<table>
<thead>
<tr>
<th>Question</th>
<th>Answers</th>
</tr>
</thead>
</table>
| 1  Is the study randomized?                                              | a. Yes  
  b. Control group but not randomized  
  c. No control arm/group  
  d. Unclear  
  e. Not stated/Full text not available (ie. Poster or abstract)  
  f. Not applicable                                           |
| 2  Blinding of participants and personnel                               | a. Double-blind  
  b. Single-blind (either participants or study personnel)  
  c. Open label  
  d. Unclear  
  e. Not stated/Full text not available (ie. Poster or abstract)                                           |
| 3  Blinding of outcome assessment (e.g., specimens were tested without knowledge of pre/post PCV status or study arm) | a. Yes  
  b. No (.e., not blinded or no control arm for the relevant outcome of interest)  
  c. Unclear  
  d. Not stated/Full text not available (ie. Poster or abstract)                                           |
| 4  Incomplete outcome data (e.g., the percent of those randomized to those analyzed) | a. 90% or more of those randomized were included in the analysis of the relevant outcome of interest  
  b. Fewer than 90% were analyzed  
  c. Unclear  
  d. Not stated/Full text not available (ie. Poster or abstract)                                           |
| 5  Was industry (i.e., GSK or Pfizer) involved in this study?            | a. No  
  b. Yes, funded all or in part by Industry but conducted entirely by independent investigators  
   (e.g., no co-authors from industry; lab work not performed by Industry)  
  c. Yes, conducted all or in part by industry (e.g., analyses or lab work performed by Industry)  
  d. Unclear  
  e. Not stated/Full text not available (ie. Poster or abstract)                                           |
<p>| 6  Other Risk of Bias                                                     | Please comment on other factors that may introduce bias |</p>
<table>
<thead>
<tr>
<th>Reference (Author,Year)</th>
<th>Study Design</th>
<th>Study Details</th>
<th>Bias Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esposito, 2010</td>
<td>Double-blind, multicenter trial</td>
<td>Subjects were randomly assigned in a 1:1 ratio to one of the two vaccine groups. Treatment allocation was concealed from all subjects, study staff, and those assessing the outcomes.</td>
<td>Study was funded by a grant from Wyeth and several of the author affiliations listed are for Wyeth.</td>
</tr>
<tr>
<td>Jalal, 2004</td>
<td>Randomized controlled trial</td>
<td>The study was conducted in an open manner, as the participants from the different groups received the study vaccine according to different vaccination schedules.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Jos, 2016</td>
<td>Double-blind, multicenter trial</td>
<td>Study staff allocated participants with a participant number and randomly assigned a 4:4:5 ratio to receive PCV13 or PCV7 or no vaccine until age 10 and 11 months.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Tarantola, 2015</td>
<td>Double-blind, multicenter trial</td>
<td>Study staff members and parents were aware of the intervention.</td>
<td>Study was conducted in an open-label setting.</td>
</tr>
<tr>
<td>Van Weezenbeek, 2011</td>
<td>Open-label study</td>
<td>Laboratory staff were blind to intervention group assignment.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Stirn, 2015</td>
<td>Double-blind, multicenter trial</td>
<td>Study staff members and parents were aware of the child's allocated immunization schedule, but laboratory staff was not.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Weckx, 2012</td>
<td>Randomized controlled trial</td>
<td>Subjects were randomly assigned in a 1:1 ratio to receive PCV13+P80 or PCV13 without P80.</td>
<td>Randomization was performed by Pfizer’s Vaccine Research Clinical Testing Laboratory.</td>
</tr>
<tr>
<td>Martínón, 2015</td>
<td>Parallel-group study</td>
<td>Study staff members and parents were aware of the child’s allocated immunization schedule, but laboratory staff was not.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Spijkerman, 2013</td>
<td>Randomized controlled trial</td>
<td>Subjects were randomly assigned in a 1:1 ratio to receive PCV13+P80 or PCV13 without P80.</td>
<td>Randomization was performed by Pfizer’s Vaccine Research Clinical Testing Laboratory.</td>
</tr>
<tr>
<td>Aparicio, 2015</td>
<td>Double-blind, multicenter trial</td>
<td>Study staff members and parents were aware of the child’s allocated immunization schedule, but laboratory staff was not.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
<tr>
<td>Weckx, 2012</td>
<td>Double-blind, multicenter trial</td>
<td>Subjects were randomly assigned in a 1:1 ratio to receive PCV13+P80 or PCV13 without P80.</td>
<td>Study was conducted and funded by GSK.</td>
</tr>
</tbody>
</table>
1034 Martinón-Torres, 2012

- Subjects were randomly allocated to 1:1 ratio
- This was a double-blind, multicenter trial
- Not stated
- According to the text, 74.8% of the 449 randomized children were included for analysis after the blood draw
- Some authors are affiliated with Wyeth. Wyeth sponsored the study and contributed to the study’s design, data collection, analysis, etc.
- LOW

1077 Ooldijkstra, 2014

- 6-11 weeks old infants were 1:1:1:1 randomized
- Observer-blinded study
- Not stated (poster)
- Not stated (poster)
- Partly blind to treatment
- NC/CA: GSK, full personnel and completeness of outcome data not stated

1075 Rodolfo, 2016

- Not stated, Full text not available (ie. Poster or abstract)
- Not stated (presentation from SAGE WG)
- Not stated (presentation from SAGE WG)
- Not stated (presentation from SAGE WG)
- NC/CA: Not enough information to evaluate

1088 Aziz, unpublished

- Infants and toddlers randomized using random number generator function based on uniform probability distribution, performed in blocks of 20, after stratification by clinic for eligible group
- Open label study
- All study staff were aware of treatment allocation
- Some authors are affiliated with industry
- HIGH: Study was conducted in Belgium

1091 Opek, 2016

- Pre-vaccination time point for the comparator for pre-vaccine GMT
- Not applicable since only 1 intervention
- Not stated
- Not stated
- GSK affiliated study, high burden of IPD in SA,
- Small sample size LOW

1101 Grimprel, 2011

- Eligible subjects were randomly allocated to 1:1:1:1:1:1 ratio
- Double-blind, multicenter trial
- Not stated
- According to Figure 1, 79.1% of the 613 randomized children were included for analysis.
- Co-author has Pfizer affiliation, study was supported by Wyeth and Pfizer contributed to the study’s conduct and analysis.
- LOW

1105 Kim, 2011

- Infants were randomized (3:1 treatment allocation ratio)
- Single-blind, randomized, controlled trial
- Not stated
- According to Figure 1, 83.3% of the 503 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- LOW

1106 Lamb, 2011

- Infants were randomized (1:1 treatment allocation ratio)
- Single-blind, randomized, controlled trial
- Not stated
- According to Figure 1, 86.5% of the 360 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- LOW

1122 Kruken, 2011

- Infants were assigned a vaccine schedule based on age, and only 1 vaccine product was used. The reference group was children who had received the vaccine through the normal national vaccine scheme.
- Open label
- Not stated
- According to Figure 1, 88.9% of the 230 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- LOW

1088 Ochotonka, 2013

- "A randomization blocking scheme (2:1 ratio)…" was used to ensure that balance between treatments was maintained
- In this open, randomized, controlled study...
- Not stated
- According to the Trial Profile figure, 90% of the 120 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- Small sample size

1142 Braas-Plassen, 2011

- No control group present - "The objectives of this phase II, single-arm, open-labeled study..."
- The objectives of this phase II, single-arm, open-labeled study...
- Not stated
- According to Figure 1, 85.2% of the 200 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- Comparison to European cohort

1144 Senyure, 2014

- Eligible infants were randomly assigned as 1:1:1 ratio to receive PCV7 or PCV10
- Not stated
- According to Figure 1, 86.8% of the 300 randomized children were included for analysis.
- Some authors are affiliated with Pfizer & Wyeth, and Pfizer sponsored the study.
- Small sample size

1145 van Beurden, 2014

- This is a follow-up to an earlier study that randomized children to PCV10 or PCV7 with observation or to a control group. Previously randomized and control group children were then invited to participate in this booster phase study.
- Since this study assessed different vaccine schedule during nature, it was open label
- Not stated
- According to Figure 1, 85.8% of the 180 randomized children were included for analysis.
- Some authors are affiliated with GSK, and GSK sponsored the study and was involved in all stages of conduct and analysis.
- Small sample size
588 Togashi, 2013 c This was an open-label study that had only 1 treatment arm.
589
590 Pan, Benigno, 2013 c Subjects were randomized 1:1 ratio.
591
592 Payton, 2013 a This was a phase 3, open-label, single-arm, multicenter trial.
593
594 Dagan, 2013 a Healthy infants were randomized (1:1) to receive PCV7 or PCV13.
595
596 Dicko, 2013 c Study had no control group.
597
598 Brito, 2013 c This phase 3, open-label, single-arm, multicenter trial.
599
600 Volfo, 2014 c Study had to control group.
601
602 Hose, 2016 c About 1.4% of GMFR infants randomized to 2:2:1 to PCV or PCV13 and different schedules.
603
604 Morse, 2016 a Infants randomized to either PCV10 or PCV13, no control group.
605
606 Babiak, 2016 a Infants randomized to receive one of two schedules, no control group.
607
608 Silfverdal, 2009 a Infants randomized to receive one of two schedules, no control group.
609
610 Tovar, 2009 a Primary schedule: infants randomized, booster schedule: partially randomized based on what vaccines received as primary. 
611
612
American, 2009
don’t know but not controlled
one side
blinded analysis conducted at Lab
assessed for immunogenicity (measured as immune response after safety) and preprocessed as only 15/23 per group
Study of safety and immunogenicity with different coadministered vaccines
LOW: Wyeth study, primary objective: safety

Hatonen, 2012
Subjects were randomized in a parallel-group, double-blind, multi-center trial
Not stated
Including in Figure 1, 95% of the 300 randomized children completed the toddler series for safety analysis.
None authors are affiliated with Pﬁzer, and Wyeth sponsored the study.
LOW

Zuck, 2011
The objectives of this phase II, randomized, open, controlled study
Not stated
Including in Figure 1, 95% of the 300 randomized children were included for in the ATP immunogenicity cohort.
None authors are affiliated with GSK and Wyeth sponsored the study.
LOW

Niel-Pedersen, 2010
Children randomized to 1 of 3 dosing schedules
One side
Laboratory personnel responsible for immunogenicity testing were blinded to the treatment group. *
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

Van den Bergh, 2016
Randomized to PCV10 or PCV7 arms
Not stated
Laboratory technicians not aware of study arm allocations
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

Kabelle, 2014
Double-blind multicenter trial
Not stated
Participant involved in data gathering, processing, and analysis and safety assessments were blinded to vaccine allocation
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
About 54 infants excluded from immunogenicity arms because of incorrect consent forms. High rate of attrition between primary and booster time points.
Topile, 2014
Low at study, still large numbers in immunogenicity analysis
LOW

Berrel, 2011
Infants randomized to receive either PCV10 or PCV7
Double-blind
Sera were analyzed in a blinded manner
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
Blinder phase continued from primary phase of comparison RCT between PCV10 and PCV7
LOW

Helm, 2015
Double-blind, controlled: true
Not stated
Children group available for analyti; 78% of catch up group included in analysis
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

Bryant, 2010
Infants (n v 249) were randomly assigned to
Not stated
91.6% of the infants (228 of 249) completed the primary vaccination series.
Dr Bryant has been an investigator on clinical trials funded by Wyeth Pharmaceuticals, GlaxoSmithKline, Novartis, Johnson and Johnson, has served as a consultant to Wyeth and Astellas, received honoraria from Sanofi Pasteur and Abbott for lectures and from GlaxoSmithKline for service on an advisory board; Dr Block has been an investigator on clinical trials funded by Wyeth; Drs. H. Block and T. Block have served as a consultant to Wyeth at the time the study was conducted; and Drs
LOW

1320 Timo, 2010
A total of 1650 subjects (1235 in the PHiD-CV groups and 415 in the 7vCRM group) were enrolled for the primary vaccination phase and 1112 subjects for the booster phase (712 in the PHiD-CV primed and booster group, 319 in the 7vCRM primed and booster group and 283 in the 7vCRM primed and PCV6 booster group)
Not stated
Not stated
Not stated
Not stated
None: not used
Blinder analysis was blinded
UNCLEAR: lots of missing info

1423 Ladhani, 2015
This was an open, non-randomized study, conducted by the same investigator in 2 of the same geographical areas (Gloucestershire/northwestern Europe) in 2011–2012 that assessed antibody responses in infants 1 month after primary immunization with the same vaccines and schedules and with samples tested by the same laboratories and assays as in this evaluation
Not stated
Not stated
Not stated
Not stated
UNCLEAR: lots of missing info

1491 van den Bergh, 2016
Not stated
Not stated
GSK laboratories, Knaesart, Belgium. A
Not stated
Not stated
Not stated

1546 Hajkowicz, 2015
Not stated
Not stated
19% completeness
Unclear: some data is included in the PCV13 era
Historical control 2011-2014: Study 2012-2014
LOW: historical control

1626 Tregnaghi, 2014
Not stated
Not stated
93% of subjects completed the toddler series.
Lowest phase continued from primary phase of comparison RCT between PCV10 and PCV7
LOW

3723 Wysocki, 2009
A randomized but no control open label
evaluated for immunogenicity (measured as immune response after safety) and preprocessed as only 15/23 per group
Study of safety and immunogenicity with different coadministered vaccines
LOW: Wyeth study, primary objective: safety

1298 Dicko, 2011
The objectives of this phase III, randomized, parallel-group, double-blind, multi-center trial
Not stated
According to Figure 1, 94.3% of the 300 randomized children were included in the ATP immunogenicity cohort.
None authors are affiliated with GSK and Wyeth sponsored the study.
LOW

910 Vanderkooi, 2012
Subjects were randomized 1:1
This was a phase III, parallel-group, double-blind, multi-center trial
Lowest phase continued from primary phase of comparison RCT between PCV10 and PCV7
LOW

Ruiz-Palacios, 2013
Toddlers randomized to 1 of 3 dosing schedules
Open side
Laboratory personnel responsible for immunogenicity protocol for immunogenicity analysis
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

3754 van den Bergh, 2016
Subjects were randomized to 1 of 3 dosing schedules
Open side
Laboratory personnel responsible for immunogenicity protocol for immunogenicity analysis
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

2226 Tregnaghi, 2014
The objectives of this phase III, randomized, double-blind multicenter study
Not stated
According to Figure 1, 91.9% of the 300 randomized children were included in the ATP immunogenicity cohort.
None authors are affiliated with GSK and Wyeth sponsored the study.
LOW

798, 2011
Children randomized to receive either PCV10 or PCV7
Double-blind
Serum were analyzed in a blinded manner
GSK funded study and involved in design, coauthors employed at GSK, GSK labs
LOW

3363 Vesikari, 2016
Randomized, controlled cluster trial
Double-blind
Not stated
Not stated
Not stated
Not stated
None: not used
Blinder analysis was blinded
UNCLEAR: lots of missing info

3725 Wysocki, 2009
This was a phase II, parallel-group, double-blind, multi-center trial
Not stated
Including in Figure 1, 95% of the 300 randomized children completed the toddler series for analysis.
None authors are affiliated with Pﬁzer, and Wyeth sponsored the study.
LOW
This phase III, randomized, open-label, multicenter study (NCT01027845) conducted in Japan assessed the immunogenicity, safety, and reactogenicity of 10-valent pneumococcal nontypeable Haemophilus influenzae protein D conjugate vaccine (PHiD-CV, given intramuscularly) co-administered with diphtheria-tetanus-acellular pertussis vaccine (DTPa, given subcutaneously).

There were 360 individuals who could be randomized and after the whole series there were 216 evaluable immunogenicity cohort. GlaxoSmithKline provided the funding and was involved in all stages of the study conduct and development and publishing of the present manuscript.

Low health infants were randomly assigned in an open, controlled trial. Participants, study staff, and those assessing the outcomes were blinded to the group assignment.

This was a parallel group, randomized, double-blind, multicenter (9 centers in Poland) trial.

In this open-label study, 325 healthy children aged 12-15 months were randomized to 1 of 2 groups.
Overall, 751 healthy infants (age: 55–89 days) were enrolled to receive 3 or 4 doses of MenACWY-CRM (2/4/12 or 2/4/12 months of age, respectively) with PCV13 (routine vaccinations [ACWY3 and ACWY4 groups, respectively] or PCV13-routine vaccinations, city routine group).

Results of a Phase 2b, Randomized, Open-label Trial

All serological analyses were performed by staff blinded to vaccine group assignment.

Novartis Vaccines and Diagnostics, Inc. provided financial support for the conduct of the research, including study design as well as data collection, analysis and interpretation, and paid all costs associated with the manuscript development. L.H. and I.S. were employees of Novartis group companies and hold stock ownership from the sponsoring company at the time of the study but are now employees of GlaxoSmithKline group companies. F.X. was a contractor associate at Novartis Vaccines and Diagnostics, Inc. but is now a contractor associate at GlikasBio, Inc., United States. P.M.D. was a permanent employee of Novartis Vaccines and Diagnostics, Inc. at the time of the study. Some of the authors and institutions have received funding from industry.

This phase III, open-label, multicenter study was conducted in 9 health centres. Not stated (Figure 2), only 13.5% of the total vaccinated cohort from the previous study that were eligible to participate in this study were included in the ATP immunogenicity cohort. Some authors are affiliated with Pfizer, and Wyeth sponsored the study. One author is affiliated with GSK and GSK sponsored the study. Two authors are affiliated with Pfizer, and Wyeth sponsored the study.

This long-term follow-up study included children from 2 previous primary/booster study, 110 (from 2 of the 4 countries in that study) were enrolled in the present follow-up study, 75 in the PHiD-CV 2 v 1 group and 55 in the PHiD-CV 3 v 1 group. A total of 45 unprimed, age-matched controls were also enrolled in this for this follow-up study. Figure 1 shows reason for exclusion and the number of children included in the ATP immunogenicity cohort per group. The study groups in the ATP immunogenicity cohort were comparable with regard to demographic characteristics (Table 2), that is, age at the time of administration of the PHiD-CV dose ranged from 20 to 40 months across groups, gender distribution (46%–52% girls across groups), and ethnicity (95%–100% white Caucasian or European heritage across groups).

"120 children… were randomized (1:1) to receive…" ISPPD abstract does not state.

"The study population consisted of PHiD-CV unprimed Malian children previously enrolled in the control group of study NCT00678301 receiving a 2-dose catch-up vaccination with PHiD-CV in the second year of life."
## PRIME: IPD Case Control Risk of Bias Tool

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Representativeness of cases</td>
<td>a) consecutive or obviously representative series of cases</td>
</tr>
<tr>
<td></td>
<td>b) potential for selection biases or not stated</td>
</tr>
<tr>
<td></td>
<td>c) Unclear</td>
</tr>
<tr>
<td></td>
<td>d) Not stated/Full text not available (ie. Post or abstract)</td>
</tr>
<tr>
<td>2 Selection of Controls</td>
<td>a) community controls</td>
</tr>
<tr>
<td></td>
<td>b) hospital controls</td>
</tr>
<tr>
<td></td>
<td>c) test-negative controls (e.g. non-vaccine type cases)</td>
</tr>
<tr>
<td></td>
<td>d) no description</td>
</tr>
<tr>
<td></td>
<td>e) Unclear</td>
</tr>
<tr>
<td></td>
<td>f) Not stated/Full text not available (ie. Post or abstract)</td>
</tr>
<tr>
<td>3 Definition of Controls</td>
<td>a) no history of disease (endpoint)</td>
</tr>
<tr>
<td></td>
<td>b) no description of source</td>
</tr>
<tr>
<td></td>
<td>c) Unclear</td>
</tr>
<tr>
<td></td>
<td>d) Not stated/Full text not available (ie. Post or abstract)</td>
</tr>
<tr>
<td>4 Potential confounders measured and adjusted for in the analysis</td>
<td>Please list out factors that were controlled for in the analysis</td>
</tr>
<tr>
<td>5 Ascertainment of exposure</td>
<td>a) secure record (eg provider history; immunization registry)</td>
</tr>
<tr>
<td></td>
<td>b) parent/guardian written record</td>
</tr>
<tr>
<td></td>
<td>c) parent/guardian verbal record</td>
</tr>
<tr>
<td></td>
<td>d) no description</td>
</tr>
<tr>
<td></td>
<td>e) Unclear</td>
</tr>
<tr>
<td></td>
<td>f) Not stated/Full text not available (ie. Post or abstract)</td>
</tr>
<tr>
<td>6 Same method of ascertainment for cases and controls?</td>
<td>a) yes</td>
</tr>
<tr>
<td></td>
<td>b) no</td>
</tr>
<tr>
<td></td>
<td>c) Unclear</td>
</tr>
<tr>
<td></td>
<td>d) Not stated/Full text not available (ie. Post or abstract)</td>
</tr>
<tr>
<td>7 Other Risk of Bias</td>
<td>Please comment on other factors that may introduce bias</td>
</tr>
</tbody>
</table>
cases identified through national laboratory-based surveillance

South Africa, von Hoffner, 2016

- cases identified through national laboratory-based surveillance
- matched hospital controls sought
- one can infer that the controls are those with no history of the disease, but it does not state it explicitly
- laboratory-based surveillance
- matched hospital controls sought
- HIGH

UK, Andrews, 2014

- "To assess vaccine effectiveness, we used 14 cases of invasive pneumococcal disease in the cohort eligible for PCV13 vaccination in England, Wales, and Northern Ireland identified up to Oct 31, 2013, through enhanced national surveillance by Public Health England"*
- matched hospital controls
- one can infer that the controls are those with no history of the disease, but it does not state it explicitly
- laboratory-based surveillance
- matched hospital controls sought
- LOW

UK, Andrews, 2014 (abstract cohort study)

- cases were identified through laboratory-based surveillance in 10 states in Brazil from March 2010 to December 2012. Cases were defined as S. pneumoniae detected from a normally sterile site (e.g., blood or nonpneumococcal fluid) in a child age 2 to 59 months who received ≤1 PCV10 dose. Initially cases were identified by culture only; however starting in December 2010, some study sites were started. Cases were confirmed using PCR
- matched hospital controls
- indirect cohort study design -- controls are individuals with invasive pneumococcal disease caused by the non-PCV13 serotypes* in the same neighborhood in which the case resided at the time of illness.
- We obtained vaccination history, from general practitioners through postal questionnaires and telephone calls
- matched hospital controls
- LOW

Veras.et al. 2015

- cases included in the study were those that met the following criteria: (a) contact and living in the same household as the case, (b) age of at least 6 months, (c) absence of under 6 months of age, and (d) case and control were hospitalized in the same hospital. Children with non-culture methods were assessed by PCC
- matched hospital controls
- indirect cohort study design -- controls are individuals with invasive pneumococcal disease caused by the non-PCV13 serotypes* in the same neighborhood in which the case resided at the time of illness.
- Vaccination histories were abstracted from case-patients' immunisation cards
- matched hospital controls
- LOW

Kurander et al 2014

- abstract thus the selection of controls not stated
- abstract thus the definition of controls not stated
- abstract thus the method of ascertainment for cases and controls
- N/A
- N/A
- N/A
- N/A
- abstract thus the method of ascertainment for cases and controls
- UNCLAR

Pakistan, Ali 2016

- controls are matched on age, neighborhood, and season, to mention of where they were recruited
- abstract thus the method of ascertainment for cases and controls
- abstract thus the method of ascertainment for cases and controls
- N/A
- N/A
- N/A
- N/A
- N/A
- UNCLAR

Romania-Republic, Cancea, 2016

- abstract thus the method of ascertainment for cases and controls
- abstract thus the method of ascertainment for cases and controls
- abstract thus the method of ascertainment for cases and controls
- N/A
- N/A
- N/A
- N/A
- N/A
- UNCLAR

Reference: Country, Author, Year (Abstract)
We used data from a nationwide surveillance program of IPD for children <16 years based on cases identified by the German pediatric- and adult vaccination registers. Eligible cases were: IPD cases in children <16 years identified by the German pediatric- or adult vaccination registers. The Navarra Health Service provides healthcare, free at point of service, to 97% of the inhabitants of the region. Clinical records have been computerized since 2000 and include reports from primary care, hospital admissions, the regional vaccination register, and labor
tory test results. Vaccination history was obtained from the regional vaccine-creation register (21), which includes all doses received by children, including those acquired in the private market.

A case-control study, nested within the cohort, indicates that the underlying cohorts which is made up of the cases controls the information collection methods in the same

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</thead>
</table>
| **1** Was the outcome measured consistently across the study period (e.g. surveillance methodology changes; was % all IPD cases serotyped consistent pre and post) | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| **2** Does the surveillance initiation predate the time period used as baseline (i.e. did the data collection start before the study baseline period?) | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| **3** Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre to post changes? | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| **4** Were the outcome measures of interest taken multiple times before the intervention? (ex. were multiple time points reported for the baseline period; was baseline averaged for more than one year?) | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| **5** Were the outcome measures of interest taken multiple times after the intervention? (ex. were multiple time points reported for the post-intervention period; was post-intervention period averaged for more than one year?) | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| **6** Was industry (i.e., GSK or Pfizer) involved in this study?        | a. Yes  
|                                                                         | b. No  
|                                                                         | c. Unclear  
<p>|                                                                         | d. Not stated/Full text not available (ie. Poster or abstract) |
| <strong>7</strong> Other risk of bias                                                | Comments                                                                 |</p>
<table>
<thead>
<tr>
<th>RefID</th>
<th>Reference (Country, Author, Year)</th>
<th>Q1consis_ans</th>
<th>Q1consis_comments</th>
<th>Q2base_ans</th>
<th>Q2base_comments</th>
<th>Q3prepost_ans</th>
<th>Q3prepost_comments</th>
<th>Q5after_ans</th>
<th>Q5after_comments</th>
<th>Q6industry_ans</th>
<th>Q6industry_comments</th>
<th>PICO I</th>
<th>PICO II</th>
<th>Overall Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>63</td>
<td>Finland, Jokinen, 2015</td>
<td>a</td>
<td>10% missing serotype data in 2001/02 and only 10% missing serotype data after PCV13 intro. Also in 2010, reporting became mandatory, before then it was voluntary.</td>
<td>x</td>
<td>surveillance system NEDR since 1995</td>
<td>x</td>
<td>0% Cs provided</td>
<td>x</td>
<td>2 years for PCV13 data, but 2 years for PCV7 data</td>
<td>a</td>
<td>National Institute for Health and Welfare received funding from UK for FinnFlap trial</td>
<td>Authors attempted to correct for indirect effects and serotype data</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>137</td>
<td>UK, Weight, 2015</td>
<td>b</td>
<td>All NPS isolates were serotyped, national reference lab at SSI</td>
<td>x</td>
<td>surveillance system commenced before 2010</td>
<td>x</td>
<td>0% Cs provided for serotype groups and O9A</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>Public Health England is funder</td>
<td>Authors modeled for cyclic variation in serotype prevalence</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>262</td>
<td>Denmark, Harboe 2014</td>
<td>a</td>
<td>All NPS isolates were serotyped, national reference lab at SSI</td>
<td>x</td>
<td>surveillance system commenced before 2010</td>
<td>x</td>
<td>0% Cs provided for serotype groups and O9A</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>National Institute for Public Health and the Environment</td>
<td>Very low incidence of SA and 6C disease, may not be powered to detect differences</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>3515</td>
<td>Netherlands, Jou, ISPPED2016</td>
<td>a</td>
<td>Authors mention serotype specific data from 1993 onwards</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>8 years pre-PCV data</td>
<td>x</td>
<td>3 years for PCV7 and 3 years for PCV13</td>
<td>a</td>
<td>THL and Univ of Tampere</td>
<td>Excluded years of FinnFlap trial and a transition year</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>3656</td>
<td>Israel, Regev-Yochay, 2016</td>
<td>a</td>
<td>All clinical labs submit Ssp isolates to THL for serotyping</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>8 years pre-PCV data</td>
<td>x</td>
<td>3 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>IAPO Group</td>
<td>Capture-recapture method assured reporting of &gt;95% cases</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>3672</td>
<td>Finland, Nuorti, 2016</td>
<td>a</td>
<td>All clinical labs submit Ssp isolates to THL for serotyping</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>8 years pre-PCV data</td>
<td>x</td>
<td>3 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>THL and Univ of Tampere</td>
<td>Excluded years of FinnFlap trial and a transition year</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>3677</td>
<td>Finland, Cencoran, 2016</td>
<td>d</td>
<td>No information on the source of the isolates and completeness of reporting</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>1 year of pre-PCV data</td>
<td>x</td>
<td>2 years for PCV7 and 5 years of PCV13</td>
<td>a</td>
<td>partly funded by Pfizer Ireland</td>
<td>Unclear what % of all isolates this study represents</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>4454</td>
<td>Australia, Jayasinghe, 2017</td>
<td>a</td>
<td>% isolates serotyped not stated</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>1 year of pre-PCV data</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>a</td>
<td>NCIRS funded by govt dept of health</td>
<td>Adjusted for missing serotype data</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>1276</td>
<td>Ben-Ormiri (2015)</td>
<td>b</td>
<td>The proportion of isolates for which a serotype was determined increased from 40% to 70% in the period between July 2004 and June 2009 to &gt;95% since July 2009 to December 2012.</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>6 years pre-PCV7 data</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>Israeli and Pediatric Bacteremia and Meningitis Group</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>326</td>
<td>Ben-Ormiri et al. 2014</td>
<td>b</td>
<td>No isolates for which a serotype was determined increased</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>6 years pre-PCV7 data</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>Bacteremia and</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>420</td>
<td>Von Gottberg 2014</td>
<td>a</td>
<td>Surveillance for</td>
<td>x</td>
<td>surveillance system commenced by 1 year, not stated for adult sentinel surveillance</td>
<td>x</td>
<td>6 years pre-PCV7 data</td>
<td>x</td>
<td>2 years for PCV7 and 3 years for PCV13</td>
<td>b</td>
<td>Neuromuscular</td>
<td>reports receiving grant</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>
527 Steens 2013

- observational-retrospective population study; routine collection of serotype specific data in MSIS started in 2006. For 2004, 2004, and 2006, serotype specific data was linked to notified data from MSIS retrospectively.

1538 Diawara et al. 2015

- Surveillance started in Jan 2004 and PCV7 was introduced in July 2006.
- IRR with 95% CIs provided: 
  - 2 years pre PCV7 data
  - 1 year post PCV13 data

3217 Pusat et al. Vaccine 2016

- Serotyping of Sp6A and Sp6B was conducted by medical microbiological laboratories and clinicians in Norway.

160 Raynaudre 2023

- A. Lepoutre declares no potential conflicts of interest. E. Varon received fees from Pfizer and GlaxoSmithKline for participation in working groups on pneumococcal vaccines. S. Georges, F. Données, C. Janot, L. Gutmann and D. Lévy-Bruhl declare no potential conflicts of interest.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1839</td>
<td>Sweden</td>
<td>Low: methods sound, mandatory reporting coincides with intro of PCV7, wide CIs so findings are not statistically sig</td>
</tr>
<tr>
<td>1839_Jokinen_2012.pdf</td>
<td>England</td>
<td>Low number of cases in neonates so CIs are very wide</td>
</tr>
<tr>
<td>1908</td>
<td>England</td>
<td>abstract, not stated how the measured the outcome</td>
</tr>
<tr>
<td>1908_Scott_2012.pdf</td>
<td>Denmark</td>
<td>abstract, not stated about this</td>
</tr>
<tr>
<td>1908</td>
<td>Denmark</td>
<td>abstract, not stated how the measured the outcome</td>
</tr>
<tr>
<td>1917</td>
<td>Denmark</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>1917_Slotved_2016</td>
<td>Denmark</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>1939</td>
<td>England</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2013</td>
<td>England</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2015</td>
<td>England</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2015</td>
<td>Sweden</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2016</td>
<td>Denmark</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2016</td>
<td>Sweden</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2016</td>
<td>Denmark</td>
<td>funded by SSI</td>
</tr>
<tr>
<td>2016</td>
<td>England</td>
<td>funded by SSI</td>
</tr>
</tbody>
</table>

**England manages the largest national invasive pneumococcal disease dataset in the world, with around 5000 annual reports of invasive pneumococcal disease from England and Wales, of which more than 90% are serotyped.**

Using this national dataset, we assessed the effect of the PCV13 programme on the serotype-specific incidence of invasive pneumococcal disease in unvaccinated cohorts and older unvaccinated age groups.

We calculated incidence rate ratio (IRR) for invasive pneumococcal disease by comparing incidence in the epidemiological year 2003/04 with the average incidence in the 2 years preceding PCV13 introduction (July, 2000, to June, 2002) and the average of the pre-PCV7 baseline years (July, 2000, to June, 2006) using Poisson regression. Significance (for testing the null hypothesis of IRR=1) was set at 5% for serotype-specific analyses and at 1% for serotype-specific regression.

Average incidence in the 2 years preceding PCV13 introduction (July, 2000, to June, 2002) and the average of the pre-PCV7 baseline years (July, 2000, to June, 2006) were used for serotype-specific regression.

As an abstract, only had incidence rates from pre post periods with out having p values or CIs stated might be a part of the full text.

No mention of industry in text.
| authors adjusted for proportion serotyped and in the pre-PCV period for improvements in surveillance. Public Health England surveillance system, % serotyped increased over time from 49% to 93% | authors refer to extracting data for the study period | % change reported but no p-values given | 5 years of pre-PCV data | 2 years of PCV7 and 4 years of PCV13 | No mention of industry in poster | authors extrapolated counts from 5 months before surveillance started and for a period of 1 month when flooding halted surveillance (2010). This only impacts the annual incidence estimates, these two extrapolated time points were not used in the pre/post | 
| --- | --- | --- | --- | --- | --- | --- | --- |
| UK, Collins 2016 | Yes (Poster version) | No | No | No | No | No | Low |

<table>
<thead>
<tr>
<th>surveillance began 12May2008, annual incidence reported for 2006 was extrapolated back to 1Jan2008 using 2009 data. However, IRRs report only use the actual data from 12May2008 as the baseline comparison</th>
<th>p-value set at 0.05, 95% CI for IRR reported with overdispersed poisson distribution taken into account for two age groups</th>
<th>prePCV baseline 2 years (May 12, 2008-May 11, 2010)</th>
<th>last 2 years post PCV13 (2013-2014)</th>
<th>Funded by Gavi, BMGF, UE MRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Gambia, Mackenzie, 2016</td>
<td>Yes (Poster version)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>abstract, not stated. Surveillance part of Landspítal University Hospital</th>
<th>unclear if surveillance was already in place</th>
<th>p-values provided, exact statistical methods are not described</th>
<th>prePCV annual average from 2008-2010</th>
<th>Post PCV was annual average from 2011-2013</th>
<th>no conflict of interest stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iceland, Haraldsson, 2014</td>
<td>No (Abstract only)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>abstract, not stated how the measured the outcome</th>
<th>abstract thus unclear if the surveillance period predates the study periods</th>
<th>IRR stated with 95% CIs</th>
<th>average of 2005-2008 (or pre vaccination period)</th>
<th>post pv period 2012</th>
<th>no conflict of interest stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2132_2132_Naene_2014.pdf</td>
<td>No stated/Full text not available (as Poster or abstract)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>We used data from a stable surveillance system with constant coverage over time, age and serotype data were nearly complete (99.9%).</th>
<th>We used data from a stable surveillance system with constant coverage over time, age and serotype data were nearly complete (99.9%).</th>
<th>incidence rate ratios (IRRs) with 95% Cs and p values were calculated. Differences between IRRs were tested by calculating p values for interaction between birth cohort and serotype; the IRR for serotypes not related to PCV10 was used as reference.</th>
<th>IRR stated with 95% CIs</th>
<th>not averaged, a cumulative number</th>
<th>no conflict of interest stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2183_Hilde-2015.pdf</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

| As our laboratory is the National Public Health Reference Center for S. pneumoniae surveillance, we regularly receive isolates with enroled relevant patient information. Our routine protocol assigns a laboratory number to identify each isolate. After that the patient record/information is anonymized and de-identified prior to analysis. | Laboratory-based surveillance of IPD started in 1987 [12] and became nationwide in 1994, when a regional pneumococcal network called SIREVA, was organized. While the study period starts in 2003 | Changes in incidence rates (IR) were presented as incidence rate ratio with 95% confidence intervals (CI) and percent changes. Proportions of pneumococcal isolates by clinical diagnosis were tested with Chi-square test or Fisher exact test, as required. A p<0.05 was considered to be significant | not averaged, a cumulative number | no conflict of interest stated |
| 247_JVT_Galbarot_2014.pdf | No | No | No | No | No | No | Low |

<table>
<thead>
<tr>
<th>At 17 sites part of nationwide active surveillance, all isolates were serotyped in central laboratory</th>
<th>surveillance began in 2000 with PCV7 intro</th>
<th>CI bars shown on annual incidence graph</th>
<th>first year of surveillance was 1st year of PCV7 use</th>
<th>1 year of PCV7 and 4 years of PCV13 use</th>
<th>No mention of industry in poster</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel, Regev-Yochay, 2016</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Report ID</td>
<td>Source</td>
<td>Year</td>
<td>Surveillance System</td>
<td>Data Collection</td>
<td>Data Source</td>
<td>Serotyping</td>
</tr>
<tr>
<td>-----------</td>
<td>--------</td>
<td>------</td>
<td>---------------------</td>
<td>-----------------</td>
<td>-------------</td>
<td>------------</td>
</tr>
<tr>
<td>3540</td>
<td>South Africa, von Gottberg, 2016</td>
<td>d</td>
<td>no information describing surveillance system in poster</td>
<td>d</td>
<td>not stated in poster</td>
<td>95% CIs provided for change pre-post</td>
</tr>
<tr>
<td>3773</td>
<td>Denmark, Sloved, 2016</td>
<td>b</td>
<td>mandatory reporting to Danish reference laboratory initiated in 2007, but estimated 95% coverage of all IPD isolates in a</td>
<td>a</td>
<td>national surveillance system in place since the 1950's</td>
<td>95% CI for IRR reported</td>
</tr>
<tr>
<td>4034</td>
<td>Canada, Ways, 2015</td>
<td>a</td>
<td>population-based surveillance since 2000 with IPD being a notifiable disease, all isolates are forwarded to the public health lab</td>
<td>b</td>
<td>surveillance system since 2000, 1st year of data reported in study</td>
<td>no CIs provided for incidence rates</td>
</tr>
<tr>
<td>4285</td>
<td>Canada, Desai, 2016</td>
<td>a</td>
<td>IPD a notifiable disease, all isolates serotyped in central labs. 75% of cases had serotypes documented, but not sure if this proportion varied between early and later years</td>
<td>b</td>
<td>routine reporting began in 2007 the 1st year of the study</td>
<td>p-values reported for pre-post trends</td>
</tr>
<tr>
<td>4286</td>
<td>UK, Kandasamy, 2017 (unpublished)</td>
<td>a</td>
<td>surveillance system is Public Health England, no description provided in manuscript</td>
<td>d</td>
<td>not stated in text</td>
<td>95% CIs for IRR provided</td>
</tr>
<tr>
<td>3417</td>
<td>Chang-2014.pdf</td>
<td>d</td>
<td>abstract, not stated how the measured the outcome</td>
<td>d</td>
<td>abstract</td>
<td>d</td>
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<tr>
<td>3504</td>
<td>NPDD-22.pdf</td>
<td>a</td>
<td>poster and the full text is not provided, only states that this comes from state based morbidity data and commonwealth data</td>
<td>d</td>
<td>not fully articulated when the data source began</td>
<td>x</td>
</tr>
</tbody>
</table>

Unclear: not enough info in poster to assess surveillance system

Poster or abstract not stated/Full text not available (ex. Poster or abstract): poster and the full text is not provided, only states that this comes from state based morbidity data and commonwealth data

Abstract: not stated/Full text not available (ex. Poster or abstract): abstract, not stated about this

Notes: No mention of industry, however this is the abstract and need the full text to make sure
<table>
<thead>
<tr>
<th>ID</th>
<th>Title/Authors, Year</th>
<th>Details</th>
<th>Methods</th>
<th>Surveillance System</th>
<th>Start Date</th>
<th>End Date</th>
<th>Funding</th>
<th>Study Funding</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3515</td>
<td>UK, Callan 2015, ISPPDpdf</td>
<td>d. Not stated</td>
<td>poster not fully stated if data collection predicts study period</td>
<td>poster not fully stated</td>
<td>prePCV from 2000/2001 - 2005/2006</td>
<td>post PCV 7 period is 2 years (04/09-09/10)</td>
<td>poster not stated about funding sources or potential sources of conflicts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3555</td>
<td>Argentina, Papucci, 2016</td>
<td>d</td>
<td>poster, details of surveillance not reported</td>
<td>poster, not stated</td>
<td>prePCV - 4 years averaged</td>
<td>post PCV is 3 years averaged</td>
<td>poster, no funding information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>458</td>
<td>Uruguay, Pirez, 2014</td>
<td>a</td>
<td>standardized government case definitions</td>
<td>data is from hospital records</td>
<td>p-value from fisher exact two-tailed test and confidence intervals</td>
<td>prePCV (2003-2007)</td>
<td>Study funding not listed, but several authors report receiving funding from industry as a conflict of interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>508</td>
<td>UK, Moore, 2014</td>
<td>a</td>
<td>two hospitals were added partway through the study</td>
<td>this surveillance network began in 1996</td>
<td>p-values and confidence intervals</td>
<td>5 years of post PCV</td>
<td>Pfizer funds the surveillance network used</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3914</td>
<td>The Gambia, Levy, 2016</td>
<td>e</td>
<td>this is a population-based ecological study of children born in 2007–2010 in the province of Quebec, Canada, and followed up to December 31, 2010.</td>
<td>p-values and confidence intervals</td>
<td>10 years of pre-pcv</td>
<td>5 years of post PCV13</td>
<td>Pfizer funds the surveillance network used</td>
<td>Paper is a commentary, no data presented</td>
<td></td>
</tr>
</tbody>
</table>

**Methodological Details:**

- **Serotype Identification:** Serotype identification was performed using the traditional capsular swelling method (Quellung reaction). For selected serogroups, by a monoclonal antibody technique. Polymerase chain reaction (PCR) was used.

- **Statistical Methods:** Two statistical methods using SAS 9.2 software (SAS Institute, Cary, NC) were used to compute rate ratios, adjusting for age (in months), and the number of doses received. One test was performed using the number of IPD cases and the number of persons at risk in each cohort. Secondly, Poisson regression models were used.

- **Funding:** The study was supported by a research grant from the ‘Ministère de la Santé et des Services sociaux du Québec’. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of data; and preparation of the manuscript.
Disease Register data were used for calculating culture-confirmed serotype-specific IPD rates in the study cohorts. A population-based laboratory surveillance system in place since 1995, All clinical microbiology laboratories submit pneumococcal isolates to THL reference laboratories for serotyping and susceptibility testing, currently, over 97% of the case isolates are received. Case Definition: S. pneumoniae, children born 06/2010–09/2015, age range 3 to 66 months, unclear because they did not take the average of the rates rather they provided rate numbers. They did not take the average, provided rates. Not stated as this was a poster. Unclear
### PRIME: NP Carriage Randomized Controlled Trial Risk of Bias Tool

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| 1 | Is the study randomized? | a. Yes  
b. Control group but not randomized  
c. No control arm/group  
d. Unclear  
e. Not stated/Full text not available (ie. Poster or abstract)  
f. Not applicable |
| 2 | Blinding of participants and personnel | a. Double-blind  
b. Single-blind (either participants or study personnel)  
c. Open label  
d. Unclear  
e. Not stated/Full text not available (ie. Poster or abstract) |
| 3 | Blinding of outcome assessment (e.g., specimens were tested without knowledge of pre/post PCV status or study arm) | a. Yes  
b. No (i.e., not blinded or no control arm for the relevant outcome of interest)  
c. Unclear  
d. Not stated/Full text not available (ie. Poster or abstract) |
| 4 | Incomplete outcome data (e.g., the percent of those randomized to those analyzed) | a. 90% or more of those randomized were included in the analysis of the relevant outcome of interest  
b. Fewer than 90% were analyzed  
c. Unclear  
d. Not stated/Full text not available (ie. Poster or abstract) |
| 5 | Was industry (i.e., GSK or Pfizer) involved in this study? | a. No  
b. Yes, funded all or in part by Industry but for the relevant outcome was conducted entirely by independent investigators (e.g., no co-authors from industry; lab work not performed by Industry)  
c. Yes, evaluation of the relevant outcome was conducted all or in part by industry (e.g., analyses or lab work performed by Industry)  
d. Unclear  
e. Not stated/Full text not available (ie. Poster or abstract) |
<p>| 6 | Other Risk of Bias | Please comment on other factors that may introduce bias |</p>
<table>
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<tr>
<th>Question</th>
<th>Comments</th>
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<td>Q1</td>
<td>Is the study a poster abstract? Yes (50%) No (50%)</td>
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**Notes:**
- **RefID:** Verhagen, Orami; Pomat 2016
- **Prymula,** 2011
- **Temple,** Smith-Vaughn, Mullholland, 2017
- **3621:** 4475
- **b**
- **controls** were older siblings and adults so not
- **This** is a follow-up study of two randomized studies
- **(COMPAS & another study)**
- **Clusters** were randomized... using a standard SAS...
- **Each participant** was assigned to a group via a web-generated...
- **2:1 ratio** for immunization with
- **participant number** and randomly assigned
- **Q2blindpart_ans**
- **This** study is a poster abstract and did not specify anything regarding blinding.
- **Q3blindout_comments**
- **This** study is a poster abstract and did not specify anything regarding follow-up.
- **Q4incomp_comments**
- **This** study is a poster abstract and did not specify anything regarding comparability.
- **Q5othbias_comments**
- **This** study is a poster abstract and did not specify anything regarding low/high risk of bias.