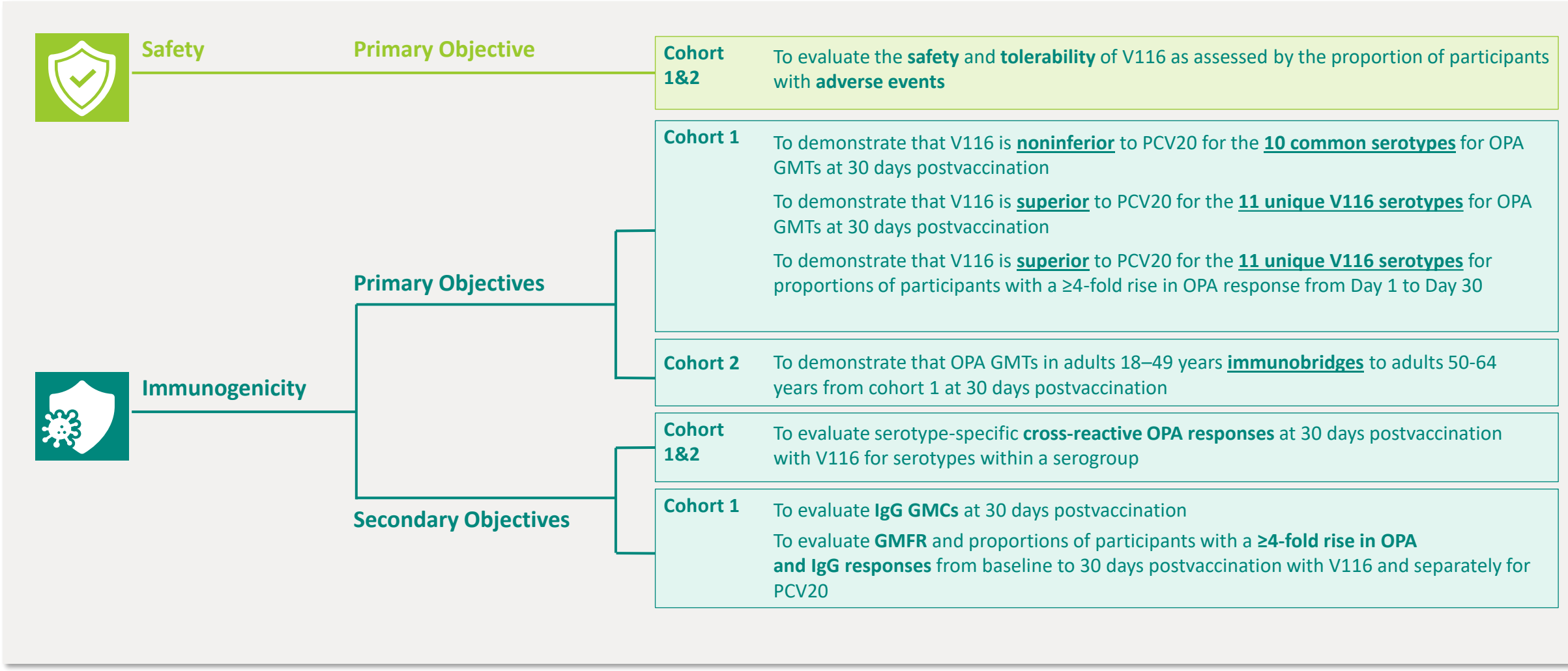
Serotypes in PCV21 Are Responsible for 81–94% of IPD in Adults Aged ≥65 years



[a]This study from Germany includes patients aged ≥60 years.

PCV13, pneumococcal conjugate vaccine, 13-valent; PCV20, pneumococcal conjugate vaccine, 20-valent; PPSV23, pneumococcal polysaccharide vaccine, 23-valent; UK, United Kingdom; PCV21, pneumococcal conjugate vaccine, 21-valent.
Omole T, et al. Presented at the BSI Congress, 2022.

Phase III Study V116-003 (STRIDE-3): Study Objectives and Endpoints



IgG, immunoglobulin G; GMC, geometric mean concentration; GMFR, geometric mean fold rise; GMT, geometric mean titer; OPA, opsonophagocytic activity; PCV20, pneumococcal conjugate vaccine, 20-valent; PCV21, pneumococcal conjugate vaccine, 21-valent.

Platt H, et al. on behalf of the STRIDE-3 Study Group. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *Lancet Infect Dis* 2024 Published: July 01, 2024. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00344-X/fulltext.