**Supplementary Table 1.** Additional characteristics and risk of bias assessment of included observational studies on vaccine effectiveness of PCV13 and PPV23 in the same or similar populations.

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| **Reference** | **Outcome measurements/case definitions** | **Assessment of PCV13 and PPV23 sequential vaccination** | **Period of follow up/time since vaccination** | **Vaccine effectiveness (VE) calculation** | **Results****VE % (95%CI)** | **Risk of bias assessment (ROBINS-I)** |
| **Pneumococcal disease outcomes** |
| McLaughlin et al 2018[1] | PCV13-type CAP, defined as patients hospitalized for CAP in whom PCV13 serotypes were identified by any method, including from ssUAD or culture from blood, respiratory tract, orpleural fluid | Not assessed; assessment of PCV13 VE adjusted for PPV23 receipt | PCV13 receipt within the previous 5 years | VE = (1- adjusted odds ratio) x 100%  | VE against PCV13-type CAP:* Unadjusted: 72.8 (12.8−91.5)
* Adjusted: 71.2 (6.1−91.2)

VE against nonbacteremic PCV13-type CAP:* Unadjusted: 70.1 (4.1−90.7)
* Adjusted: 67.6 (–6.2 to 90.1)
 | Moderate |
| Chandler et al 2022[2] | PPV23-type CAP, defined as patients hospitalized for CAP in whom PPV23 serotypes were identified by ssUAD | Not assessed. People who had received PCV13 were excluded.  | PPV23 receipt within the previous 5 years | VE = (1- adjusted odds ratio) x 100%  | VE against PPV23-type CAP:* Overall cohort (≥18y): 14 (-17–39)
* ≥65y subgroup: 2 (-50–38)
 | Moderate |
| Heo et al 2021[3] | * Pneumococcal community acquired pneumonia (P-CAP), defined as pneumococcal infection identified by ≥1 diagnostic methods (sputum/blood culture, BinaxNOW, or ssUAD assay)
* Vaccine-type community acquired pneumonia (VT-CAP), defined as PCV13- or PPV23-serotype pneumococcal infection identified by microbiological culture or ssUAD assay
 | Assessment of PCV13 VE adjusted for PPV23 receipt, and vice-versa.For sequential PCV13/PPV23 VE, two analyses were conducted- one including single-dose pneumococcal vaccination recipients in the unvaccinated group (with adjustment), and the other excluding them from analysis. Results were similar. | Variable for PCV13 (not specified); PPV23 receipt within the previous 5 years  | VE = (1-adjusted odds ratio) x 100%  | VE against VT-CAP (≥65y):* PCV13 alone (against PCV13 serotypes): 41.1 (-103.7–83.0)
* PPV23 alone (against PPV23 serotypes): 6.3 (-73.8–49.5)
* Sequential PCV13/PPV23 (against PCV13 and PPV23 serotypes): 44.6

(-84.0–83.3)VE against VT-CAP (65–74y subgroup):* PCV13 alone (against PCV13 serotypes): 58.1 (-245.5–94.9)
* PPV23 alone (against PPV23 serotypes): 15.7 (-91.4–62.9)
* Sequential PCV13/PPV23 (against PCV13 and PPV23 serotypes): 63.6

(-186.0–95.4)VE against VT-CAP (≥75y subgroup):* PCV13 alone (against PCV13 serotypes): 26.8 (-239.4–84.2)
* PPV23 alone (against PPV23 serotypes): -2.0 (-161.7–60.2)
* Sequential PCV13/PPV23 (against PCV13 and PPV23 serotypes): 24.8

(-233.1–83.0)VE against P-CAP (≥65y):* PCV13 alone: 40.0 (-10.8–67.5)
* PPV23 alone: 11.0 (-26.4–37.3)
* Sequential PCV13/PPV23: 38.5 (-21.0–68.7)

VE against P-CAP (65–74y subgroup):* PCV13 alone: 66.4 (0.8–88.6)
* PPV23 alone: 18.5 (-38.6–52.0)
* Sequential PCV13/PPV23: 80.3 (15.9–95.4)

VE against P-CAP (≥75y subgroup):* PCV13 alone: 14.0 (-83.2–59.6)
* PPV23 alone: 6.4 (-49.9–41.6)
* Sequential PCV13/PPV23: -14.8

(-152.9–47.9)VE against nonbacteremic P-CAP (≥65y):* PCV13 alone: 38.8 (-13.0–66.9)
* PPV23 alone: -0.1 (-59.4–39.0)
* Sequential PCV13/PPV23: 36.5 (-25.0–67.8)

VE against nonbacteremic P-CAP (65–74y subgroup):* PCV13 alone: 66.5 (0.7–88.7)
* PPV23 alone: 18.5 (-38.6–52.0)
* Sequential PCV13/PPV23: 80.0 (14.4–95.3)

VE against nonbacteremic P-CAP (≥75y subgroup):* PCV13 alone: 12.5 (-86.5–59.0)
* PPV23 alone: 6.4 (-49.9–41.6)
* Sequential PCV13/PPV23: -18.1

(-160.4–46.4) | Moderate |
| Love et al 2021[4] | Severe pneumococcal disease (pneumococcal meningitis, pneumococcal sepsis/bacteremia, pneumococcal pneumonia), determined by ICD-9/ICD-10 codes | Evaluated separately from PPV23 only and PCV13 only | Variable (not specified) | VE = (1-adjusted hazard ratio) x 100%, calculated from results | VE against severe pneumococcal disease:* PCV13 alone: 79 (70–85)
* PPV23 alone: -10 (-21–1)
* ≥2 doses PPV23: 20 (5–33)

Sequential PCV13/PPV23: 83 (78–86) | Moderate |
| **Pneumonia or lower respiratory tract infection outcomes** |
| Kolditz et al 2018[5] | All-cause pneumonia, defined as main diagnosis of pneumonia or a main diagnosis of sepsis togetherwith a secondary diagnosis of pneumonia, determined by ICD-10 codes. Outpatient pneumonia cases were validated by ambulatory prescription of an antibiotic within 7 days of the diagnosis. | Not assessed. This study only evaluated PPV23; no study participants had received PCV13. | PPV23 receipt within the previous 5 years | VE= (1-risk ratio) x 100%, calculated from results | PPV23 VE against all-cause pneumonia:* ≥60y: 3.2 (0.7–5.6)
* 60–79y subgroup: -1.8 (-5.8–2.0)
* ≥80y subgroup: 0.0 (-3.5–3.4)
* Male subgroup ≥60y: 0.5 (-3.3–4.8)
* Female subgroup ≥60y: 5.1 (1.7–8.4)
 | Moderate  |
| Kolditz et al 2018[6] | All-cause pneumonia, defined as primary diagnosis of pneumonia or a main diagnosis of sepsis together with a secondary diagnosis of pneumonia, determined by ICD-10 codes. Outpatient pneumonia cases were validated by ambulatory prescription of an antibiotic within 7 days of the diagnosis. | Not assessed. People who had received PPV23 after January 2012 were excluded.  | PCV13 receipt within the previous 5 years | VE= (1-risk ratio) x 100%, calculated from results | PCV13 VE against all-cause pneumonia:* ≥60y: 11.9 (3.2–19.9)
* 60–79y subgroup: 7.8 (-5.2–19.2)
* ≥80y subgroup: 11.0 (-1.9–22.3)
* Male subgroup ≥60y: 3.7 (-9.1–14.9)
* Female subgroup ≥60y: 19.0 (6.4–29.8)
 | Moderate |
| Lewnard et al 2021[7] | * All-cause, medically-attended (inpatient or outpatient, including emergency department) pneumonia, determined by ICD-10 codes
* All-cause, medically-attended (inpatient or outpatient, including emergency department) lower respiratory tract infection (LTRI), determined by ICD-10 codes

For both pneumonia and LRTI, outcomes were the first diagnosed episode during each year of follow-up. | Not assessed. Analysis of PCV13 adjusted for receipt of PPV23, and vice-versa. | Variable (not specified) | VE = (1-adjusted hazard ratio) x 100% | VE against all-cause pneumonia:* PCV13 VE 8.8 (-0.2–17.0)
* PPV23 VE 1.0 (-18.0–17.0)

VE against all-cause LRTI:* PCV13 VE 9.9 (1.1–17.9)
* PPV23 VE 3.9 (-9.4–15.6)
 | Moderate |
| Hsaio et al 2022[8] | * All-cause, hosptialized pneumonia, determined by ICD-9/ICD-10 codes (first event)
* All-cause, hospitalized LRTI, determined by ICD-9/ICD-10 codes (first event)
 |  | Variable for PCV13 (not specified); PPV23 receipt within the previous 5 years | VE = (1-adjusted relative risk) x 100% | VE against all-cause, hospitalized pneumonia:* PCV13 VE 10.0 (2.4–17.0)
* PPV23 VE -8.0 (-20–3)

VE against all-cause, hospitalized LRTI:* PCV13 VE 9.4 (2.1–16.1)
* PPV23 VE -8.0 (-20–3)
 | Moderate |
| **COVID-19** |
| Lewnard et al. 2021(30) | * COVID-19 diagnosis, defined as a positive result of a molecular test for SARS-CoV-2 infection or a clinically confirmed COVID-19 diagnosis
* COVID-19 hospitalization, defined as a new inpatient admission between 7 days before and 28 days after a COVID-19 diagnosis
 | Evaluated separately from PPV23 only and PCV13 only; compared with no pneumococcal vaccination | Variable (not specified) | VE = (1-negative control corrected adjusted hazard ratio) x 100%, calculated from results | VE against COVID-19 diagnosis:* PCV13: 35 (28–41)
* PPV23: -19 (-36–-5)
* Sequential PCV13/PPV23: 34 (24–44)

VE against COVID-19 hospitalization:* PCV13: 32 (17–43)
* PPV23: -2 (-29–22)
* Sequential PCV13/PPV23: 46 (27–59)
 | Moderate |

**Supplementary Table 2**. Characteristics of excluded observational studies on vaccine effectiveness of PCV13 and PPV23 in the same or similar populations.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Design** | **Study population or analytic cohort** | **Study period** | **Pneumococcal vaccination history of participants** | **Outcomes** | **Results****VE % (95%CI)** | **Reason for exclusion** |
| **Pneumococcal disease and pneumonia outcomes**  |
| Perniciaro et al 2021[9] | Prospective, indirect cohort study investigating vaccine status of IPD1 cases | 928 German adults ≥60y with IPD  | 2018–2019 | * 21.4% PPV23 only
* 3.6% PCV13 only
* Patients who received both PCV13 and PPV23 excluded
 | VT-IPD1 | * PPV23 VE against VT-IPD: 37 (12–55)
* PCV13 VE against VT-IPD: 21 (-68–66)
 | Low PCV13 vaccination among study population |
| Prato et al 2018[10] | Prospective cohort; test-negative design for hospitalized patients, case-control for outpatients | 186 Italian adults aged ≥65y with CAP  |  2013–2015 | * 32% PPV23
* 11% PCV13
 |  Pneumococcal CAP (pCAP); VT-CAP | * PPV23 VE against pCAP: -4 (-115.4–50.4)
* PCV13 VE against pCAP 33.2 (-106.6–82)
* PCV13 VE against VT-CAP 38.1 (-131.9–89)
 | PPV23 results only provided for a subset of analyses; serious risk of bias according to ROBINS-I |
| Ignatova et al 2021[11] | Prospective cohort with 5 year follow-up post vaccination | 302 Russian men aged ≥45y with chronic obstructive pulmonary disease | 2012–2017  | * 41% PCV13
* 11% PPV23
 | Pneumonia episodes per year | VE = (1 - rate ratio) x 100%, calculated from results; 95%CIs could not be calculated.1 year post vaccination:PCV13 VE = 67%PPV23 VE = 58%5 years post vaccination:PCV13 VE = 86%PPV23 VE = -104% | Most results were presented as figures without numerical data; Insufficient methods information to complete ROBINS-I risk of bias assessment |
| Vila-Corcoles et al 2020[12] | Cohort study using hospital database | 2,025,730 Spanish adults >50y | 2015–2016 | * 39% PPV23
* 0.2% PCV13
 | Hospitalized pneumococcal pneumonia; hospitalized all-cause pneumonia | VE = (1 - adjusted hazard ratio) x 100%, calculated form results.* PPV23 VE against pneumococcal pneumonia: -8 (-19–2)
* PCV13 VE against pneumococcal pneumonia: -52 (-97–-17)
* PPV23 VE against all-cause pneumonia: -17 ( -21–-13)
* PCV13 VE against all-cause pneumonia: -76 ( -95– -61)
 | Low PCV13 vaccination among study population |
| **COVID-19 outcomes** |
| Satue-Gracia et al 2021[13] | Population-based cohort study | 79,083 Spanish adults >50y | March–June 2020 | * 33.1% PPV23
* 1.4% PCV13
 | Laboratory confirmed COVID-19 (n=536) | * PPV23 VE against COVID-19: -5 (-35–18)
* PCV13 VE against COVID-19: -74 (-185–6)
 | Low PCV13 vaccination among study population |
| Fernandez-Prada et al 2021[14] | Case-control study, test-negative design | 188 Spanish patients tested for COVID-19  | Feb–May 2020 | * 19.1% PCV13
* 10.6% PPSV23
* 8.5% PCV13 and PPV23
 | PCR+ for COVID-19 (n=63) | VE = (1 - odds ratio) x 100%, calculated from results.* PCV13 VE against COVID-19: 60 (-0.6–83)
* PPV23 VE against COVID-19: 30 (-110–72)
* Sequential PCV13/PPV23 VE against COVID-19: 80 ( -18.2–94)
 | No adjustment for underlying conditions (serious risk of bias) |

1IPD = invasive pneumococcal disease; VT-IPD = vaccine-type IPD

2CAP= community-acquired pneumonia; VT-CAP = vaccine-type CAP

3UAD = serotype-specific urinary antigen detection assay

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