Vaccination strategies for pneumococcal disease: Update and perspectives on clinical need and impact

touch™ INFECTIOUS DISEASES

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by USF Health and touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by USF Health and touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in USF Health and touchIME activities*
- *USF Health and touchIME accept no responsibility for errors or omissions*

Identifying the need for next-generation vaccines: Pneumococcal disease in at-risk groups

Prof. Antoni Torres

University of Barcelona,
Barcelona, Spain

touch™ INFECTIOUS DISEASES

Overview of pneumococcal disease

***Streptococcus pneumoniae*[1]**

Gram-positive bacterium[1]

>90 distinct immunological serotypes[1]

A main cause of CAP[2–5]

Europe incidence:[6*] 45–2,940/100,000

Invasive pneumococcal disease

Prevalent symptoms[7]

- Otitis media
- Sinus infection
- Pneumonia
- Conjunctivitis

Hallmark clinical features[8]

- Bacteraemia (without focus in children <5 years)
- Meningitis
- Pleural infection

Epidemiology in EU/EEA, 2018[9]

Cases per 100,000 population:

- Overall: **6.4 cases**
- Infants aged <1 year: **14.4 cases**
- Adults aged ≥65 years: **18.7 cases**

*Findings from systematic literature review covering 2011 to 2021.

CAP, community-acquired pneumonia.

1. European Centre for Disease Prevention and Control. Factsheet about pneumococcal disease. 2023. Available at: www.ecdc.europa.eu/en/pneumococcal-disease/facts; 2. Rider AC, Frazee BW. *Emerg Med Clin North Am*. 2018;36:665–83; 3. Torres A, et al. *Eur J Clin Microbiol Infect Dis*. 2014;33:1065–79; 4. Niederman MS, Torres A. *Eur Respir Rev*. 2022;31:220123; 5. Martin-Loeches I, et al. *Intensive Care Med*. 2023;49:615–32; 6. Tsoumani E, et al. *Expert Rev Vaccines*. 2023;22:876–84; 7. European Centre for Disease Prevention and Control. Invasive pneumococcal disease. Available at: www.ecdc.europa.eu/en/invasive-pneumococcal-disease; 8. Scelfo C, et al. *Vaccines*. 2021;9:420; 9. European Centre for Disease Prevention and Control. September 2020. Available at: www.ecdc.europa.eu/en/pneumococcal-disease/surveillance-and-disease-data. All links accessed 16 September 2024.

touch™ INFECTIOUS DISEASES

Populations who may require vaccination

Children <5 years

All in this age group[1]

Children 6–18 years

Risk condition or immunocompromised[2]*

- CSF leak
- Chronic liver disease
- Cochlear implant
- Diabetes
- Asplenia/splenic dysfunction
- CHD
- CKD
- Chronic lung disease
- Maintenance dialysis or nephrotic syndrome

Adults 19–64 years

Risk condition or immunocompromised[2]*

- Immunodeficiency
- Immunosuppressive or radiation therapy
- HIV
- SCD/haemoglobinopathy
- Alcoholism/smoking/drug use
- Homelessness
- CHD (excl. hypertension)
- Chronic lung disease
- Chronic renal failure/ nephrotic syndrome

Adults ≥65 years

All in this age group[1]

*Please refer to guidelines for further information.

CHD, chronic heart disease; CKD, chronic kidney disease CSF, cerebrospinal fluid; HIV, human immunodeficiency virus; SCD, sickle cell disease.

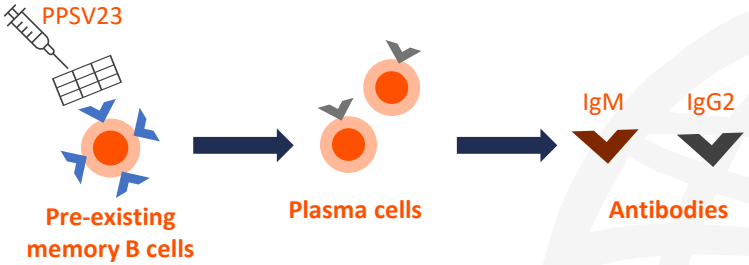
1. Centers for Disease Control and Prevention. Pneumococcal Vaccine Recommendations. 2024. Available at: www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html (accessed 16 September 2024); 2. Centers for Disease Control and Prevention. Summary of Risk-Based Pneumococcal Vaccination Recommendations. 2024. Available at: www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/risk-indications.html (accessed 16 September 2024).

touch™ INFECTIOUS DISEASES

Vaccine types and their indications

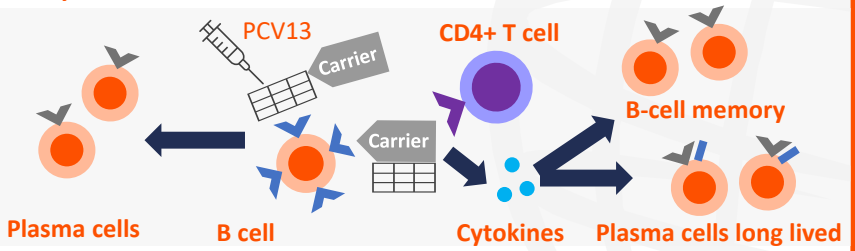
Pneumococcal polysaccharide vaccine (PPSV) 23

- Contains 23 pneumococcal polysaccharides aimed to protect against most common IPD-causing serotypes in the 1980s[1,2]
- Recommended in adults ≥65 years and anyone ≥2 years with risk conditions[3]



Pneumococcal conjugate vaccine (PCV) 7 and 13[1,2]

- Pneumococcal polysaccharide antigens covalently linked to immunogenic carrier protein[1]
- PCV7 increased 19A infections and PCV13 increased 35B infections[2]
- PCV13 may be used in certain paediatric groups and is no longer routinely recommended in adults[4,5]



Vaccine[1,2]	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	2	8	9N	10A	11A	12F	15B	17F	20	22F	33F
PCV7	■	■	■	■	■	■	■																	
PCV13	■	■	■	■	■	■	■	■	■	■	■	■	■											
PPSV23	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	■	■	■	■	■	■	■

Figure adapted from Scelfo C, et al. 2021.[1]

Ig, immunoglobulin; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.

1. Scelfo C, et al. *Vaccines*. 2021;9:420; 2. Daniels CC, et al. *J Pediatr Pharmacol Ther*. 2016;21:27-35; 3. Centers for Disease Control and Prevention. Pneumococcal Polysaccharide Vaccine (PPSV23): What You Need to Know. 2019. Available at: www.cdc.gov/vaccines/hcp/vis/vis-statements/ppv.html (accessed September 16, 2024); 4. Farrar JL, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:1072; 5. Kobayashi M, et al. *MMWR Morb Mortal Wkly Rep*. 2024;73:793–8.

touch™ INFECTIOUS DISEASES

Safety and efficacy of third-generation pneumococcal vaccines

Prof. Antoni Torres

University of Barcelona,
Barcelona, Spain

touch™ INFECTIOUS DISEASES

Evolving Burden of PD and IPD in adults

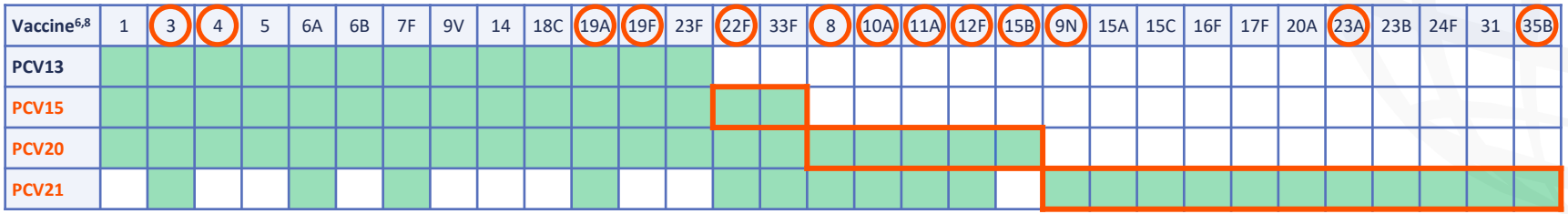
European systematic review (2010–2022)[1]
- Serotypes **8, 12F** and **22F** represent a significant proportion of PD and IPD cases
- Serotypes **10A, 11A, 15B** and **22F** represent serious/fatal cases
- Serotypes **8, 10A, 11A, 15B** and **22F** affecting adults ≥65 years, immunocompromised individuals and those with comorbidities

UK cohort study (2018–2020)[2]
- Serotypes **3** and **8** prevalent in CAP cases
- **PCV20-non13-serotype PD** more likely in younger people with fewer risk factors

Italian cohort study (2017–2020)[3]
- Serotypes **3, 8, 11A** and **22F** most common in adults ≥65 years hospitalized for CAP

Spanish studies[4,5]
- **CAPA study, 2011–2018:** Serotypes **3** and **8** prevalent in CAP cases
- **2019–2023:** Serotypes **3** (children and adults) and **4** (young adults) emergent in IPD cases

US PNEUMO study (2018–2022)[6,7]
- Serotypes **3, 22F, 19A, 35B, 9N, 19F, 23A** and **11A** most common
- **>1/3** of detected serotypes **not covered by PCV15 and PCV20**
- **Surveillance data** shows re-emergence of serotype **4** IPD



CAP, community-acquired pneumonia; IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine; PD, pneumococcal disease.

1. Teixeira R, et al. *Microorganisms*. 2023;11:1376; 2. Lansbury L, et al. *Lancet Reg Health Eur*. 2023;37:100812; 3. Orsi A, et al. *Microorganisms*. 2022;11:70; 4. Torres A, et al. *Clin Infect Dis*. 2021;73:1075–85; 5. Pérez-García C, et al. *J Infect*. 2024;89:106204; 6. Self WH, et al. *Clin Infect Dis*. 2024. doi: 10.1093/cid/ciae316; 7. Kobayashi M, et al. *MMWR Morb Mortal Wkly Rep*. 2024;73:793–8; 8. Centers for Disease Control and Prevention. About Pneumococcal Vaccines. 2024. Available at: www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html (accessed 16 September 2024).

touch™ INFECTIOUS DISEASES

Key efficacy data in infants and children

	Healthy infants		Children	
	PCV15	PCV20	PCV15	PCV20
Trial	**Phase III PNEU-PED trial[1]**	**Phase II trial[2]**	**Phase III PNEU-PLAN trial[3]**	**Phase III single-arm trial[4]**
N	1,720	460	606	831
Method	Randomized 1:1 PCV15 vs PCV13	Randomized 1:1 PCV20 vs PCV13	Randomized 1:1 PCV15 vs PCV13 Three age groups: 7–11 months, 12–23 months, 2–17 years	Ages 15 months–<5 years had ≥3 prior PCV13 doses Any PCV status for ≥5–18 years
Dosing	Four-dose regimen	Four-dose regimen	Age-appropriate catch-up schedules recommended by ACIP	One 0.5-mL PCV20 dose IM
Key outcomes	IgG GMC non-inferiority met for: • All PCV13-matched serotypes at PD4 • 12/13 PCV13 serotypes at PD3 (6A missed) • PCV15-unique serotypes 22F and 33F	IgG GMCs for shared serotypes: • Comparable but numerically lower vs PCV13 at PD3 (mostly for serotype 3) and PD4 • Boosted for PCV20-unique serotypes	IgG GCMs 30 days after last dose: • Comparable among age groups vs PCV13-matched serotypes • Higher in PCV15 groups for unique serotypes	• IgG concentrations for 7 PCV20-unique serotypes were superior 1 month after vs before a single dose of PCV20

PCV21 is designed for use in adults[5]

ACIP, Advisory Committee on Immunization Practices; GMC, geometric mean concentration; IgG, immunoglobulin G; IM, intramuscular; PCV, pneumococcal conjugate vaccine; PD3, 1-month post-dose 3; PD4, 1-month post-dose 4.

1. Lupinacci R, et al. *Vaccine*. 2023;41:1142–52; 2. Senders S, et al. *Pediatr Infect Dis J*. 2021;40:944–51; 3. Banniettis N, et al. *Vaccine*. 2022;40:6315–25; 4. Meyer J, et al. *Pediatr Infect Dis J*. 2024;43:574–81; 5. Scott P, et al. *Clin Infect Dis*. 2024. doi: 10.1093/cid/ciae383.

Key efficacy data in adults (phase III)

≥18 years

PCV20[1]

- N=3,009 adults ≥60 years randomized 1:1 to PCV20 vs PCV13/PPSV23*
- Adults 50–59 years (N=445) and 18–49 years (N=448) randomized 1:1 PCV20 vs PCV13
- **OPA GMT non-inferiority criteria met for:**
  - PCV13-matched serotypes in adults ≥60 years 1 month PD (slightly lower with PCV20)
  - 6 of 7 extra serotypes in PCV20 vs PPSV23 (8 missed)
  - Adults 50–59 and 18–49 years vs ≥60 years

≥50 years

PCV21 STRIDE-6[2]

- N=717 adults with prior PPSV23 use
- Randomized 2:1 to PCV21 or PCV15; prior combination of PPSV23 and PCV13/15 or PCV15 received open-label PCV21
- **OPA GMTs and IgG GMCs 1 month PD comparable** between PCV21 and PCV15 or PPSV23 regardless of vaccination history
- Higher response to PCV21-unique serotypes

PCV21 STRIDE-3[3]

- N=2,663 adults 18–49 years and ≥50 years
- With or without chronic conditions*
- Randomized 1:1 PCV21 vs PCV20
- Efficacy outcomes reported for ≥50 years group
- **OPA GMT non-inferiority criteria met** for 10 shared serotypes
- **Superiority criteria met** for 10 of 11 PCV21-unique serotypes (15C missed)

PCV15 PNEU-AGE trial[4]

- N=1,202 adults ≥50 years*
- Randomized 1:1 PCV15 vs PCV13
- **OPA GMT non-inferiority criteria met** for all PCV13-matched serotypes 1 month PD
- **Superiority criteria met** for PCV15-unique serotypes with ≥4-fold OPA GMT rise 1 month PD

≥65 years

PCV15 PNEU-AGE sub-analysis[5]

- N=245 Japanese adults had responses **consistent** with overall population but **stronger response for** serotype 3, 22F and 33F with PCV15 vs PCV13

PCV20 open-label[6]

- N=875 pneumococcal vaccine-experienced adults
- Robust immune responses were observed with PCV20 among all serotypes regardless of prior vaccination schedule vs PCV13/PPSV23

Studies shown used single-dose regimens. *Participants had not previously received a pneumococcal vaccine.
GMC, geometric mean concentration; GMT, geometric mean titre; IgG, immunoglobulin G; OPA, opsonophagocytic activity; PCV, pneumococcal conjugate vaccine; PD, post-dose; PPSV, pneumococcal polysaccharide vaccine.

1. Essink B, et al. *Clin Infect Dis*. 2022;75:390–8; 2. Scott P, et al. *Clin Infect Dis*. 2024. doi: 10.1093/cid/ciae383; 3. Platt HL, et al. *Lancet Infect Dis*. 2024;24:1141–50; 4. Platt HL, et al. *Vaccine*. 2022;40:162–72; 5. Kishino H, et al. *Jpn J Infect Dis*. 2022;75:575–82; 6. Cannon K, et al. *Vaccine*. 2021;39:7494–502.

touch™ INFECTIOUS DISEASES

Key safety findings from clinical trials

PCV15

AEs mostly mild-to-moderate with short duration

Infants and children

- **Infants and children 7 months to 17 years:** PCV15 and PCV13 had comparable AE rates[1,2]
- **12–33 months:** Numerically higher AE rates with PCV15 vs PCV13[2]

Adults

- **Most adults ≥50 years** had ≥1 AE with PCV15 and PCV13[3]
- Higher injection-site pain with PCV15 vs PCV13; 54.0% vs 42.3%, p<0.001)[3]
- **Japanese adults ≥65 years:** greater injection-site pain and myalgia with PCV15 vs PCV13[4]

PCV20

AEs mostly mild-to-moderate

Infants and children

- **Infants:** Comparable AE rates between PCV20 and PCV13[5]
- **Children:** Injection-site pain most common local AE[6]
- Most common systemic AE was fatigue in **≥2–<5 years** and muscle pain in **≥5–<18 years**[6]

Adults

- Comparable AE rates/severity between PCV20 and PCV13 in **adults ≥18 years** and between age groups (**≥60 years, 50–59 years, 18–49 years**)[7]
- **Adults ≥65 years:** Comparable AE rates for PCV20 vs PCV13 or PPSV23[8]

PCV21

AEs mostly mild-to-moderate

Adults

- **Vaccine-naive adults ≥50 years:** Comparable AE rates between PCV21 (58.2%) or PCV20 (66.2%), injection-site pain slightly lower for PCV21[9]
- **18–49 years:** Overall, more patients reported AEs vs adults ≥50 years across groups[9]
- **Vaccine-experienced adults ≥50 years:** AEs generally comparable between PCV21 vs PCV15 or PPSV23[10]
  - Rate of injection-site swelling was higher after PPSV23 (16.5%) vs PCV21 (4.6%) [10]

AE, adverse event; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.

1. Lupinacci R, et al. *Vaccine*. 2023;41:1142–52; 2. Banniettis N, et al. *Vaccine*. 2022;40:6315–25; 3. Platt HL, et al. *Vaccine*. 2022;40:162–72;
4. Kishino H, et al. *Jpn J Infect Dis*. 2022;75:575–82; 5. Senders S, et al. *Pediatr Infect Dis J*. 2021;40:944–51; 6. Meyer J, et al. *Pediatr Infect Dis J*. 2024;43:574–81;
7. Essink B, et al. *Clin Infect Dis*. 2022;75:390–8; 8. Cannon K, et al. *Vaccine*. 2021;39:7494–502; 9. Platt HL, et al. *Lancet Infect Dis*. 2024;24:1141–50;
10. Scott P, et al. *Clin Infect Dis*. 2024. doi: 10.1093/cid/ciae383.

touch™ INFECTIOUS DISEASES

Understanding guidelines updates in pneumococcal disease

Prof. Antoni Torres

University of Barcelona,
Barcelona, Spain

touch™ INFECTIOUS DISEASES

Updated ACIP guidance for children, 2023*

2–23 months old

All PCV-naïve children to receive PCV15 or PCV20

24–71 months old

To receive PCV15 or PCV20 if PCV vaccination incomplete

- **24–59 months, healthy:** one dose 8 weeks after last PCV dose
- **24–71 months, risk condition, <3 PCV doses:** two doses 8 weeks apart
- **24–71 months, risk condition, 3 PCV doses before 12 months:** one dose 8 weeks after last PCV dose

2–18 years old

Risk condition

- **Completed PCV series before 6 years of age**
- **If complete with ≥1 PCV20 dose:** no action required
- **If complete with PCV13or PCV15 dose:** one dose PCV20 or ≥1 dose PPSV23
- **If PPSV23 used and immunocompromised:** one dose PCV20 or PPSV23 ≥5 years after first PPSV23 dose

6–18 years old

Risk condition

- **Not received any PCV:** Single dose of PCV15 (+ PPSV23 8 weeks after if never given) or PCV20 ≥8 weeks after last dose

- PCV13 can be used if other PCVs unavailable
- Healthy children aged 24–59 months with complete PCV13 schedule do not need supplemental PCV15 or PCV20
- Children aged <19 years having HSCT are eligible for 4 doses of PCV20

*Refer to practice guidelines for specific conditions that are included in each section and full recommendations for all populations requiring vaccination.
ACIP, Advisory Committee on Immunization Practices; HSCT, haematopoietic stem cell transplant; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.

Farrar JL, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:1072.

touch™ INFECTIOUS DISEASES

Updated ACIP guidance for adults, 2024*

19–64 years

	Immunocompromised, CSF leak or cochlear implant	Chronic medical condition
No prior PCV or PCV7	• Single dose of PCV21, PCV20, or PCV15 + PPSV23 ≥8 weeks later	• Single dose of PCV21, PCV20, or PCV15 + PPSV23 ≥1 year later
Prior PPSV23 only	• Single dose of PCV21, PCV20, or PCV15 ≥1 year later	• Single dose of PCV21, PCV20, or PCV15 ≥1 year later
Prior PCV13 only	• Single dose of PCV21 or PCV20 ≥1 year later *OR* • PPSV23 ≥8 weeks later + PCV21, PCV20 or PPSV23 ≥5 years later	• Single dose of PCV21, PCV20, or PPSV23 ≥1 year later
Prior PCV13 + one dose PPSV23	• Single dose of PCV21 or PCV20 ≥5 years after last PCV dose *OR* • ≥1 dose PPSV23 ≥8 weeks after PCV13 dose and ≥5 years after first PPSV23 dose • Review when patient turns 65 years	• Review when patient turns 65 years of age
Prior PCV13 + two doses PPSV23	• Review when patient turns 65 years, *OR* • Single dose of PCV21 or PCV20 ≥5 years after last PCV dose	

*Refer to practice guidelines for specific conditions that are included in each section and full recommendations for all populations requiring vaccination.
ACIP, Advisory Committee on Immunization Practices; CSF, cerebrospinal fluid; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.
Kobayashi M, et al. *MMWR Morb Mortal Wkly Rep*. 2024;73:793–8.

touch™ INFECTIOUS DISEASES

Updated ACIP guidance for adults, 2024*

≥65 years[1]

No prior PCV or PCV7	• Single dose of PCV21, PCV20, or PCV15 + PPSV23 ≥1 year later or ≥8 weeks later if immunocompromised, with cochlear implant or CSF leak
Prior PPSV23 only	• Single dose of PCV21, PCV20, or PCV15 ≥1 year later
Prior PCV13 only	• Single dose of PCV21, PCV20, or PPSV23 ≥1 year later or ≥8 weeks later if immunocompromised, with cochlear implant or CSF leak
Prior PCV13 at any age + PPSV23 at age <65 years	• Single dose of PCV21 or PCV20 ≥5 years after last PCV dose, *OR* • PPSV23 ≥1 year later (or ≥8 weeks later if immunocompromised, with cochlear implant or CSF leak) and ≥5 years after last PPSV23 dose
Prior PCV13 at any age + PPSV23 at age ≥65 years	• Shared clinical decision on whether to vaccinate further • If single dose of PCV21 or PCV20 used, give ≥5 years after last PCV dose

*Refer to practice guidelines for specific conditions that are included in each section and full recommendations for all populations requiring vaccination.
ACIP, Advisory Committee on Immunization Practices; CSF, cerebrospinal fluid; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.
Kobayashi M, et al. *MMWR Morb Mortal Wkly Rep*. 2024;73:793–8.

Co-administration with other vaccines

Children

Can co-administer:

- PCV15, PCV20 or PPSV23 with most routine childhood vaccines[1]
- PCV15 or PCV20 with flu vaccine (increased risk for febrile seizure with inactivated vaccine)[1]
- No RCT data on PPSV23 co-administration

Adults

Can co-administer:

- PCV15, PCV20, PCV21 or PPSV23 with other vaccines (based on contraindications) including flu[1,2]
- Inject at different sites[1]

Flu elevates risk for PD; important to provide both vaccines where possible[1]

Special considerations

Cannot co-administer:

- PCV13 and MCV4-D in anatomic/functional asplenia and/or HIV owing to reduced immunogenicity (administer PCV13 first and MCV4-D 4 weeks later)[3]
- When both PCV13 and PPSV23 are recommended, administer separately[3]

ACIP, Advisory Committee on Immunization Practices; MCV4-D, meningococcal conjugate vaccine; PCV, pneumococcal conjugate vaccine; PD, pneumococcal disease; PPSV, pneumococcal polysaccharide vaccine; RCT, randomized controlled trial. 1. Centers for Disease Control and Prevention. Administering Pneumococcal Vaccines. 2023. Available at: www.cdc.gov/vaccines/vpd/pneumo/hcp/administering-vaccine.html (accessed 16 September 2024); 2. Kobayashi M, et al. *MMWR Morb Mortal Wkly Rep.* 2024;73:793–8; 3. Kroger A, et al. ACIP General Best Practices for Immunization. 2024. Available at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html (accessed 16 September 2024).

touch™ INFECTIOUS DISEASES