Anhang zur wissenschaftlichen Begründung für die Aktualisierung der STIKO-Empfehlungen zur Pneumokokken-Standardimpfung von Personen ≥ 60 Jahre sowie zur Pneumokokken-Indikationsimpfung von Risikogruppen

Inhaltsverzeichnis

1. Suchstrategie und Flussdiagramm des systematischen Reviews zur Sicherheit und Wirksamkeit von PCV20

Suchstrategie:
Suche in MEDLINE, EMBASE, grauer Literatur und Referenzlisten von relevanten Publikationen (Datum der Suche: 17.1.2023)

PubMed

#1	(Pneumococcal Vaccines[MeSH Terms]) OR (pneumococcus vaccine[Title/Abstract]) OR (pcv20[Title/Abstract]) OR (prevnar20[Title/Abstract]) OR (prevnar 20[Title/Abstract]) OR (20-valent[Title/Abstract])

EMBASE

#1	'pneumococcus vaccine'/mj OR 'pneumococcus vaccine':ti,ab OR 'pcv20':ti,ab OR 'prevnar 20':ti,ab OR '20-valent':ti,ab

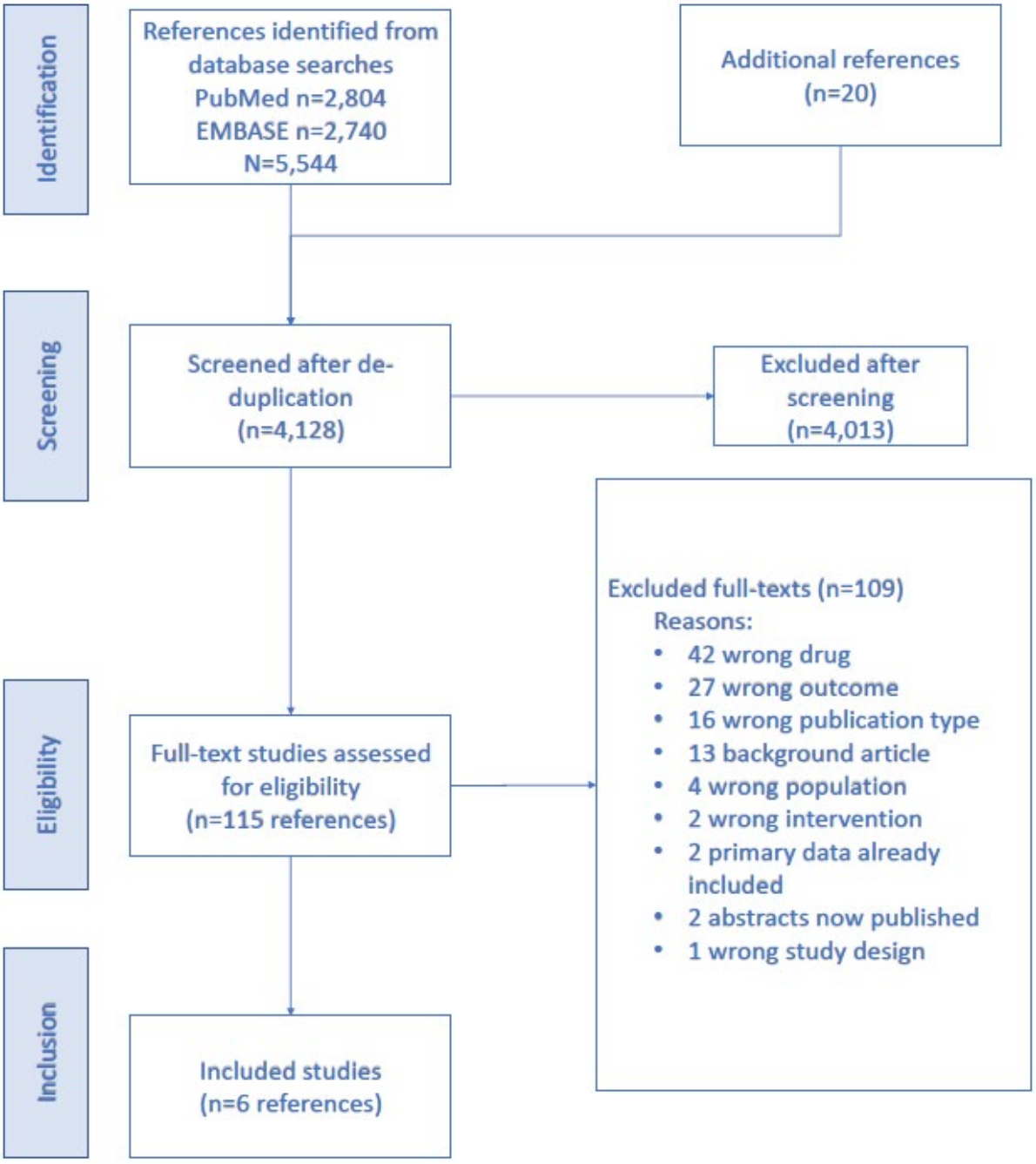


Abbildung 1: Flussdiagramm zum Review der Sicherheit und Wirksamkeit von PCV20

2. Ein- und Ausschlusskriterien für die Identifikation von relevanten Studien für den systematischen Review zur Sicherheit und Wirksamkeit von PCV20

PICO-Kriterium	Einschlusskriterium
Population	Gesunde Personen ≥ 18 Jahre jeden Geschlechts, die in Industrieländern leben und nicht zu den indigenen Minderheiten gehören[1]
Intervention	Impfung mit dem 20-valenten Pneumokokken-Konjugatimpfstoff (Einzeldosis)
Comparator	· Keine Impfung · Impfung mit Placebo · Impfung mit einem anderen Pneumokokken-Impfstoff (PPSV23 oder PCV13) · Impfung mit einem anderen (Nicht-Pneumokokken-) Impfstoff
Outcome	· Invasive Pneumokokken-Erkrankung (IPD) · Pneumokokken-Pneumonie · Krankenhausaufenthalt oder Tod aufgrund von IPD oder Pneumokokken-Pneumonie · Bei fehlenden Wirksamkeitsdaten: Immunogenitätsdaten als Surrogatmarker
Study Characteristic	Randomisierte kontrollierte Studien (RCT), Beobachtungsstudien mit einer Referenzgruppe
Study Characteristic	Sprachen: Englisch, Deutsch, Französisch, Spanisch
Veröffentlichungs-zeitraum	Ab 2016 bis 2023

[1]Die Suchstrategie enthielt keinen Term zur Population, sodass Personen mit Grunderkrankungen hätten identifiziert werden können.

3. Liste der ausgeschlossenen Studien

No.	Reference	Exclusion reason
1	Al-Lahham A, Khanfar N, Albataina N, Al Shwayat R, Altwal R, Abulfeilat T, Alawneh G, Khurd M, Alqadi Altamimi A. Urban and Rural Disparities in Pneumococcal Carriage and Resistance in Jordanian Children, 2015-2019. Vaccines (Basel). 2021 Jul 14;9(7):789. doi: 10.3390/vaccines9070789. PMID: 34358205; PMCID: PMC8309963.	Wrong drug
2	Arvind RK, Beerwala FA, Wali SC, Parihar AS, Ganachari MS, Bhandari R. A Randomized, Single Centered, Parallel and Open Labelled Interventional Study on Effectiveness of Clinical Pharmacists on Adverse Event Following Immunization (AEFI) in Pediatric Population. Curr Drug Saf. 2022;17(4):357-365. doi: 10.2174/1574886317666220103092844. PMID: 35049436.	Wrong drug
3	Averin A, Sato R, Kutrieb E, Atwood M, Weycker D. EE204 Budgetary Impact of New Recommendations for Pneumococcal Vaccination of US Adults. Value in Health. Vol. 25(7). Suppl. Jul 2022. doi: 10.1016/j.jval.2022.04.453	Wrong outcome
4	Bernth Jensen JM, Hansen AT, Söderström A, Jørgensen CS, Larsen CS, Skov Sørensen UB, Thiel S, Petersen MS. A low level of naturally occurring antibodies associates with functional antibody deficiency. Clin Immunol. 2022 Aug;241:109070. doi: 10.1016/j.clim.2022.109070. Epub 2022 Jun 30. PMID: 35779828.	Wrong drug
5	Bruhn CA, Hetterich S, Schuck-Paim C, Kürüm E, Taylor RJ, Lustig R, Shapiro ED, Warren JL, Simonsen L, Weinberger DM. Estimating the population-level impact of vaccines using synthetic controls. Proc Natl Acad Sci U S A. 2017 Feb 14;114(7):1524-1529. doi: 10.1073/pnas.1612833114. Epub 2017 Feb 1. PMID: 28154145; PMCID: PMC5321019.	Wrong outcome
6	Camargos P, Drumond E, Nascimento-Carvalho CM. Effect of pneumococcal conjugate vaccines on invasive pneumococcal disease. Lancet Infect Dis. 2021 Apr;21(4):453. doi: 10.1016/S1473-3099(21)00051-7. PMID: 33773123.	Wrong population
7	Campos-Outcalt D. Vaccine update: The latest recommendations from ACIP. J Fam Pract. 2022 Mar;71(2):80-84. doi: 10.12788/jfp.0362. PMID: 35507818.	Background article
8	Cané A, Hamelin B, Isturiz R. Effectiveness of three pneumococcal conjugate vaccines (PCV) to prevent invasive pneumococcal disease in Quebec, Canada. Vaccine. 2016 Apr 19;34(18):2051-2. doi: 10.1016/j.vaccine.2015.06.115. Epub 2015 Jul 31. PMID: 26235371.	Wrong drug
9	Cannon K, Cardona JF, Yacisin K, Thompson A, Belanger TJ, Lee DY, Peng Y, Moyer L, Ginis J, Gruber WC, Scott DA, Watson W. Safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine coadministered with quadrivalent influenza vaccine: A phase 3 randomized trial. Vaccine. 2023 Mar 24;41(13):2137-2146. doi: 10.1016/j.vaccine.2022.11.046. Epub 2023 Feb 23. PMID: 36828719.	Wrong intervention
10	Centers for Disease Control and Prevention. Recommended adult immunization schedule for ages 19 years or older - United States. 2022.	Background article

	https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf [latest accessed 2023.8.22].	
11	Chan T, Tay MZ, Kyaw WM, Chow A, Ho HJ. Epidemiology, vaccine effectiveness, and risk factors for mortality for pneumococcal disease among hospitalised adults in Singapore: a case-control study. BMC Infect Dis. 2020 Jun 17;20(1):423. doi: 10.1186/s12879-020-05140-1. PMID: 32552726; PMCID: PMC7302122.	Wrong drug
12	Chen H, Liu C. Molecular epidemiology of Streptococcus pneumoniae isosslated from children with community-acquired pneumonia under 5 years in Chengdu, China. Epidemiol Infect. 2022 Dec 14;151:e2. doi: 10.1017/S0950268822001881. PMID: 36515066; PMCID: PMC9990402.	Wrong outcome
13	Càmara J, Ardanuy C. Pneumococcal disease and conjugate vaccines. Enferm Infecc Microbiol Clin (Engl Ed). 2018 Dec;36(10):605-606. English, Spanish. doi: 10.1016/j.eimc.2018.07.012. Epub 2018 Sep 13. PMID: 30220517.	Wrong drug
14	Càmara J, Grau I, González-Díaz A, Tubau F, Calatayud L, Cubero M, Domínguez MÁ, Liñares J, Yuste J, Pallarés R, Ardanuy C. A historical perspective of MDR invasive pneumococcal disease in Spanish adults. J Antimicrob Chemother. 2021 Jan 19;76(2):507-515. doi: 10.1093/jac/dkaa465. PMID: 33254238.	Wrong outcome
15	Contreras JR. Pneumococcal conjugate vaccines. Pediatria Integral 2020 24:8 (449-456)	Wrong population
16	Crosby S, Schuh MJ, Becker M, Ivanov M, Caldera F, Farraye FA. New Pneumococcal Vaccines for Prevention of Invasive Pneumococcal Disease in Adult Patients With Inflammatory Bowel Disease. Inflamm Bowel Dis. 2023 Apr 3;29(4):661-664. doi: 10.1093/ibd/izac150. PMID: 35830419.	Wrong publication type
17	De Wals P, Deceuninck G, De Serres G. Effectiveness of three pneumococcal conjugate vaccines to prevent invasive pneumococcal disease in Quebec, Canada. Vaccine. 2016 Apr 19;34(18):2053-4. doi: 10.1016/j.vaccine.2015.06.104. PMID: 27021043.	Wrong drug
18	Dendle C, Stuart RL, Mulley WR, Holdsworth SR. Pneumococcal vaccination in adult solid organ transplant recipients: A review of current evidence. Vaccine. 2018 Oct 8;36(42):6253-6261. doi: 10.1016/j.vaccine.2018.08.069. Epub 2018 Sep 11. PMID: 30217523.	Wrong drug
19	Dorange AC. EE423 Cost-Effectiveness of Vaccinating Adults ≥65 Years and at-Risk Individuals 18-64 Years With the 20-Valent Pneumococcal Conjugate Vaccine Versus Currently Recommended Vaccine Regimens in Sweden. DOI: 10.1016/j.jval.2022.09.669	Wrong outcome
20	Duarte FG, Barberino MG, da Silva Moreira S, Reis JN, Spinardi JR, de Almeida RS, Allen KE, Alexander-Parrish R, Brim R, de Araújo Neto CA, Moreira ED. Incidence, aetiology and serotype coverage for pneumococcal vaccines of community-acquired pneumonia in adults: a population-based prospective active surveillance study in Brazil. BMJ Open. 2022 Apr 15;12(4):e059824. doi: 10.1136/bmjopen-2021-059824. PMID: 35428648; PMCID: PMC9014102.	Wrong outcome
21	El-Bardissy AHe, Al-Adawi RM, Shible AA, Albu-Mahmood Z, Elgaily DE, Abdelaziz H. Evaluating the effectiveness of pneumococcal vaccines against hospitalization and intensive care unit admission in adults. J Pharm Health Serv Res, 2019; 10: 427-431. doi: 10.1111/jphs.12321	Wrong drug

22	El-Beyrouty C, Buckler R, Mitchell M, Phillips S, Groome S. Pneumococcal vaccination-A literature review and practice guideline update. Pharmacotherapy. 2022 Sep;42(9):724-740. doi: 10.1002/phar.2723. Epub 2022 Aug 4. PMID: 35876213.	Background article
23	Esden JL. Pneumococcal vaccination for adults: History and updates. Nurse Pract. 2022 Nov 1;47(11):40-47. doi: 10.1097/01.NPR.0000897220.84850.82. PMID: 36287736.	Wrong publication type
24	Essink B, Peterson J, Yacisin K, Lal H, Mirza S, Xu X, Scully IL, Scott DA, Gruber WC, Jansen KU, Watson W. A randomized phase 1/2 study of the safety and immunogenicity of a multivalent pneumococcal conjugate vaccine in healthy adults 50 through 85 years of age. Hum Vaccin Immunother. 2021 Aug 3;17(8):2691-2699. doi: 10.1080/21645515.2021.1890511. Epub 2021 Mar 4. PMID: 33661716; PMCID: PMC8475590.	Wrong drug
25	Essink B, Sabharwal C, Xu X, Sundaraiyer V, Peng Y, Moyer L, Pride MW, Scully IL, Jansen KU, Gruber WC, Scott D, Watson W. Phase 3 pivotal evaluation of 20-valent pneumococcal conjugate vaccine (PCV20) safety, tolerability, and immunologic noninferiority in participants 18 years and older. Open Forum Infect Dis 2020;7(Supplement_1):S2. doi: 10.1093/ofid/ofaa417.002	Abstract now published
26	Farrar JL, Childs L, Ouattara M, Akhter F, Britton A, Pilishvili T, Kobayashi M. Systematic Review and Meta-Analysis of the Efficacy and Effectiveness of Pneumococcal Vaccines in Adults. medRxiv 2022.10.06.22280772; doi: https://doi.org/10.1101/2022.10.06.22280772	Wrong drug
27	Farrar JL, Kobayashi M, Childs L, Pilishvili T. Systematic Review and Meta-Analysis of Pneumococcal Vaccine Effectiveness against Invasive Pneumococcal Disease among Adults. Open Forum Infectious Diseases, Volume 8, Issue Supplement_1, November 2021, Pages S134–S135, https://doi.org/10.1093/ofid/ofab466.223	Wrong drug
28	Food and Drug Administration. Summary basis for regulatory action—PREVNAR20. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration, 2021. https://www.fda.gov/media/150388/download [latest accessed 2023.8.22].	Background article
29	Fitz-Patrick D, Young M, Scott D, Scully IL, Baugher G, Peng Y, Jansen KU, Gruber WC, Watson W. A randomized phase 1 study of a novel pneumococcal conjugate vaccine in healthy japanese adults in the united states. Open Forum Infectious Diseases - Volume 7, Issue 0, pp. S30-S31 - published 2020-01-01 DOI: 10.1093/ofid/ofaa417.061	Wrong publication type
30	Fitz-Patrick D, Jennings T, Young M, et al. Safety, tolerability, and immunogenicity of a booster dose of BNT162b2 COVID-19 vaccine coadministered with 20-valent pneumococcal conjugate vaccine (PCV20) in adults 65 years of age and above [abstract and poster no. 2245]. In: 32nd ECCMID. 2022.	Wrong intervention
31	Flores-Copete M, Reolid-Martínez R, López-García M, Alcantud-Lozano P, Mudarra-Tercero E, Azorín-Ras M, Del Campo-Giménez M, Ayuso-Raya MC, Escobar-Rabadán F. Riesgo de enfermedad neumocócica en pacientes ancianos con y sin vacunación previa [Risk of pneumococcal disease in elderly patients with and without previous vaccination]. Aten Primaria. 2019 Nov;51(9):571-578.	Wrong drug

	Spanish. doi: 10.1016/j.aprim.2018.07.009. Epub 2018 Nov 1. PMID: 30391017; PMCID: PMC6945128.	
32	Froes F, Roche N, Blasi F. Pneumococcal vaccination and chronic respiratory diseases. Int J Chron Obstruct Pulmon Dis. 2017 Dec 5;12:3457-3468. doi: 10.2147/COPD.S140378. PMID: 29255353; PMCID: PMC5723118.	Wrong drug
33	Golos M, Eliakim-Raz N, Stern A, Leibovici L, Paul M. Conjugated pneumococcal vaccine versus polysaccharide pneumococcal vaccine for prevention of pneumonia and invasive pneumococcal disease in immunocompetent and immunocompromised adults and children. Cochrane Database of Systematic Reviews, Volume 2016, Issue 8. doi: 10.1002/14651858.CD012306	Wrong drug
34	Goonewardene ST, Tang C, Tan LT, Chan KG, Lingham P, Lee LH, Goh BH, Pusparajah P. Safety and Efficacy of Pneumococcal Vaccination in Pediatric Nephrotic Syndrome. Front Pediatr. 2019 Aug 13;7:339. doi: 10.3389/fped.2019.00339. PMID: 31456997; PMCID: PMC6700369.	Wrong drug
35	Greenberg GM, Koshy PA, Hanson MJS. Adult Vaccination. American Family Physician 2022. Vol. 106(5), pp. 534-542.	Background article
36	Hausdorff WP. Pneumococcal conjugate vaccines in different settings. Lancet Infect Dis. 2019 Dec;19(12):1283-1284. doi: 10.1016/S1473-3099(19)30623-1. PMID: 31782390.	Wrong outcome
37	Hoshi SL, Shono A, Seposo X, Okubo R, Kondo M. Cost-effectiveness analyses of 15- and 20-valent pneumococcal conjugate vaccines for Japanese elderly. Vaccine. 2022 Nov 22;40(49):7057-7064. doi: 10.1016/j.vaccine.2022.10.010. Epub 2022 Oct 21. PMID: 36273987.	Wrong outcome
38	Hsiao A, Klein NP. All Older Adults Benefit From Pneumococcal Vaccinations-The Case for Evaluating Vaccine Effectiveness Using All-Cause Pneumonia. JAMA Intern Med. 2023 Jan 1;183(1):48-49. doi: 10.1001/jamainternmed.2022.5456. PMID: 36469330.	Wrong publication type
39	Huang L, Wasserman M, Grant L, Farkouh R, Snow V, Arguedas A, Chilson E, Sato R, Perdrizet J. Burden of pneumococcal disease due to serotypes covered by the 13-valent and new higher-valent pneumococcal conjugate vaccines in the United States. Vaccine. 2022 Aug 5;40(33):4700-4708. doi: 10.1016/j.vaccine.2022.06.024. Epub 2022 Jun 24. PMID: 35753839.	Wrong outcome
40	Hurley D, Griffin C, Young M, Scott D, Pride MW, Scully IL, Ginis J, Peng Y, Jansen KU, Gruber WC, Watson W. 1240. Persistence of Circulating Antibody Through 12 Months Following Vaccination With a 20-Valent Pneumococcal Conjugate Vaccine in Adults 60–64 Years of Age	Abstract now published
41	Isturiz R, Grant L, Gray S, Alexander-Parrish R, Jiang Q, Jodar L, Peyrani P, Ford KD, Pride MW, Self WH, Counselman F, Volturo G, Ostrosky-Zeichner L, Wunderink RG, Sherwin R, Overcash JS, File T, Ramirez J. Expanded Analysis of 20 Pneumococcal Serotypes Associated With Radiographically Confirmed Community-acquired Pneumonia in Hospitalized US Adults. Clin Infect Dis. 2021 Oct 5;73(7):1216-1222. doi: 10.1093/cid/ciab375. PMID: 33982098; PMCID: PMC8492118.	Wrong outcome
42	Jaiswal V, Ang SP, Lnu K, Ishak A, Pokhrel NB, Chia JE, Hajra A, Biswas M, Matetic A, Dhatt R, Mamas MA. Effect of Pneumococcal Vaccine on Mortality and Cardiovascular Outcomes: A Systematic Review and	Wrong publication type

	Meta-Analysis. J Clin Med. 2022 Jun 30;11(13):3799. doi: 10.3390/jcm11133799. PMID: 35807082; PMCID: PMC9267914.	
43	Janssens E, Flamaing J, Vandermeulen C, Peetermans WE, Desmet S, De Munter P. The 20-valent pneumococcal conjugate vaccine (PCV20): expected added value. Acta Clin Belg. 2023 Feb;78(1):78-86. doi: 10.1080/17843286.2022.2039865. Epub 2022 Feb 16. PMID: 35171752.	Wrong publication type
44	Jimbo Sotomayor R, Toscano CM, Sánchez Choez X, Vilema Ortíz M, Rivas Condo J, Ghisays G, Haneuse S, Weinberger DM, McGee G, de Oliveira LH. Impact of pneumococcal conjugate vaccine on pneumonia hospitalization and mortality in children and elderly in Ecuador: Time series analyses. Vaccine. 2020 Oct 21;38(45):7033-7039. doi: 10.1016/j.vaccine.2020.09.032. Epub 2020 Sep 25. PMID: 32981782.	Wrong drug
45	Jit M, Flasche S. The role of pneumococcal conjugate vaccination in reducing pneumonia mortality. Lancet Glob Health. 2019 Feb;7(2):e173-e174. doi: 10.1016/S2214-109X(18)30540-0. PMID: 30683228.	Wrong drug
46	Kim KS, Kim HJ, Oh IS, Park MS, Shin JY. Detection of adverse events after pneumococcal vaccines immunization from Korea adverse events reporting system database, 2005-2016. Abstracts of the 35th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Pennsylvania Convention Center, Philadelphia, PA, USA, August 24-28, 2019. Pharmacoepidemiol Drug Saf. 2019 Aug;28 Suppl 2:5-586. doi: 10.1002/pds.4864. PMID: 31429168.	Wrong drug
47	Kim KS, Oh IS, Kim HJ, Song I, Park MS, Shin JY. Signal Detection of Adverse Events Following Pneumococcal Vaccines from the Korea Adverse Event Reporting System Database, 2005-2016. Yonsei Med J. 2020 Mar;61(3):243-250. doi: 10.3349/ymj.2020.61.3.243. PMID: 32102125; PMCID: PMC7044688.	Wrong drug
48	Klugman KP, Rodgers GL. Impact of Pneumococcal Conjugate Vaccine on Vaccine Serotype-Specific Pneumonia. Clin Infect Dis. 2021 Oct 5;73(7):e1434-e1435. doi: 10.1093/cid/ciaa1867. PMID: 33338195; PMCID: PMC8492200.	Wrong drug
49	Klugman KP, Rodgers GL. Time for a third-generation pneumococcal conjugate vaccine. Lancet Infect Dis. 2021 Jan;21(1):14-16. doi: 10.1016/S1473-3099(20)30513-2. Epub 2020 Jul 20. PMID: 32702301.	Wrong drug
50	Kobayashi M. Considerations for age-based and risk-based use of PCV15 and PCV20 among U.S. adults and proposed policy options. ACIP meeting Pneumococcal Vaccines 2021.	Wrong publication type
51	Kobayashi M. Considerations for use of PCV15 and PCV20 in U.S. adults. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/24-25/05-Pneumococcal-Kobayashi.pdf [latest accessed 2023.8.22].	Wrong publication type
52	Kobayashi M, Farrar JL, Gierke R, Britton A, Childs L, Leidner AJ, Campos-Outcalt D, Morgan RL, Long SS, Talbot HK, Poehling KA, Pilishvili T. Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022 Jan 28;71(4):109-117. doi: 10.15585/mmwr.mm7104a1. PMID: 35085226; PMCID: PMC9351524.	Wrong outcome

53	Kobayashi M, Spiller MW, Wu X, Wang R, Chillarige Y, Wernecke M, MaCurdy TE, Kelman JA, Deng L, Shang N, Whitney CG, Pilishvili T, Lessa FC. Association of Pneumococcal Conjugate Vaccine Use With Hospitalized Pneumonia in Medicare Beneficiaries 65 Years or Older With and Without Medical Conditions, 2014 to 2017. JAMA Intern Med. 2023 Jan 1;183(1):40-47. doi: 10.1001/jamainternmed.2022.5472. Erratum in: JAMA Intern Med. 2023 Jan 23;: PMID: 36469350; PMCID: PMC9857509.	Wrong drug
54	Kurt TL, Forrester MB. 145. Vaccine adverse events among older adults in The United States. NACCT Abstracs 2020. DOI: 10.1080/15563650.2020.1804238	Wrong drug
55	La Torre G, Mannocci A, Colamesta V, D'Egidio V, Sestili C, Spadea A. Influenza and Pneumococcal Vaccination in Hematological Malignancies: a Systematic Review of Efficacy, Effectiveness, and Safety. Mediterr J Hematol Infect Dis. 2016 Sep 1;8(1):e2016044. doi: 10.4084/MJHID.2016.044. PMID: 27648207; PMCID: PMC5016013.	Wrong publication type
56	La Verde NM, Dalu D, Ridolfo AL, Cona MS, De Francesco D, Riva A, Antinori S, Rota S, Tricella C, Oldani S, Fasola C, Ferrario S, Gambaro A, Filipazzi V, Chizzoniti D, Cattaneo M, Di Carlo F, Lombardi Stocchetti B, Tosca N, Galli M. 1712P Safety and efficacy of influenza and pneumococcal vaccines in cancer patients on active therapy: A prospective study. Abstract| Volume 32, SUPPLEMENT 5, S1191, September 2021. doi: 10.1016/j.annonc.2021.08.1684	Wrong outcome
57	Lee H, Kim JH, Shin JY. Pneumococcal vaccine safety surveillance using three statistical methods: Disproportionality analysis, tree-based scan statistics, and empirical Bayes geometric mean. Abstracts of the 35th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Pennsylvania Convention Center, Philadelphia, PA, USA, August 24-28, 2019. Pharmacoepidemiol Drug Saf. 2019 Aug;28 Suppl 2:5-586. doi: 10.1002/pds.4864. PMID: 31429168.	Wrong drug
58	Leidner AJ. Summary of three economic models evaluating pneumococcal vaccines in adults in the United States. Presented at the September 29, 2021 ACIP meeting. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-09-29/02-Pneumococcal-Leidner-508.pdf [latest accessed 2023.8.22].	Wrong publication type
59	Lenzing E, Rezahosseini O, Burgdorf SK, Nielsen SD, Harboe ZB. Efficacy, immunogenicity, and evidence for best-timing of pneumococcal vaccination in splenectomized adults: a systematic review. Expert Rev Vaccines. 2022 May;21(5):723-733. doi: 10.1080/14760584.2022.2049250. Epub 2022 Mar 20. PMID: 35236233.	Wrong publication type
60	Lombardi N, Crescioli G, Bettiol A, Tuccori M, Rossi M, Bonaiuti R, Ravaldi C, Levi M, Mugelli A, Bonanni P, Vannacci A. Predictors of serious adverse events following immunization: 1-year pharmacovigilance study in general population. 18th ISoP Annual Meeting "Pharmacovigilance without borders" Geneva, Switzerland, 11-14 November, 2018. Drug Saf. 2018 Nov;41(11):1103-1273. doi: 10.1007/s40264-018-0719-2. Erratum in: Drug Saf. 2018 Oct 31;:1441. PMID: 30284218.	Wrong drug

61	López Gobernado M, Pérez-Rubio A, Eiros Bouza JM. Vacunación frente al neumococo en adultos mayores de 65 años [Pneumococcal vaccine for adults over 65]. Aten Primaria. 2020 Dec;52(10):802-803. Spanish. doi: 10.1016/j.aprim.2019.12.007. Epub 2020 Mar 5. PMID: 32147234; PMCID: PMC8054274.	Wrong drug
62	Mac Mullen M, Carballo C, Seyahian E. EE390 Cost-Effectiveness of the 20-Valent Pneumococcal Conjugate Vaccine vs 15-Valent Pneumococcal Conjugate Vaccine for Adults in Argentina. Abstract, Value in Health Vol. 25(12). Suppl. Dec 2022. doi: 10.1016/j.jval.2022.09.636	Wrong outcome
63	Mackenzie GA, Osei I, Salaudeen R, Secka O, D'Alessandro U, Clarke E, Schmidt-Chanasit J, Licciardi PV, Nguyen C, Greenwood B, Mulholland K. Pneumococcal conjugate vaccination schedules in infants-acquisition, immunogenicity, and pneumococcal conjugate and yellow fever vaccine co-administration study. Trials. 2022 Jan 15;23(1):39. doi: 10.1186/s13063-021-05949-4. PMID: 35033180; PMCID: PMC8760872.	Wrong population
64	Mamouris P, Henrard S, Molenberghs G, Verhaegen J, Lin G, Vaes B. Pneumococcal vaccination prevented severe LRTIs in adults: a causal inference framework applied in registry data. J Clin Epidemiol. 2022 Mar;143:118-127. doi: 10.1016/j.jclinepi.2021.12.008. Epub 2021 Dec 8. PMID: 34896235.	Wrong drug
65	Mendes D, Averin A, Atwood M, Sato R, Vyse A, Campling J, Weycker D, Slack M, Ellsbury G, Mugwagwa T. Cost-effectiveness of using a 20-valent pneumococcal conjugate vaccine to directly protect adults in England at elevated risk of pneumococcal disease. Expert Rev Pharmacoecon Outcomes Res. 2022 Dec;22(8):1285-1295. doi: 10.1080/14737167.2022.2134120. Epub 2022 Nov 3. PMID: 36225103.	Wrong outcome
66	Mt-Isa S, Abderhalden LA, Musey L, Weiss T. Matching-adjusted indirect comparison of pneumococcal vaccines V114 and PCV20. Expert Rev Vaccines. 2022 Jan;21(1):115-123. doi: 10.1080/14760584.2021.1994858. Epub 2021 Oct 27. PMID: 34672224.	Primary data already included
67	Mugwagwa T, Averin A, Atwood M, Sato R, Vyse A, Campling J, Weycker D, Slack M, Ellsbury G, Mendes D. Public health and budgetary impact of 20-valent pneumococcal conjugate vaccine for adults in England. Expert Rev Vaccines. 2022 Sep;21(9):1331-1341. doi: 10.1080/14760584.2022.2104250. Epub 2022 Aug 8. PMID: 35929956.	Wrong outcome
68	Mullard A. GSK buys Affinivax for up to $3.3 billion, bolstering its vaccine pipeline. Nat Rev Drug Discov. 2022 Jul;21(7):480-481. doi: 10.1038/d41573-022-00103-4. PMID: 35681028.	Wrong publication type
69	Murdoch DR. Assessing the Impact of Pneumococcal Conjugate Vaccines. Clin Infect Dis. 2020 Apr 10;70(8):1589-1590. doi: 10.1093/cid/ciz484. PMID: 31175809.	Wrong drug
70	Muris J, Verhees R. Pneumococcal vaccination in patients with COPD. Huisarts en Wetenschap 2017 60:10 (534). doi: 10.1007/s12445-017-0331-1	Wrong drug
71	Olsen J, Schnack H, Skovdal M, Vietri J, Mikkelsen MB, Poulsen PB. Cost-effectiveness of 20-valent pneumococcal conjugate vaccine in Denmark compared with PPV23. J Med Econ. 2022 Jan-	Wrong outcome

	Dec;25(1):1240-1254. doi: 10.1080/13696998.2022.2152235. PMID: 36426797.	
72	Pike J, Leidner AJ, Chesson H, Stoecker C, Grosse SD. Data-Related Challenges in Cost-Effectiveness Analyses of Vaccines. Appl Health Econ Health Policy. 2022 Jul;20(4):457-465. doi: 10.1007/s40258-022-00718-z. Epub 2022 Feb 9. PMID: 35138601; PMCID: PMC9233035.	Wrong drug
73	Polistena B, Icardi G, Orsi A, Spandonaro F, Di Virgilio R, d'Angela D. Cost-Effectiveness of Vaccination with the 20-Valent Pneumococcal Conjugate Vaccine in the Italian Adult Population. Vaccines (Basel). 2022 Nov 28;10(12):2032. doi: 10.3390/vaccines10122032. PMID: 36560441; PMCID: PMC9784405.	Wrong outcome
74	Rasmussen SL, Fuursted K, Nielsen KA, Laurberg NP, Sørensen MB, Fagerberg SK, Leutscher P, Rasmussen C. Pneumococcal antibody protection in patients with autoimmune inflammatory rheumatic diseases with varying vaccination status. Scand J Rheumatol. 2020 Sep;49(5):353-360. doi: 10.1080/03009742.2020.1732459. Epub 2020 May 29. PMID: 32468899.	Wrong outcome
75	Roberts MB, Bak N, Wee LYA, Chhetri R, Yeung DT, Lewis I, Hiwase DK. Clinical Effectiveness of Conjugate Pneumococcal Vaccination in Hematopoietic Stem Cell Transplantation Recipients. Biol Blood Marrow Transplant. 2020 Feb;26(2):421-427. doi: 10.1016/j.bbmt.2019.10.006. Epub 2019 Oct 15. PMID: 31627016.	Wrong drug
76	Rose N, Storch J, Mikolajetz A, Lehmann T, Reinhart K, Pletz MW, Forstner C, Vollmar HC, Freytag A, Fleischmann-Struzek C. Preventive effects of influenza and pneumococcal vaccination in the elderly - results from a population-based retrospective cohort study. Hum Vaccin Immunother. 2021 Jun 3;17(6):1844-1852. doi: 10.1080/21645515.2020.1845525. Epub 2021 Jan 7. PMID: 33412080; PMCID: PMC8115600.	Wrong drug
77	Sabharwal C, Sundaraiyer V, Peng Y, Moyer L, Belanger TJ, Gessner BD, Jodar L, Jansen KU, Gruber WC, Scott DA, Watson W. Immunogenicity of a 20-valent pneumococcal conjugate vaccine in adults 18 to 64 years old with medical conditions and other factors that increase risk of pneumococcal disease. Hum Vaccin Immunother. 2022 Nov 30;18(6):2126253. doi: 10.1080/21645515.2022.2126253. Epub 2022 Nov 11. PMID: 36368038; PMCID: PMC9746485.	Primary data already included
78	Scheen, A. J.; Louis, R.; Moutschen, M. Apexxnar®, 20-valent pneumococcal conjugate vaccine. Revue medicale de Liege 2022 77:11 (678-683)	Background article
79	Scully IL, Cutler MW, Gangolli S, Belanger T, Cooper D, Jones T, McKeen A, Tan C, Watson W, Anderson AS, Jansen KU, Pride MW. Development, maintenance, and application of opsonophagocytic assays to measure functional antibody responses to support a 20 valent pneumococcal conjugate vaccine. Doi: 10.1093/ofid/ofz360.1201	Wrong outcome
80	Sempere J, Llamosí M, López Ruiz B, Del Río I, Pérez-García C, Lago D, Gimeno M, Coronel P, González-Camacho F, Domenech M, Yuste J. Effect of pneumococcal conjugate vaccines and SARS-CoV-2 on antimicrobial resistance and the emergence of Streptococcus pneumoniae serotypes with reduced susceptibility in Spain, 2004-20: a national surveillance study. Lancet Microbe. 2022 Oct;3(10):e744-	Wrong outcome

	e752. doi: 10.1016/S2666-5247(22)00127-6. Epub 2022 Aug 3. PMID: 35932764; PMCID: PMC9348823.	
81	Senders S, Klein NP, Lamberth E, Thompson A, Drozd J, Trammel J, Peng Y, Giardina PC, Jansen KU, Gruber WC, Scott DA, Watson W. Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Healthy Infants in the United States. Pediatr Infect Dis J. 2021 Oct 1;40(10):944-951. doi: 10.1097/INF.0000000000003277. PMID: 34525007; PMCID: PMC8443440.	Wrong population
82	Shah AA. Simplifying Pneumococcal Immunizations for Adults. American Family Physician 2022 105:6 (580-581). doi: 10.1164/RCCM.2019P17	Background article
83	Shah P, Woytanowski JR, Hadeh A, Sockrider M. Pneumococcal (Pneumonia) Vaccines. Am J Respir Crit Care Med. 2020 May 1;201(9):P17-P18. doi: 10.1164/rccm.2019P17. PMID: 32356685.	Background article
84	Shirley M. 20-Valent Pneumococcal Conjugate Vaccine: A Review of Its Use in Adults. Drugs. 2022 Jun;82(9):989-999. doi: 10.1007/s40265-022-01733-z. Epub 2022 Jul 6. PMID: 35793027.	Wrong publication type
85	Silva PH, Vázquez Y, Campusano C, Retamal-Díaz A, Lay MK, Muñoz CA, González PA, Kalergis AM, Bueno SM. Non-capsular based immunization approaches to prevent Streptococcus pneumoniae infection. Front Cell Infect Microbiol. 2022 Sep 26;12:949469. doi: 10.3389/fcimb.2022.949469. PMID: 36225231; PMCID: PMC9548657.	Wrong outcome
86	Smith KJ, Wateska AR, Nowalk MP, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK. Higher-Valency Pneumococcal Conjugate Vaccines: An Exploratory Cost-Effectiveness Analysis in U.S. Seniors. Am J Prev Med. 2021 Jul;61(1):28-36. doi: 10.1016/j.amepre.2021.01.023. Epub 2021 Apr 29. PMID: 34148625; PMCID: PMC8221100.	Wrong outcome
87	Smith KJ, Wateska AR, Nowalk MP, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK. Cost-Effectiveness of Newly Recommended Pneumococcal Vaccination Strategies in Older Underserved Minority Adults in the USA. Infect Dis Ther. 2022 Aug;11(4):1683-1693. doi: 10.1007/s40121-022-00669-x. Epub 2022 Jul 13. PMID: 35831685; PMCID: PMC9334503.	Wrong outcome
88	Stocker C. Economic assessment of PCV15 & PCV20. ACIP meeting Pneumococcal Vaccines 2021. https://stacks.cdc.gov/view/cdc/109109	Wrong publication type
89	Streeter AJ, Masoli JAH, Blé A, Melzer D, Henley WE. Pneumococcal vaccine effectiveness and its interaction with age: A UK population based study in older adults. Pharmacoepidemiology and Drug Safety 2017 26 (242-243) Supplement 2. Doi: 10.1002/pds.4275	Wrong drug
90	Sözen T, Bajin MD, Kara A, Sennaroğlu L. The Effect of National Pneumococcal Vaccination Program on Incidence of Postmeningitis Sensorineural Hearing Loss and Current Treatment Modalities. J Int Adv Otol. 2018 Dec;14(3):443-446. doi: 10.5152/iao.2018.6169. PMID: 30541736; PMCID: PMC6354544.	Wrong outcome
91	Tan TQ. Asthma and Invasive Pneumococcal Disease in the Age of Pneumococcal Conjugate Vaccines. Pediatrics. 2020 Jan;145(1):e20193360. doi: 10.1542/peds.2019-3360. Epub 2019 Dec 16. PMID: 31843862.	Wrong publication type
92	Theilacker C, Vyse A, Jodar L, Gessner BD. Evaluations of the Public Health Impact of Adult Vaccination with Pneumococcal Vaccines Should Include Reductions in All-Cause Pneumonia. Clin Infect Dis.	Wrong drug

	2020 May 23;70(11):2456-2457. doi: 10.1093/cid/ciz882. PMID: 31624826.	
93	Tiley KS, Ratcliffe H, Voysey M, Jefferies K, Sinclair G, Carr M, Colin-Jones R, Smith D, Bowman J, Hart T, Kandasamy R, Hinds J, Gould K, Berbers G, Tcherniaeva I, Robinson H, Plested E, Aley P, Snape MD. Nasopharyngeal Carriage of Pneumococcus in Children in England up to 10 Years After 13-Valent Pneumococcal Conjugate Vaccine Introduction: Persistence of Serotypes 3 and 19A and Emergence of 7C. J Infect Dis. 2023 Mar 1;227(5):610-621. doi: 10.1093/infdis/jiac376. PMID: 36130327; PMCID: PMC9978316.	Wrong outcome
94	Van Buynder P. Reducing pneumococcal risk in people aged 65 years and over. Medicine Today 2019 20:3 (11-14)	Background article
95	van de Garde MDB, Knol MJ, Rots NY, van Baarle D, van Els CACM. Vaccines to Protect Older Adults against Pneumococcal Disease. Interdiscip Top Gerontol Geriatr. 2020;43:113-130. doi: 10.1159/000504490. Epub 2020 Apr 9. PMID: 32294656.	Background article
96	van der Linden M. The real impact of pneumococcal conjugate vaccines. Lancet Child Adolesc Health. 2018 Aug;2(8):544-545. doi: 10.1016/S2352-4642(18)30183-4. Epub 2018 Jun 19. PMID: 30119707.	Wrong drug
97	Vietri, J.; Meyers, K.; Poulos, C.; Chilson, E.; Sweeney, C.; Davis, K.; Snow, V. United States Healthcare Provider Preferences for Adult Pneumococcal Vaccine Recommendations. Open Forum Infectious Diseases 2021 8:SUPPL 1 (S127). Doi: 10.1093/ofid/ofab466.209	Wrong outcome
98	Vivancos-Gallego MJ, Muriel A, Serrano-Villar S, Moreno-Zamora A, Pérez-Elías MJ, Quereda C, Casado JL, Sánchez-Conde M, Del Campo S, Dronda F, Sánchez-Díaz AM, Valencia-Martín JL, Moreno S. Pneumococcal vaccination in adult people living with HIV on suppressive antiretroviral therapy: a case-control study. Int J STD AIDS. 2020 Feb;31(2):174-182. doi: 10.1177/0956462419882128. Epub 2019 Dec 22. PMID: 31865862.	Wrong drug
99	Wateska AR, Nowalk MP, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK, Smith KJ. Cost-Effectiveness of Pneumococcal Vaccination and Uptake Improvement Programs in Underserved and General Population Adults Aged < 65 Years. J Community Health. 2020 Feb;45(1):111-120. doi: 10.1007/s10900-019-00716-8. PMID: 31401746; PMCID: PMC6957758.	Wrong drug
100	Wateska AR, Nowalk MP, Lin CJ, Zimmerman RK. COST EFFECTIVENESS OF NEWLY RECOMMENDED PNEUMOCOCCAL VACCINATION STRATEGIES IN OLDER UNDERSERVED MINORITY ADULTS IN THE US: KEEP IT SIMPLE Kenneth J. Smith1. Journal of General Internal Medicine 2022 37 (S252-S253) Supplement 2. doi: 10.1007/s11606-022-07653-8	Wrong publication type
101	Wateska AR, Patricia Nowalk M, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK, Smith KJ. Cost-effectiveness of revised US pneumococcal vaccination recommendations in underserved minority adults < 65-years-old. Vaccine. 2022 Nov 28;40(50):7312-7320. doi: 10.1016/j.vaccine.2022.10.066. Epub 2022 Nov 3. PMID: 36336526; PMCID: PMC9999373.	Wrong outcome
102	Weinberger DM, Harboe ZB, Shapiro ED. Developing Better Pneumococcal Vaccines for Adults. JAMA Intern Med. 2017 Mar	Background article

	1;177(3):303-304. doi: 10.1001/jamainternmed.2016.8289. PMID: 28099668; PMCID: PMC5568894.	
103	Weinberger DM, Shapiro ED. Pneumococcal Vaccines for Adults: What's Next? Clin Infect Dis. 2020 Jun 10;70(12):2493-2495. doi: 10.1093/cid/ciz743. PMID: 31402388.	Background article
104	Weinberger DM, Shapiro ED. Prevention of Pneumococcal Infections in Adults Using Conjugate Vaccines: No Easy Answers. Clin Infect Dis. 2019 Jun 18;69(1):50-51. doi: 10.1093/cid/ciy873. PMID: 30312380; PMCID: PMC6579952.	Wrong drug
105	Welte T. Pneumococcal Conjugate Vaccine--Equally Effective for Everyone? Dtsch Arztebl Int. 2016 Mar 4;113(9):137-8. doi: 10.3238/arztebl.2016.0137. PMID: 26987461; PMCID: PMC4802350.	Wrong drug
106	Womack J, Kropa J. Community-Acquired Pneumonia in Adults: Rapid Evidence Review. American Family Physician 2022 105:6 (625-630)	Wrong study design
107	Yin M, Huang L, Zhang Y, Yu N, Xu X, Liang Y, Ni J. Effectiveness and safety of dual influenza and pneumococcal vaccination versus separate administration or no vaccination in older adults: a meta-analysis. Expert Rev Vaccines. 2018 Jul;17(7):653-663. doi: 10.1080/14760584.2018.1495077. Epub 2018 Jul 16. PMID: 29961353.	Wrong drug
108	Pneumococcal conjugate vaccine: Do not routinely vaccinate adults aged 65 years and older. Prescrire International 2016 25:172 (157-158).	Wrong drug
109	Two New Pneumococcal Vaccines-Prevnar 20 and Vaxneuvance. JAMA. 2021 Dec 28;326(24):2521-2522. doi: 10.1001/jama.2021.22119. PMID: 34962532.	Background article

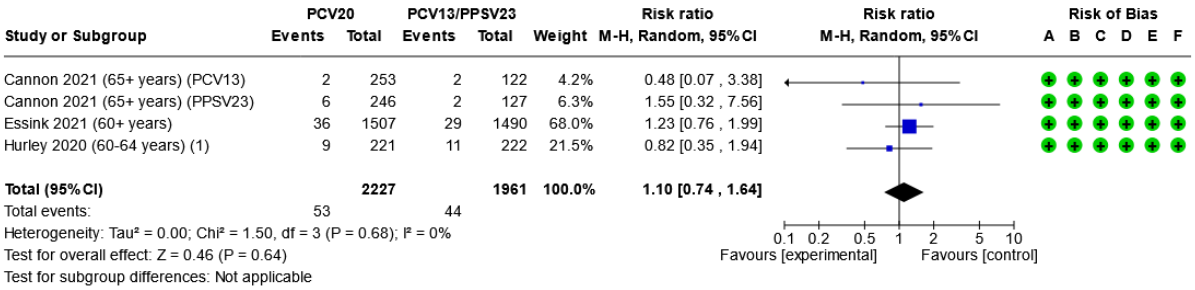
4. Sicherheitsdaten von PCV20 nach Endpunkt und Subgruppe

4.1 Mortalität

	PCV20 Events	PCV20 Total	Control Events	Control Total
Altersgruppe 18-59 Jahre	0	2.132	0	468
Altersgruppe ≥ 60 Jahre	1	2.227	0	1.961
Total	**1**	**4.359**	**0**	**2.429**

4.2 Schwere unerwünschte Ereignisse (SAE)

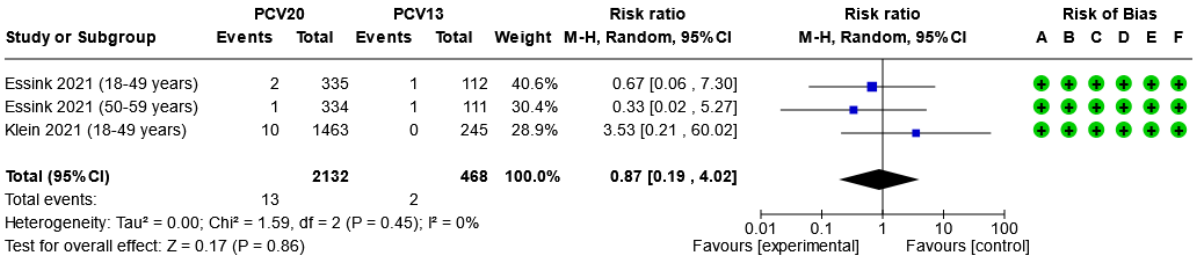
≥ 60 Jahre



Footnotes
(1) Follow-up periode after vaccination for SAE was 12 months

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

18-59 Jahre



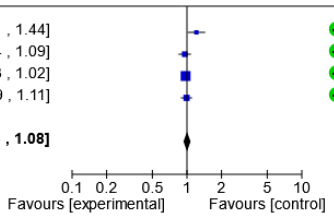
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

4.3 Andere unerwünschte Ereignisse (AE)

≥ 60 Jahre

Study or Subgroup	PCV20 Events	PCV20 Total	PCV13 Events	PCV13 Total	Weight	Risk ratio M-H, Random, 95% CI
Cannon 2021 (65+ years)	173	253	69	122	12.5%	1.21 [1.01 , 1.44]
Cannon 2021 (65+ years) (PPSV23) (1)	178	246	96	127	20.2%	0.96 [0.84 , 1.09]
Essink 2021 (60+ years)	1047	1507	1063	1490	44.1%	0.97 [0.93 , 1.02]
Hurley 2020 (60-64 years)	162	221	164	222	23.2%	0.99 [0.89 , 1.11]
Total (95% CI)		**2227**		**1961**	**100.0%**	**1.00 [0.93 , 1.08]**
Total events:	1560		1392			

Heterogeneity: Tau² = 0.00; Chi² = 5.67, df = 3 (P = 0.13); I² = 47%
Test for overall effect: Z = 0.04 (P = 0.97)
Test for subgroup differences: Not applicable



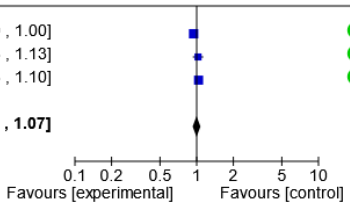
Footnotes
(1) Comparison group received PPSV23

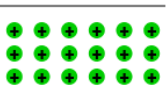
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

18-59 Jahre

Study or Subgroup	PCV20 Events	PCV20 Total	PCV13 Events	PCV13 Total	Weight	Risk ratio M-H, Random, 95% CI
Essink 2021 (18-49 years)	302	335	107	112	37.9%	0.94 [0.89 , 1.00]
Essink 2021 (50-59 years)	281	334	91	111	25.6%	1.03 [0.93 , 1.13]
Klein 2021 (18-49 years)	1275	1463	206	245	36.6%	1.04 [0.98 , 1.10]
Total (95% CI)		**2132**		**468**	**100.0%**	**1.00 [0.93 , 1.07]**
Total events:	1858		404			

Heterogeneity: Tau² = 0.00; Chi² = 7.24, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 0.06 (P = 0.95)
Test for subgroup differences: Not applicable



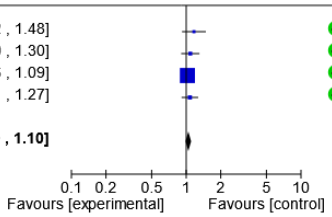


Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

4.4 Schmerzen an der Einstichstelle

≥ 60 Jahre

Study or Subgroup	PCV20 Events	PCV20 Total	PCV13 Events	PCV13 Total	Weight	Risk ratio M-H, Random, 95% CI
Cannon 2021 (65+ years)	127	253	52	121	5.5%	1.17 [0.92 , 1.48]
Cannon 2021 (65+ years) (PPSV23) (1)	150	245	71	126	9.4%	1.09 [0.90 , 1.30]
Essink 2021 (60+ years)	834	1505	802	1483	73.8%	1.02 [0.96 , 1.09]
Hurley 2020 (60-64 years)	127	220	119	222	11.3%	1.08 [0.91 , 1.27]
Total (95% CI)		**2223**		**1952**	**100.0%**	**1.04 [0.99 , 1.10]**
Total events:	1238		1044			



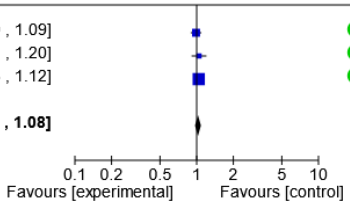
Heterogeneity: Tau² = 0.00; Chi² = 1.48, df = 3 (P = 0.69); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Not applicable

Footnotes
(1) Comparison group received PPSV23

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

18-59 Jahre

Study or Subgroup	PCV20 Events	PCV20 Total	PCV13 Events	PCV13 Total	Weight	Risk ratio M-H, Random, 95% CI
Essink 2021 (18-49 years)	272	335	92	112	30.7%	0.99 [0.89 , 1.09]
Essink 2021 (50-59 years)	240	331	77	111	15.7%	1.05 [0.91 , 1.20]
Klein 2021 (18-49 years)	1146	1456	184	243	53.6%	1.04 [0.96 , 1.12]
Total (95% CI)		**2122**		**466**	**100.0%**	**1.02 [0.97 , 1.08]**
Total events:	1658		353			

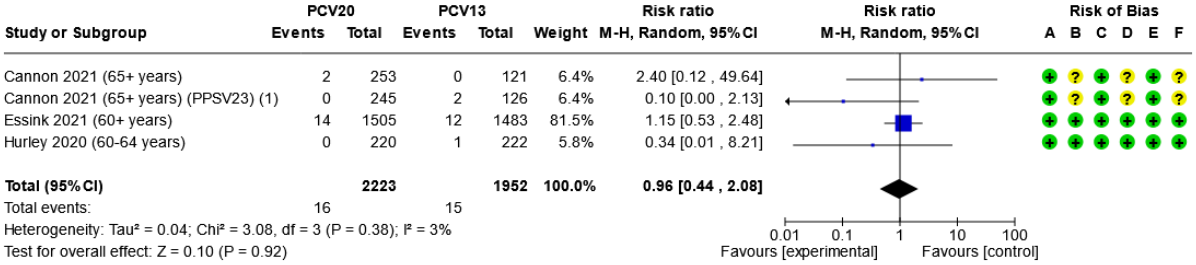


Heterogeneity: Tau² = 0.00; Chi² = 0.72, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.85 (P = 0.40)
Test for subgroup differences: Not applicable

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

4.5 Fieber ≥ 38°C

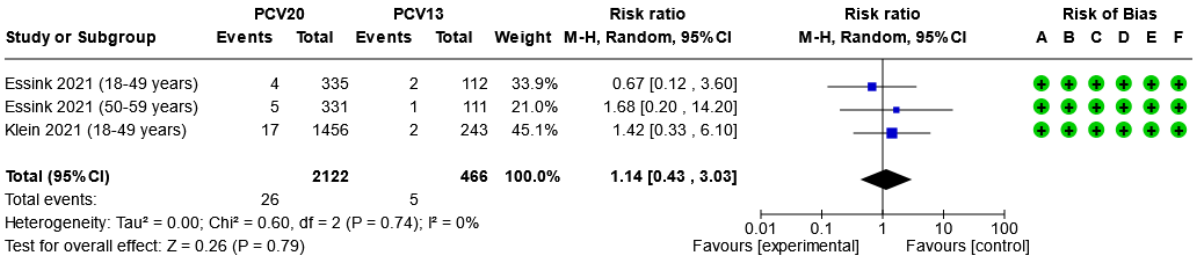
≥ 60 Jahre



Footnotes
(1) Comparison group received PPSV23

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

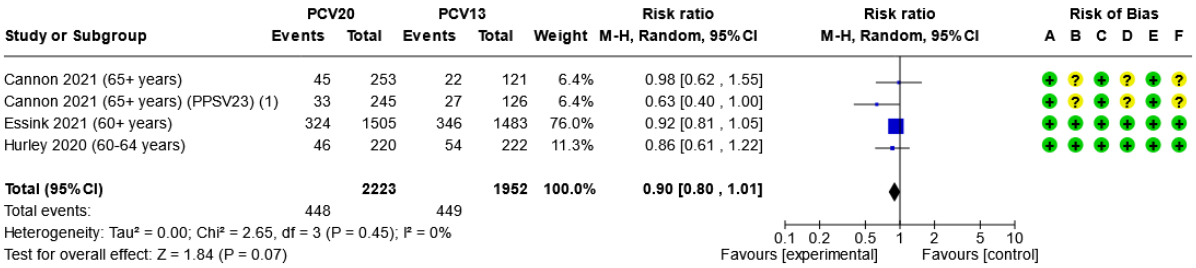
18-59 Jahre



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

4.6 Kopfschmerzen

≥ 60 Jahre



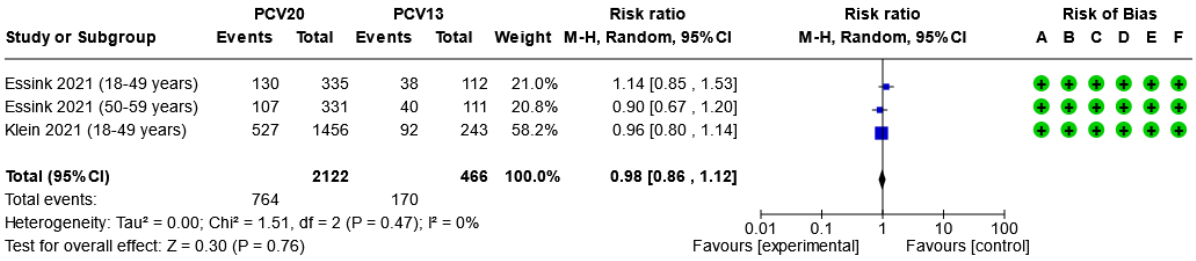
Footnotes

(1) Comparison group received PPSV23

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

18-59 Jahre

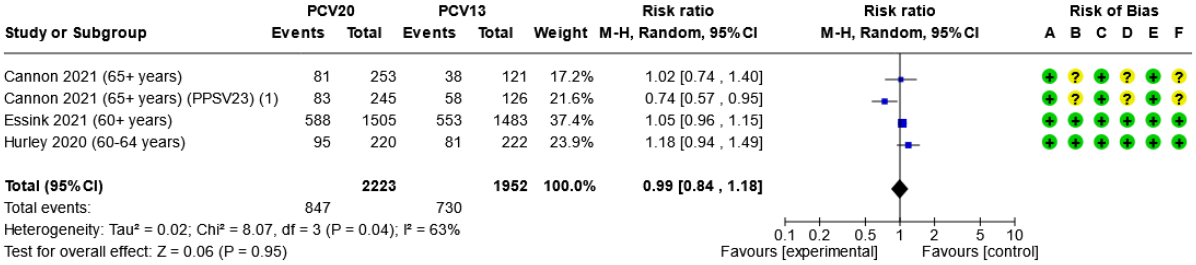


Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

4.7 Muskel- oder Gliederschmerzen

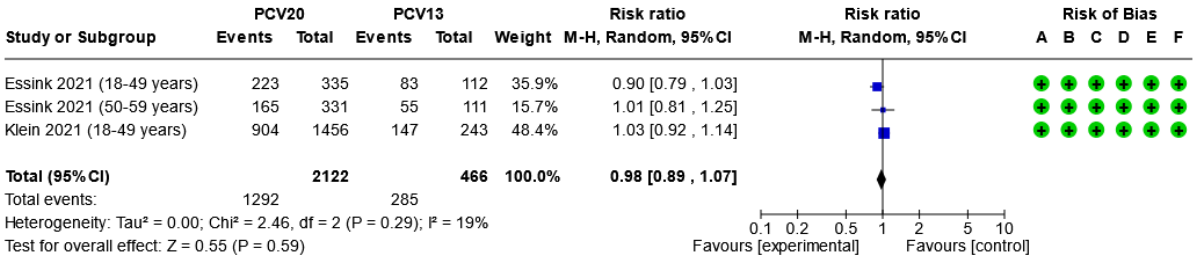
≥ 60 Jahre



Footnotes
(1) Comparison group received PPSV23

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

18-59 Jahre



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

5. Immunogenitätsdaten von PCV20

5.1 Geometric Mean Ratio (GMR) und 95% Konfidenzintervall (KI) für den Vergleich der ausgelösten Immunreaktion von PCV20 gegenüber PCV13

Serotyp	Studie	GMR	Unteres 95% KI	Oberes 95% KI
1	Essink_2021	0,8	0,71	0,9
	Hurley_2020	0,68	0,47	0,94
	Klein_2021	0,71	0,58	0,87
3	Essink_2021	0,85	0,78	0,93
	Hurley_2020	0,81	0,62	1,02
	Klein_2021	0,89	0,77	1,03
4	Essink_2021	0,81	0,71	0,93
	Hurley_2020	0,77	0,53	1,1
	Klein_2021	0,81	0,66	1,01
5	Essink_2021	0,83	0,74	0,94
	Hurley_2020	0,68	0,48	0,94
	Klein_2021	0,69	0,57	0,85
6A	Essink_2021	0,76	0,66	0,88
	Hurley_2020	0,8	0,54	1,13
	Klein_2021	0,91	0,75	1,12
6B	Essink_2021	0,83	0,73	0,95
	Hurley_2020	0,92	0,64	1,27
	Klein_2021	0,89	0,73	1,09
7F	Essink_2021	0,86	0,77	0,96
	Hurley_2020	0,82	0,66	1,02
	Klein_2021	0,81	0,67	0,99
9V	Essink_2021	0,93	0,82	1,05
	Hurley_2020	0,73	0,54	0,96
	Klein_2021	0,91	0,76	1,1
14	Essink_2021	1	0,89	1,13
	Hurley_2020	0,88	0,64	1,18
	Klein_2021	1	0,83	1,2
18C	Essink_2021	0,85	0,74	0,97
	Hurley_2020	0,81	0,58	1,09
	Klein_2021	0,87	0,7	1,09
19A	Essink_2021	0,8	0,71	0,9
	Hurley_2020	0,84	0,64	1,08
	Klein_2021	0,87	0,73	1,03
19F	Essink_2021	0,8	0,7	0,91
	Hurley_2020	0,63	0,43	0,88
	Klein_2021	0,67	0,54	0,83
23F	Essink_2021	0,83	0,7	0,97
	Hurley_2020	0,82	0,51	1,25
	Klein_2021	0,96	0,74	1,23

5.2 Geometric Mean Ratio (GMR) und 95% Konfidenzintervall (KI) für den Vergleich der ausgelösten Immunreaktion von PCV20 gegenüber PPSV23

Serotyp	Studie	GMR	Unteres 95% KI	Oberes 95% KI
8	Essink_2021	0,55	0,49	0,62
	Hurley_2020	0,65	0,48	0,86
10A	Essink_2021	1,86	1,63	2,12
	Hurley_2020	2,68	1,82	3,81
11A	Essink_2021	1,75	1,52	2,01
	Hurley_2020	1,08	0,8	1,43
12F	Essink_2021	1,48	1,27	1,72
	Hurley_2020	1,56	1,03	2,28
15B	Essink_2021	3,12	2,62	3,71
	Hurley_2020	2,68	1,74	3,94
22F	Essink_2021	1,99	1,7	2,32
	Hurley_2020	1,81	1,31	2,44
33F	Essink_2021	1,38	1,21	1,57
	Hurley_2020	1,44	1,02	1,97

6. GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) Evidenzprofile und "summary of findings"-Tabellen

6.1 PCV20 im Vergleich zu PPSV23 und/oder PCV13 für Personen ≥ 60 Jahre

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With PPSV23 and/or PCV13	With PCV20		Risk with PPSV23 and/or PCV13	Risk difference with PCV20
Serious Adverse Events (follow-up: 6 months)											
4188 (3 RCTs)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	44/1961 (2.2%)	53/2227 (2.4%)	**RR 1.10** (0.74 to 1.64)	22 per 1.000	**2 more per 1.000** (from 6 fewer to 14 more)
Fever ≥ 38°C (follow-up: 7 days)											
4175 (3 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	15/1952 (0.8%)	16/2223 (0.7%)	**RR 0.96** (0.44 to 2.08)	8 per 1.000	**0 fewer per 1.000** (from 4 fewer to 8 more)
Headache (follow-up: 7 days)											

Certainty assessment							Summary of findings				
4175 (3 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	449/1952 (23.0%)	448/2223 (20.2%)	**RR 0.90** (0.80 to 1.01)	230 per 1.000	**23 fewer per 1.000** (from 46 fewer to 2 more)

Immunogenicity (follow-up: 1 month)

3273 (2 RCTs)	serious[b]	not serious	serious[c]	not serious	none	⨁⨁◯◯ Low	1628	1645	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Sample size too small to detect rare or very rare events. (Rare events: 1 in 1000 – 1 in 10,000; 0.01% to 0.1%; very rare: <1 in 10,000; < 0.01%.)

b. Large percentage of missing data on OPA results for some serotypes.

c. No data on VE. Immunogenicity as surrogate but without clear limit of protection.

6.2 PCV20 im Vergleich zu PCV13 für Personen 18-59 Jahre

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With PCV13	With PCV20		Risk with PCV13	Risk difference with PCV20
Serious Adverse Events (follow-up: 6 months)											
2600 (2 RCTs)	not serious	not serious	serious[a]	serious[b]	none	⨁⨁◯◯ Low	2/468 (0.4%)	13/2132 (0.6%)	**RR 0.87** (0.19 to 4.02)	4 per 1.000	**1 fewer per 1.000** (from 3 fewer to 13 more)
Fever ≥ 38°C (follow-up: 7 days)											
2588 (2 RCTs)	not serious	not serious	serious[a]	not serious	none	⨁⨁⨁◯ Moderate	5/466 (1.1%)	26/2122 (1.2%)	**RR 1.14** (0.43 to 3.03)	11 per 1.000	**2 more per 1.000** (from 6 fewer to 22 more)
Headache (follow-up: 7 days)											
2588 (2 RCTs)	not serious	not serious	serious[a]	not serious	none	⨁⨁⨁◯ Moderate	170/466 (36.5%)	764/2122 (36.0%)	**RR 0.98** (0.86 to 1.12)	365 per 1.000	**7 fewer per 1.000** (from 51 fewer to 44 more)
Immunogenicity (follow-up: 1 month)											
1618 (1 RCT)	serious[c]	not serious	very serious[a,d]	not serious	none	⨁◯◯◯ Very low	232	1386	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Data only available for healthy persons without comorbidities.

b. Sample size too small to detect rare or very rare events. (Rare events: 1 in 1000 – 1 in 10,000; 0.01% to 0.1%; very rare: <1 in 10,000; < 0.01%.)

c. Large percentage of missing data on OPA results for some serotypes.

d. No data on VE. Immunogenicity as surrogate but without clear limit of protection.

7. Evidence-to-Decision (EtD)-Tabellen

7.1 Soll PCV20 für die Impfung von Personen ≥ 60 Jahre empfohlen werden?

Shall PCV20 replace PPSV23 for people aged ≥ 60 years?

Goal of vaccination: Reduction of burden of IPD and its consequences such as hospitalization, disability and death in people aged ≥ 60 years

<table>
<tr><th colspan="2">Criteria</th><th>Judgments</th><th colspan="4">Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is the problem a priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td colspan="4">National office of statistic data (destatis)
- Hospitalizations due to pneumococcal pneumonia:
- Annual mean 2007-2019: N=2,674
- Annual mean age standardized incidence: 3.2/100.000 inhabitants
- Highest incidence in elderly population
- Hospitalizations due to pneumococcal sepsis:
- Annual mean 2007-2019: N=2,417;
- Annual mean age standardized incidence: 2.9/100.000 inhabitants
- Highest incidence in elderly population
- Deaths due to pneumococcal pneumonia/sepsis/meningitis: annual mean 2007-19: N= 130
- From age 55 rise in mortality, most death occur in people aged ≥ 60 years</td><td>- Degree of underestimation of IPD and death due to IPD in National office of statistic data unknown
- for Germany no nationwide data on non-hospitalized cases available
- mandatory notification of invasive pneumococcal disease in Germany was issued in March 2020; implementation is ongoing</td></tr>
<tr><td>Benefits and harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
○ Moderate
○ High</td><td colspan="4"><table><tr><th>Outcome</th><th>Relative importance</th><th>GRADE</th></tr><tr><td>VE</td><td></td><td></td></tr><tr><td>Prevention of IPD</td><td>critical</td><td rowspan="3">No evidence available</td></tr><tr><td>Prevention of pneumococcal pneumonia</td><td>critical</td></tr><tr><td>Prevention of deaths due to IPD</td><td>critical</td></tr><tr><td>Immunogenicity[1]</td><td>critical</td><td>Low</td></tr><tr><td>Safety</td><td></td><td></td></tr><tr><td>Fever</td><td>important</td><td>High</td></tr><tr><td>Headache</td><td>important</td><td>High</td></tr><tr><td>SAE[2]</td><td>important</td><td>Moderate</td></tr></table></td><td>- PCV20 Studies provide data on people aged ≥ 60 and 18-59 years separately</td></tr>
</table>

			[1] Downgrading due to indirectness of immunogenicity parameters for vaccine effectiveness and due to large percentage of missing data on OPA results for some serotypes. [2] Downgrading due to small number of individuals in studies which makes it impossible to detect rare SAE.	
	Is there important uncertainty about how much people value the main outcomes?	○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes		

	Are the desirable anticipated effects large?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	**<u>Vaccine effectiveness (VE)</u>:** no information **<u>Immunogenicity</u>**: non-inferiority to PCV13 or PPSV23 shown, except for Serotype 8 **<u>Modelling data</u>:** considerable positive effects of switch from PPSV23 to PCV20 in the elderly, while PCV13 is used in infant program (scenario I). Effects are reduced by approximately 70% when PCV20 is used in infant program instead of PCV13 (scenario II). <u>Scenario I</u>: **infant program with PCV13**, vaccination coverage in people aged ≥ 60 years: 30% When switching from PPSV23 to PCV20 (the numbers refer to lifetime effects in 10 age cohorts vaccinated between 2024 and 2033): - additional **IPD cases** prevented: +98% - additional **hospitalized pneumonia cases** prevented: +173% - additional **death** prevented: +157% <u>Number needed to vaccinate (NNV) to prevent one hospitalization due to IPD or Pneumonia:</u> - PPSV23: 742 - PCV20: 301 <u>NNV to prevent 1 death due to IPD or Pneumonia:</u> - PPSV23: 5,935 - PCV20: 2,308 <u>Scenario II</u>: **infant program with PCV20** (PCV20 replaces PCV13 in January 2024), vaccination coverage in people aged ≥ 60 years: 30% When switching from PPSV23 to PCV20 (the numbers refer to lifetime effects in 10 age cohorts vaccinated between 2024 and 2033): - additional **IPD cases** prevented: +52% - additional **hospitalized pneumonia cases** prevented: +92% - additional **death** prevented: +86% <u>NNV to prevent one hospitalization due to IPD or Pneumonia:</u> - PPSV23: 1,339 - PCV20: 754 <u>NNV to prevent 1 death by due to IPD or Pneumonia:</u> - PPSV23: 10,722 - PCV20: 5,752	- No VE data, immunogenicity data as proxy/surrogate

<table>
<tr><td></td><td>Are the undesirable anticipated effects small?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td colspan="2">Meta-analysis performed, using 3 RCTs
<table><tr><th rowspan="2">Outcome</th><th colspan="2">PV20 group</th><th colspan="2">PCV13/PPSV23 group</th><th rowspan="2">Risk Ratio (95% CI)</th></tr><tr><th>included individuals</th><th>number of events</th><th>included individuals</th><th>number of events</th></tr><tr><td>Serious Adverse Events (SAE)</td><td>2,227</td><td>53*</td><td>1,961</td><td>44*</td><td>1.10 (0.74 – 1.64)</td></tr><tr><td>fever ≥ 38° C</td><td>2,223</td><td>16</td><td>1,952</td><td>15</td><td>0.96 (0.44 – 2.08)</td></tr><tr><td>headache</td><td>2,223</td><td>448</td><td>1,952</td><td>449</td><td>0.90 (0.80 – 1.01)</td></tr><tr><td>mortality</td><td>2,227</td><td>1*</td><td>1,961</td><td>0</td><td>-</td></tr></table>*none of the reported events were judged to be vaccine related.

Overall number of included individuals in safety analysis too small to detect rare events. PCV20 was well tolerated, no evidence for relevant safety differences between PCV20 and PCV13 and/or PPSV23 in people aged ≥ 60 years.</td></tr>
<tr><td></td><td>Are the desirable effects large relative to undesirable effects?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td colspan="2"></td></tr>
<tr><td>Resource use</td><td>Are the resources required small?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td colspan="2" rowspan="2">Cost effectiveness analysis:
- Price for PCV20 is estimated to be approximately 200% higher than price for PPSV23
<u>Scenario I:</u>
- Additional public cost per quality-adjusted life year (QALY) gained when switching from PPSV23 to PCV20: 12,281 EUR/QALY
<u>Scenario II</u>:
- Additional public cost per quality-adjusted life year (QALY) gained when switching from PPSV23 to PCV20: 45,690 EUR/QALY</td></tr>
<tr><td></td><td>Is the incremental cost small relative to the net benefits?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td></tr>
</table>

Equity	What would be the impact on health inequities?	- Increased - Probably increased - Uncertain - Probably reduced - Reduced - Varies	○ Vaccination with both vaccines are covered by health insurance. ○ PCV20 confers better protection of vulnerable group (elderly) thus it improves equity	

Acceptability	Is the option acceptable to key stakeholders?	○ No
		○ Probably no
		○ Uncertain
		○ Probably yes
		○ Yes
		○ Varies
			- Currently recommendation not well implemented: low vaccination coverage (2022):
			  - Age 60 years: 3.2%
			  - Age 60-74 years: 23.3%
			  - Age 74 years: 41.9%
			- Vaccination coverage in elderly also low for other vaccines.
			- Anticipated improvement of acceptability by doctors due to simpler recommendation (same vaccine for all) and preference of doctors for conjugate vaccines
				- What can be done to improve compliance?

Feasibility	Is the option feasible to implement?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	- Coadministration with adjuvanted influenza vaccine and mRNA-covid-19 vaccines possible - No data on coadministration with influenza high dose vaccine - Use of only 1 vaccine for all makes communication and implementation easier (storage of only one vaccine type)	

Recommendation	**Shall PCV20 replace PPSV23 for people aged ≥ 60?**				
Balance of consequences	Undesirable consequences clearly outweigh desirable consequences	Undesirable consequences probably outweigh desirable consequences	The balance between desirable and undesirable consequences is closely balanced or uncertain	Desirable consequences probably outweigh undesirable consequences	Desirable consequences clearly outweigh undesirable consequences
	○	○	○	○	○ X
Recommendation	Vaccination with PCV20 as standard vaccination for people aged ≥ 60 years				
Justification	Mathematical modelling suggests that vaccination with PCV20 prevents more IPD cases and deaths than vaccination with PPSV23 in the elderly while having a similar safety profile.				

Subgroup considerations	- In case of a shortage, vaccination with PCV20 should be postponed - Depending on the duration and the patient's risk profile, it may make sense not to wait but to use PPSV23 or PCV15. In both cases, if PCV20 is again available, sequential vaccination at a minimum interval of 1 year should be considered. - Persons aged ≥ 60 years, who have already received PPSV23 should receive PCV20 earliest 6 years after PPSV23 - No information can currently be given on the need for repeat vaccinations after PCV20
Implementation considerations	Coadministration with COVID-19 mRNA vaccines or influenza vaccines is possible
Monitoring and evaluation	- PCV coverage is regularly analyzed by "RKI Impfsurveillance" in people ≥ 60 years - Use of national surveillance data to measure impact of recommendation on IPD incidence - Surveillance of Pau-Ehrlich-Institute (PEI) for safety signals of PCV20 - Close monitoring of serotype distribution and replacement effects on a national/international level
Research priorities	- Studies investigating duration of protection of PCV20 - Clinical vaccine effectiveness studies - Further development of pneumococcal vaccines in order to provide better protection from serotype 3 or serotype independent protection

7.2 Soll PCV20 für die Impfung von Personen 18-59 Jahren mit Grunderkrankungen empfohlen werden?

What is the additional benefit of sequential vaccination (PCV20+PPSV23) compared with PCV20 only for adults with underlying medical conditions?

Goal of vaccination: Reduction of burden of IPD and its consequences such as hospitalization, disability and death in persons with underlying medical conditions.

<table>
<tr><th colspan="2">Criteria</th><th>Judgments</th><th>Research evidence</th><th>Additional considerations</th></tr>
<tr><td>Problem</td><td>Is the problem a priority?</td><td>○ No
○ Probably no
○ Uncertain
○ Probably yes
○ Yes
○ Varies</td><td>National office of statistics data (destatis) provides no specific data on persons with underlying medical conditions
- Risk groups defined in EpidBull 37/2016:
1. Persons with congenital or acquired immunodeficiencies or immunosuppression
2. People with other chronic diseases
3. Anatomical and foreign body-associated risks for pneumococcal meningitis
- STIKO has not performed new evidence searches on risk groups for severe disease
- Indication groups remain the same as for previous recommendation</td><td>- for Germany no nationwide data on non-hospitalized cases available
- mandatory notification of invasive pneumococcal disease in Germany was issued in March 2020; implementation is ongoing</td></tr>
<tr><td>Benefits and harms of the options</td><td>What is the overall certainty of this evidence?</td><td>○ No included studies
○ Very low
○ Low
○ Moderate
○ High</td><td>
<table>
<tr><th>Outcome</th><th>Relative importance</th><th>GRADE</th></tr>
<tr><td>VE</td><td></td><td></td></tr>
<tr><td>Prevention of IPD</td><td>critical</td><td rowspan="3">No evidence available</td></tr>
<tr><td>Prevention of pneumococcus pneumonia</td><td>critical</td></tr>
<tr><td>Prevention of deaths due to IPD</td><td>critical</td></tr>
<tr><td>Immunogenicity[1]</td><td>critical</td><td>Very low</td></tr>
<tr><td>Safety</td><td></td><td></td></tr>
<tr><td>Fever</td><td>important</td><td>Moderate</td></tr>
<tr><td>Headache</td><td>important</td><td>Moderate</td></tr>
<tr><td>SAE[2]</td><td>important</td><td>Low</td></tr>
</table>
</td><td>- PCV20 Studies provide data on people aged ≥ 60 and 18-59 years separately</td></tr>
</table>

			[1] Downgrading due to indirectness of immunogenicity parameters for vaccine effectiveness, for indirectness regarding study population without underlying medical conditions, and due to large percentage of missing data on OPA results for some serotypes. [2] Downgrading due to small number of individuals in studies which makes it impossible to detect rare SAE.	
	Is there important uncertainty about how much people value the main outcomes?	○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes		

	Are the desirable anticipated effects large?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	**<u>Vaccine effectiveness (VE):</u>** no information **<u>Immunogenicity</u>**: non-inferiority of PCV20 to PCV13 shown **<u>Modelling data</u>:** The additional beneficial effect of a sequential vaccination (PCV20 + PPSV23) is small compared to PCV20 only, when PCV13 is used in the infant routine program (scenario I). The additional benefit of the 3 serotypes in PPSV23 and thus of a sequential vaccination becomes more apparent when infants are routinely vaccinated with PCV20 (scenario II). NNV of sequential vaccination for prevention of one IPD case or one death is about 15 times higher than NNV of PCV20 only in scenario I and less than 5 times higher in scenario II. <u>Scenario I</u>: **infant program with PCV13**, vaccination coverage in adults: 30% Comparison sequential vaccination PCV20+ PPSV23 to PCV20 only (the numbers refer to lifetime effects in 10 age cohorts vaccinated between 2024 and 2033): - additional **IPD cases** prevented: +9% compared with PCV20 only - additional **hospitalized pneumonia cases** prevented: +7% compared with PCV20 only - additional **death** prevented: +7% compared with PCV20 only <u>Number needed to vaccinate (NNV) to prevent one hospitalization due to IPD or Pneumonia:</u> - PCV20: 301 - for the additional PPSV23 dose: 4,046 <u>NNV to prevent 1 death due to IPD or Pneumonia:</u> - PCV20: 2,308 - for the additional PPSV23 dose: 31,900 <u>Scenario II</u>: **infant program with PCV20**, vaccination coverage in adults: 30% Comparison sequential vaccination PCV20+ PPSV23 to PCV20 only (the numbers refer to lifetime effects in 10 age cohorts vaccinated between 2024 and 2033):	- Immunocompromised and people with unstable underlying medical conditions were excluded from studies - Modeling results are based on a comparison of vaccine effects in non-immunocompromised people. It is expected that the effectiveness of PPSV23 in immunocompromised people is substantially reduced and thus the benefits of sequential vaccination much smaller than in non-immunocompromised people. Absolute additional effects of sequential vaccination are only slightly higher than in scenario I but the effects of PCV20 only are substantially lower than in scenario I. Hence, NNVs to prevent one hospitalization or one death for the additional dose of PPSV23 are still considerably higher than for PCV20 only.

- additional **IPD cases** prevented: +31% compared with PCV20 only
- additional **hospitalized pneumonia cases** prevented: +26% compared with PCV20 only
- additional **death** prevented: +27% compared with PCV20 only

<u>NNV to prevent one hospitalization due to IPD or Pneumonia:</u>
- PCV20: 754
- for the additional PPSV23 dose: 2,740

<u>NNV to prevent 1 death by due to IPD or Pneumonia:</u>
- PCV20: 5,752
- for the additional PPSV23 dose: 21,589

Are the undesirable anticipated effects small?

- o No
- o Probably no
- o Uncertain
- o Probably yes
- o Yes
- o Varies

Meta-analysis performed, using 2 RCTs

outcome	**PV20 group**		**PCV13 group**		**Risk Ratio (95% CI)**
	included individuals	**number of events**	**included individuals**	**number of events**	
Serious Adverse Events (SAE)	2,132	13*	468	2*	0.87 (0,19 – 4.02)
fever ≥ 38° C	2,122	26	466	5	1.14 (0,43 – 3,03)
headache	2,122	764	466	170	0.98 (0.86 – 1,12)
mortality	2,132	0	468	0	-

*none of the reported events were judged to be vaccine related

Overall number of included individuals in safety analysis too small to detect rare events. PCV20 was well tolerated, no evidence for relevant safety differences between PCV20 and PCV13 in adults aged 18-59 years.

Are the desirable effects large relative to undesirable effects?

- o No
- o Probably no
- o Uncertain
- o Probably yes
- o Yes
- o Varies

Resource use	Are the resources required small?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	**Cost effectiveness analysis:** - Price for PCV20 is estimated to be 10% higher than for PCV13 and more than 200% higher than price for PPSV23 - Cost of PCV20 lower than cost for sequential vaccination - <u>Scenario I:</u> - Additional public cost per quality-adjusted life year (QALY) gained when switching from PPSV23 to PCV20: 76,655 EUR/QALY - <u>Scenario II</u>: - Additional public cost per quality-adjusted life year (QALY) gained when switching from PPSV23 to PCV20: 50,861 EUR/QALY	- Cost effectiveness results are based on a comparison of vaccine effects in non-immunocompromised people. It is expected that the effectiveness of PPSV23 in immunocompromised people is substantially reduced and thus the cost-effectiveness of sequential vaccination much smaller than in non-immunocompromised people.
	Is the incremental cost small relative to the net benefits?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies		
Equity	What would be the impact on health inequities?	○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies	- Vaccination with both vaccines are covered by health insurance.	
Acceptability	Is the option acceptable to key stakeholders?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	- Currently recommendation not well implemented: low vaccination coverage - Adults with underlying condition aged 18-59 years (2022): 25.6% - Vaccination coverage in adults with underlying conditions also low for other vaccines. - Anticipated improvement of acceptability with simpler recommendation (same vaccine for all, only one appointment)	- What can be done to improve compliance?
Feasibility	Is the option feasible to implement?	○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies	- Coadministration with adjuvanted influenza vaccine and mRNA-covid-19 vaccines possible - No data on coadministration with other influenza vaccines - Use of only 1 vaccine for all makes communication and implementation easier (storage of only one vaccine type)	

Recommendation	Shall PCV20 replace sequential vaccination with PCV13+PPSV23 for adults with underlying conditions?				
Balance of consequences	Undesirable consequences clearly outweigh desirable consequences	Undesirable consequences probably outweigh desirable consequences	The balance between desirable and undesirable consequences is closely balanced or uncertain	Desirable consequences probably outweigh undesirable consequences	Desirable consequences clearly outweigh undesirable consequences
	○	○	○	○ X	○
Recommendation	Vaccination with PCV20 for adults with underlying conditions (no sequential vaccination any more)				
Justification	Mathematical modelling suggests a small additional beneficial effect of a sequential vaccination (PCV20 + PPSV23) compared to PCV20 only in adults. Acceptability is likely to be better when only one vaccination/appointment is needed.				
Subgroup considerations	- In case of a shortage, vaccination with PCV20 should be postponed - Depending on the duration and the patient's risk profile, it may make sense not to wait but to use PPSV23 or PCV15. In both cases, if PCV20 is again available, sequential vaccination at a minimum interval of 1 year should be considered. - Persons, who have already received PCV13+PPSV23 should receive PCV20 earliest 6 years after PPSV23. In the case of a pronounced immune deficiency, vaccination with PCV20 can be carried out in individual cases at least 1 year after the PPSV23 vaccination - No information can currently be given on the need for repeat vaccinations after PCV20				
Implementation considerations	Coadministration with COVID-19 mRNA vaccines or influenza vaccines is possible				
Monitoring and evaluation	- PCV coverage is regularly analyzed by “RKI Impfsurveillance” in adults with underlying conditions - Use of national surveillance data to measure impact of recommendation on IPD incidence - Surveillance of Pau-Ehrlich-Institute (PEI) for safety signals of PCV20 - Close monitoring of serotype distribution and replacement effects on a national international level undertaken by reference laboratories				
Research priorities	- Studies investigating duration of protection of PCV20 - Clinical vaccine effectiveness studies including persons 18-59 years with underlying medical conditions - Further development of pneumococcal vaccines in order to provide better protection from serotype 3 or serotype independent protection				