



Proposed Updates to Clinical Guidance on Pneumococcal Vaccine Use among Adults

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Pneumococcal Vaccines

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Current Recommendations

- **Adults aged ≥ 65 years***. Adults aged ≥ 65 years* who have not previously received **PCV** or whose previous vaccination history is unknown **should** receive 1 dose of PCV (either PCV20 or PCV15). When PCV15 is used, it should be followed by a dose of PPSV23.
- **Adults with previous PPSV23 only**. Adults who have only received PPSV23 **may** receive a PCV (either PCV20 or PCV15) ≥ 1 year after their last PPSV23 dose. When PCV15 is used in those with history of PPSV23 receipt, it need not be followed by another dose of PPSV23.

*Same recommendations for adults aged 19–64 years with certain underlying medical conditions or other risk factors.
Kobayashi et al. MMWR 2022. <https://www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm>

Questions received

- Does “who have not previously received **PCV**” include adults who have previously received **PCV7**?
- Wouldn't adults who received **PPSV23 only** be part of adults “**who have not previously received PCV or whose vaccination history is unknown**”?
- If an adult inadvertently received PPSV23 first instead of PCV15, is it a “**may**” or “**should**” for a person to complete the series with **PCV15**?
- If an adult **aged <65 years** with indications receives **both PCV15 and PPSV23**, does the person need **another dose of PPSV23** in the future?
- What should we do if we do not have access to PCV15 or PCV20?

Proposed Clarifications

- **Adults aged ≥ 65 years***. Adults aged ≥ 65 years* who have not previously received **PCV13, PCV15, or PCV20** or whose previous vaccination history is unknown **are recommended to** receive 1 dose of PCV20 or PCV15. When PCV15 is used, it should be followed by a dose of PPSV23 **to complete the recommended vaccine series. If PPSV23 is inadvertently given before PCV15, a dose of PCV15 or PCV20 should be given at least 1 year later**

Footnote: If PCV15 or PCV20 is not available, a dose of PCV13 may be given followed by a dose of PPSV23 as previously recommended.

- **Adults who received PPSV23 only.** Adults who have only received PPSV23 **are recommended to receive a dose of either PCV20 or PCV15** ≥ 1 year after their last PPSV23 dose. When PCV15 is used in those with history of PPSV23 receipt, it need not be followed by another dose of PPSV23.

*Same recommendations for adults aged 19 –64 years with certain underlying medical conditions or other risk factors.

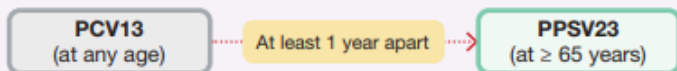
Rationale

- **Recommending new PCVs for adults who previously received PCV7**
 - It has been at least 10 years since PCV7 was available in the U.S.
 - The new PCVs cover ≥ 8 more pneumococcal serotypes
 - The WG is proposing use of PCV20 for adults who previously received PCV13
- **Not recommending additional doses of PPSV23 for adults who receive PCV15 followed by PPSV23**
 - HCPs have been confused by the recommendations of repeat PPSV23 doses
 - Reported coverage of PCV13 and PPSV23 among adults aged 19–64 years with IC has been very low¹.
 - Unknown impact of new PCV use among children
 - New pneumococcal vaccines are in advanced stages of development

Pneumococcal vaccine timing for adults who previously received PCV13 but who have not received all recommended doses of PPSV23

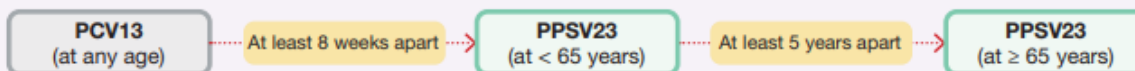
The previous pneumococcal recommendations remain in effect pending further evaluation. Use the following information for guidance on the number of and interval between any remaining recommended doses of PPSV23.

Adults 65 years or older without an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant



CDC recommends 1 dose of PPSV23 at age 65 years or older.** Administer a single dose of PPSV23 at least 1 year after PCV13 was received. Their pneumococcal vaccinations are complete.

Adults 19 years or older with a cerebrospinal fluid leak or cochlear implant

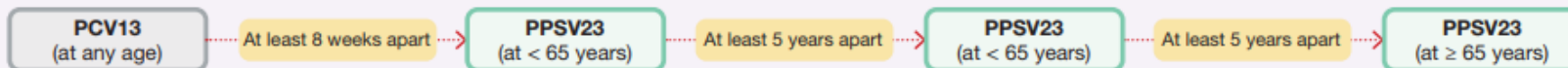


CDC recommends 1 dose of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**

Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

- If the adult is 65 years or older, their pneumococcal vaccinations are complete.
- If the adult was younger than 65 years old when the first dose of PPSV23 was given, then administer a final dose of PPSV23 once they turn 65 years old and at least 5 years have passed since PPSV23 was first given. Their pneumococcal vaccinations are complete.

Adults 19 years or older with an immunocompromising condition



CDC recommends 2 doses of PPSV23 before age 65 years and 1 dose of PPSV23** at age 65 years or older.**

Administer a single dose of PPSV23 at least 8 weeks after PCV13 was received.

- If the patient was younger than 65 years old when the first dose of PPSV23 was given and has not turned 65 years old yet, administer a second dose of PPSV23 at least 5 years after the first dose of PPSV23. This is the last dose of PPSV23 that should be given prior to 65 years of age.
- Once the patient turns 65 years old and at least 5 years have passed since PPSV23 was last given, administer a final dose of PPSV23 to complete their pneumococcal vaccinations.

** For adults who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available. If PCV20 is used, their pneumococcal vaccinations are complete.

Rationale (continued)

- **Recommending PCV15 or PCV20 for adults who inadvertently received PPSV23 first for the PCV15–PPSV23 series**
 - Avoiding use of “should” vs “may”
 - Similar recommendation was in place when adults were recommended to receive PCV13 followed by PPSV23
- **Recommending either PCV15 or PCV20 for adults who have received PPSV23 only**
 - Under the new recommendations, all adults with indications for pneumococcal vaccines are recommended to receive a PCV
 - An interval of “at least 1 year” is consistent with the PPSV23–PCV13 sequence that was previously recommended

Proposed changes to address gaps in current adult pneumococcal vaccine recommendations

Hematopoietic Stem Cell Transplant Recipients

Adults who received hematopoietic stem cell transplant are currently not included as part of the pneumococcal risk conditions

Underlying medical condition or other risk factor	19 through 64 years old	≥ 65 years old
None	Not recommended	Administer 1 dose of PCV20 OR 1 dose of PCV15 followed by 1 dose of PPSV23 at least 1 year later
Alcoholism	Administer 1 dose of PCV20 OR 1 dose of PCV15 followed by 1 dose of PPSV23 at least 1 year later <i>The minimum interval (8 weeks) can be considered in adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak.</i>	Administer 1 dose of PCV20 OR 1 dose of PCV15 followed by 1 dose of PPSV23 at least 1 year later <i>The minimum interval (8 weeks) can be considered in adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak.</i> <i>Reminder: No additional doses are indicated at this age if PCV15 or PCV20 were administered at a younger age.</i>
Chronic heart disease [†]		
Chronic liver disease		
Chronic lung disease [§]		
Cigarette smoking		
Diabetes mellitus		
Cochlear implant		
Cerebrospinal fluid leak		
Chronic renal failure*		
Congenital or acquired asplenia*		
Congenital or acquired immunodeficiency* [¶]		
Generalized malignancy*		
HIV infection*		
Hodgkin disease*		
Iatrogenic immunosuppression* [‡]		
Leukemia*		
Lymphoma*		
Multiple myeloma*		
Nephrotic syndrome*		
Sickle cell disease/other hemoglobinopathies*		
Solid organ transplant*		

Existing Guidance 1. CDC's General Best Practice Guidelines for Immunization

- *“Sequential administration of 3 doses of pneumococcal conjugate vaccine is recommended, beginning 3-6 months after the transplant, followed by a dose of PPSV23”.*
- *“Some sources state a 4-week interval between these doses as reasonable with the dose of PPSV23 being replaced by a dose of PCV13 in the context of graft-versus-host disease. Other sources support 3 doses of PCV13 at 8-week intervals, with a dose of PPSV23 recommended 8 weeks after the last dose of PCV13 and 12 months after the HSCT”.*

Existing Guidance 2. IDSA's Clinical Practice Guideline for Vaccination of the Immunocompromised Host

- *“Three doses of PCV13 should be administered to adults and children starting at 3–6 months after HSCT (strong, low). **At 12 months after HSCT, 1 dose of PPSV23 should be given** provided the patient does not have chronic GVHD (strong, low). For patients with chronic GVHD, a fourth dose of PCV13 can be given at 12 months after HSCT (weak, very low).”*

Proposed updates

- Adults who are hematopoietic stem cell transplant (HSCT) recipients are recommended to receive three doses of PCV20 4 weeks apart starting 3 months after HSCT. This should be followed by a fourth PCV20 dose at least 6 months after the 3rd PCV20 dose, or at least 12 months after HSCT, whichever is later.
- HSCT recipients who have started their pneumococcal vaccine series with PCV13 or PCV15 may complete their 4-dose pneumococcal vaccine series with PCV20.
- If PCV20 is not available, three doses of PCV15 4 weeks apart, followed by a dose of PPSV23 at least 12 months after HSCT may be given. For patients with chronic graft-versus-host disease, a fourth dose of PCV15 can be given in place of PPSV23.

Rationale: Use of PCV20 among HSCT recipients

- HSCT recipients have poor immune response to PPSV23 when given during the first year of transplantation or longer, especially in those with chronic graft versus host disease (GVHD)^{1,2}.
- PCV20 currently has the broadest serotype coverage among available PCVs
- In this high-risk population, a regimen that provides broad pneumococcal serotype coverage early on is warranted

1. Hammarström V, et al. *Support Care Cancer*. 1993.

2. Tomblyn M. et al. *Bone Marrow Transplant*. 2009.

Evidence on use of 4 doses of PCV among HSCT recipients

- No PCV20 studies among HSCT recipients
- Two studies assessed the use of four PCV13 doses^{1,2}:
 - 3 PCV13 doses given 1 month apart followed by a booster dose 6 months after the 3rd PCV dose + a dose of PPSV23
 - Immune responses* against the PCV13 serotypes increased from baseline to after the 3rd PCV13 dose, and from after the 3rd dose to after the 4th dose.
- In one study, local and systemic reactions occurred more frequently after the 4th PCV13 dose, compared with after 1st–3rd dose of PCV13, but most were mild–moderate reactions¹.

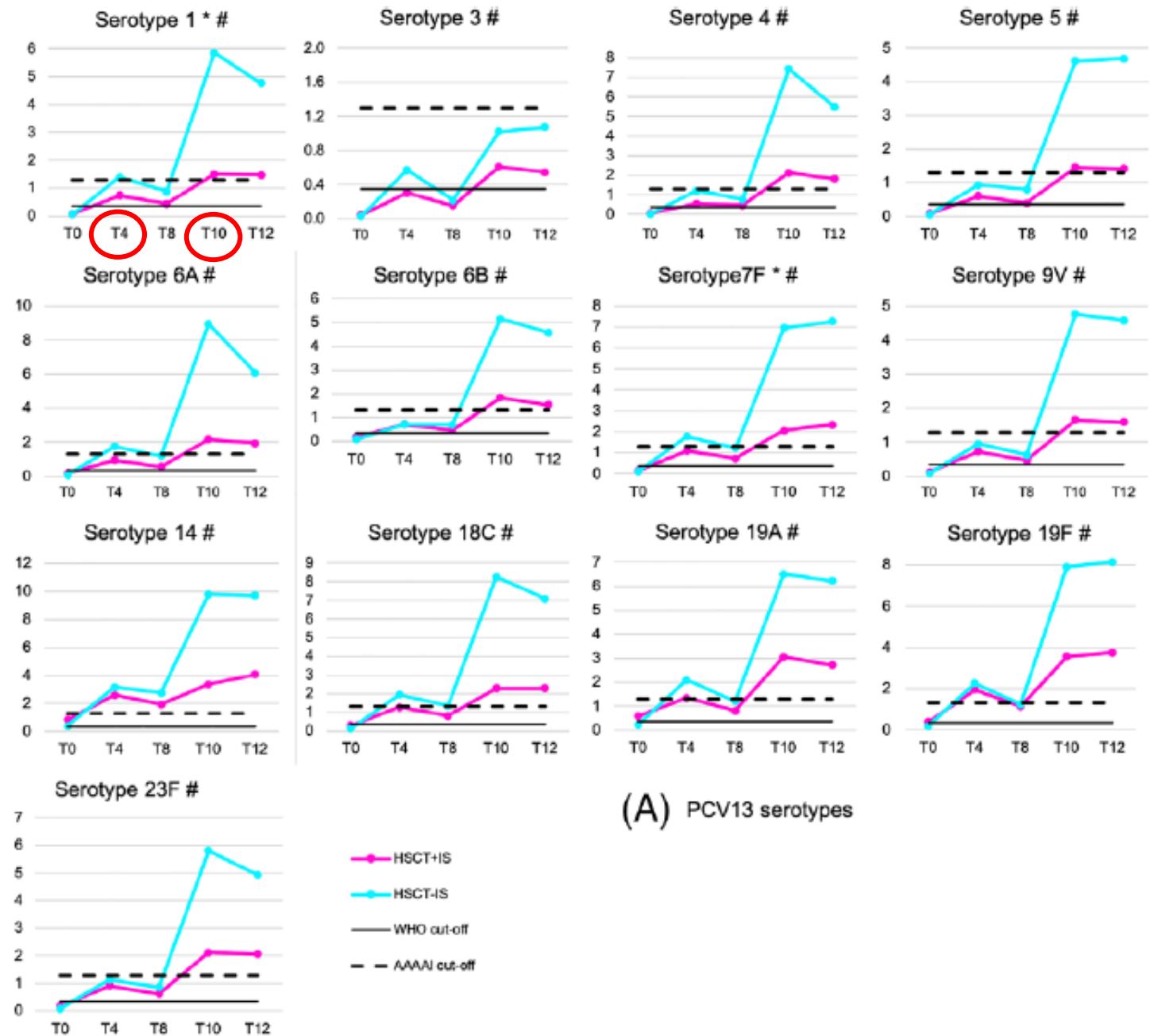
*IgG Geometric Mean Concentrations (GMC), Geometric Mean Fold Rise of GMC, and OPA titers in Cordonnier et al. 2015; serotype-specific IgG levels and proportion of patients with postimmunization IgG concentration above a certain threshold in Garcia Garrido et al. 2022

1. Cordonnier C, et al. *Clin Infect Dis*. 2015
2. Garcia Garrido HM, et al. *Am J Hematol*. 2022

Serotype-specific IgG levels in mcg/ml over time.

T4: 2 months after 3rd PCV13 dose

T10: 2 months after 4th PCV13 dose



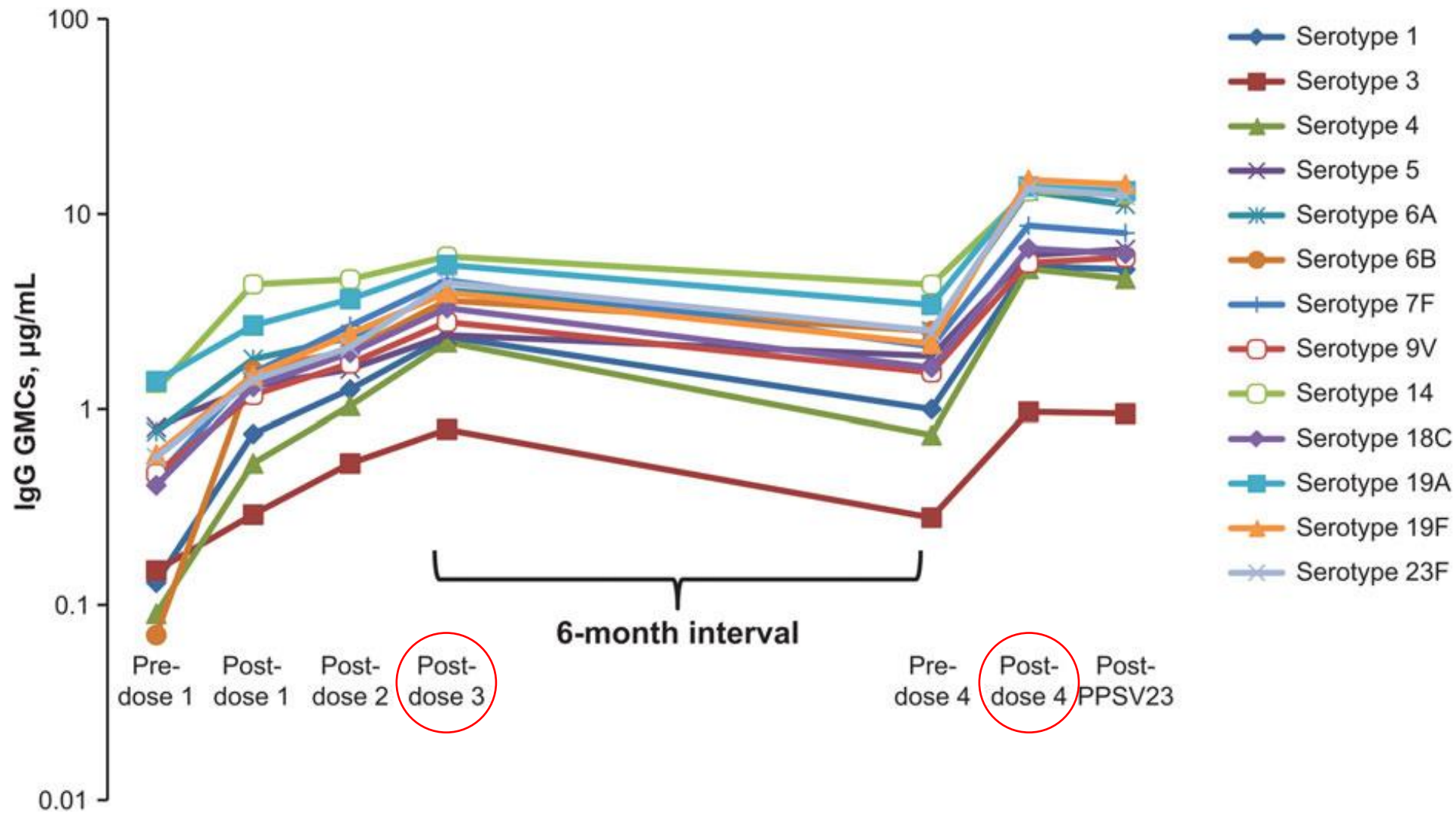
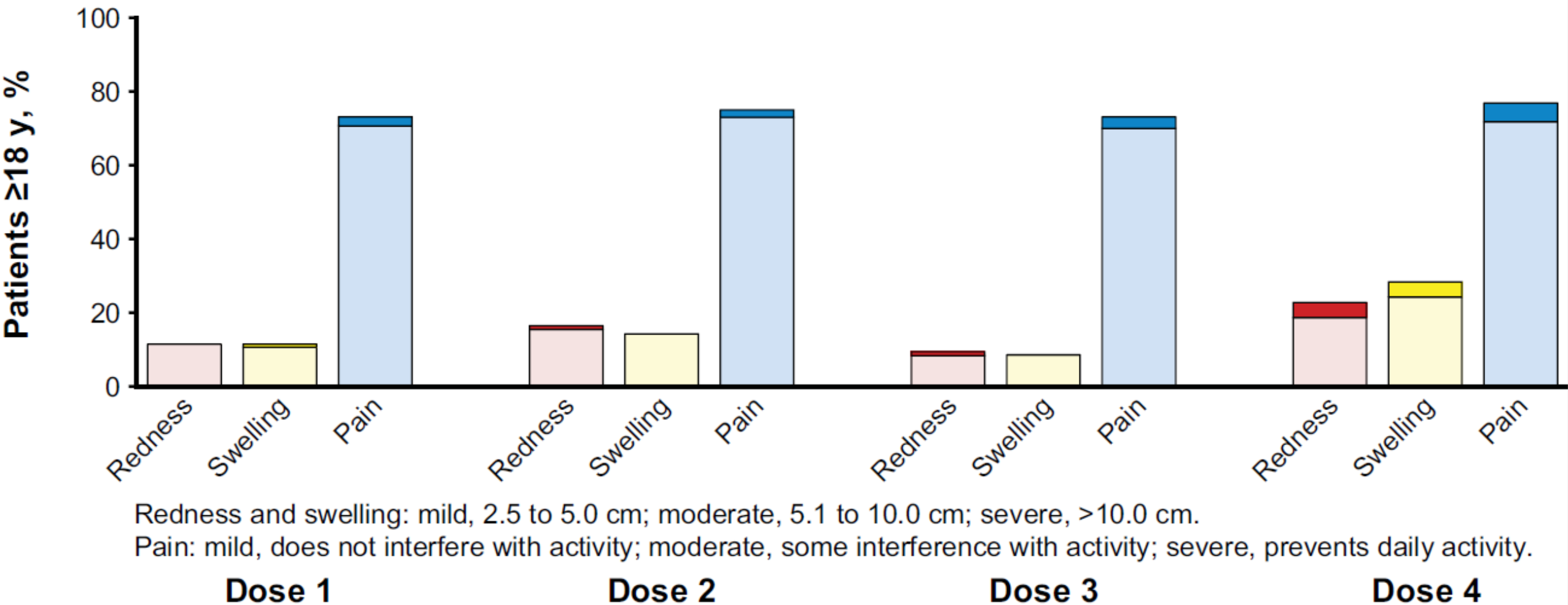


Figure 2. Pneumococcal immunoglobulin G (IgG) geometric mean concentrations (GMCs) in the evaluable immunogenicity population after 3 doses of 13-valent pneumococcal conjugate vaccine (monthly), a booster dose (6 months later), and a dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) (1 month later).

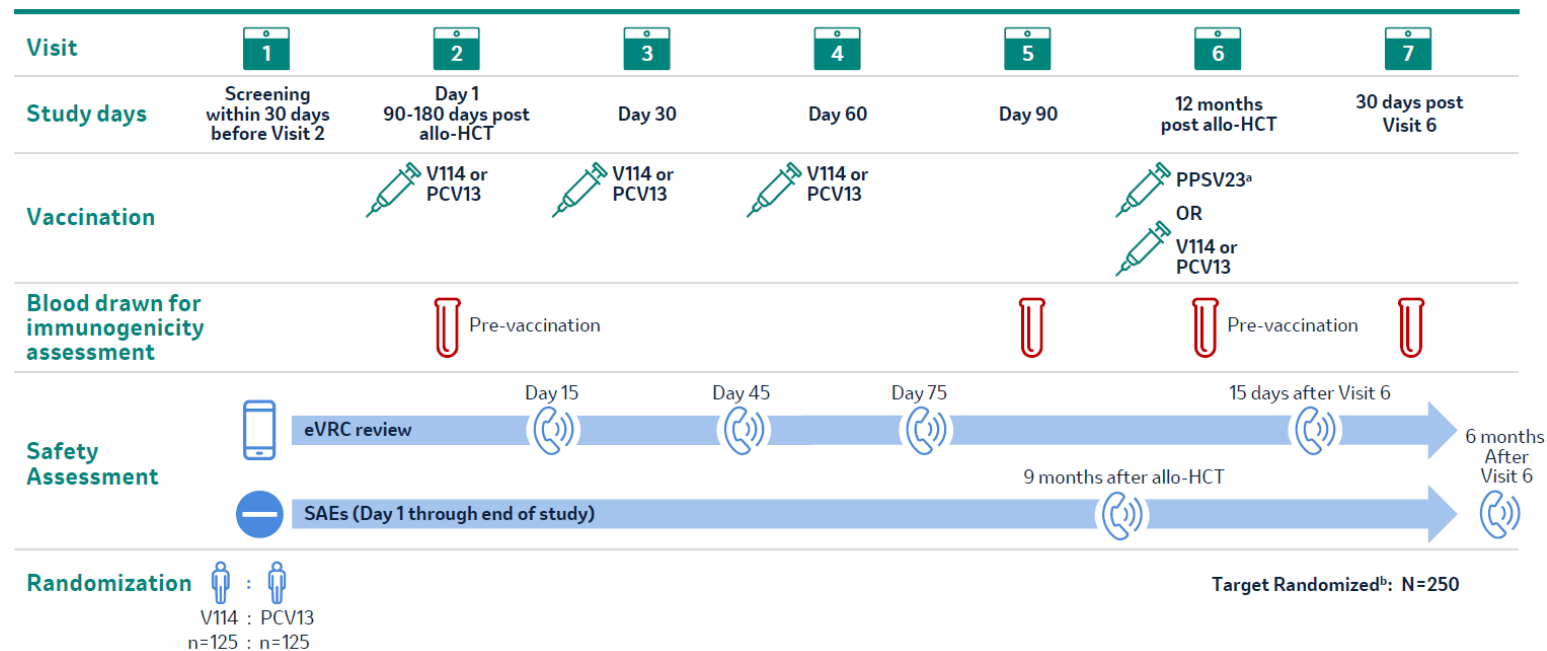


Supplementary Figure 2. Percentage of patients reporting local reactions within 14 days of PCV13.

Evidence on PCV15 use among HSCT recipients

- In a phase 3 randomized controlled trial among HSCT recipients, participants received **three doses of PCV** (either PCV13 or PCV15) followed by a dose of **PPSV23 at 12 months** (or a dose of PCV13 or PCV15 in those who developed GVHD)

V114-022 study design



^aParticipants received PPSV23 if they did not develop GVHD, or a 4th PCV dose (blinded V114 or PCV13) if they developed GVHD.

^bRandomization target determined by the number of ≥18 year old participants.

Evidence on PCV15 use among HSCT recipients

- Between those who received PCV13 or PCV15:
 - Immunogenicity* was generally comparable for the 13 shared PCV13 serotypes
 - PCV15 recipients had higher immunogenicity for 2 additional serotypes not included in PCV13
 - Injection-site adverse events and solicited systemic events were reported more frequently among those who received PCV15, but most were mild to moderate

*IgG CMG and OPA GMT

A Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 in Allogeneic Hematopoietic Stem Cell Transplant Recipients (V114-022/PNEU-STEM) <https://ClinicalTrials.gov/show/NCT03565900>

Thank You!!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

