UK Health Security Agency

Effect of maternal pertussis vaccination on pneumococcal carriage in infants

A rapid systematic review

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Main messages

1. This rapid systematic review (search up to 4 June 2026) identified and summarised evidence that assessed whether pertussis vaccination with Tdap (tetanus, diphtheria and acellular pertussis) vaccine given to mothers during pregnancy increased nasopharyngeal carriage of pneumococcal vaccine serotypes in infants who had pneumococcal conjugate vaccination (PCV).

2. Seven studies were included in this review, of which one was a systematic review with an individual participant data (IPD) meta-analysis (1), one was a randomised controlled trial (RCT) (2), one was a non-randomised study (3), and 4 were cohort studies (4 to 7). The IPD meta-analysis synthesised 4 studies that were all identified for inclusion in this review (3, 5 to 7).

3. One study, the IPD meta-analysis, assessed the impact of maternal Tdap vaccination on anti-PCV antibody concentrations in infants vaccinated with PCV13. Four studies were included with between 565 and 613 infants. There were significantly lower antibody concentrations of 12 of 13 pneumococcal vaccine serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 18C, 19A, 19F and 23F) in infants whose mothers had been given Tdap vaccine during pregnancy compared to those whose mothers had not (1).

4. The IPD meta-analysis also assessed the number of infants vaccinated with PCV13 who achieved the protective antibody threshold for *Streptococcus pneumoniae* (antibody concentrations against *Streptococcus pneumoniae* equal or greater than 0.35 µg per mL per serotype) (1). They found that significantly fewer infants whose mothers had been given Tdap vaccine met the protective antibody threshold in 5 of 13 pneumococcal vaccine serotypes (5, 6B, 9V, 19A, and 23F) compared to infants whose mothers had not (1). There were no significant differences of maternal Tdap vaccination for any of the other 8 pneumococcal vaccine serotypes.

5. One study assessed anti-PCV antibody concentrations and protective antibody thresholds in infants vaccinated with PCV10 (2). This study was a RCT of 103 infants, it reported that infants whose mothers had been given Tdap vaccine had significantly lower concentrations of anti-PCV antibodies for serotype 19F at 6 months of age, but not 12 months of age. No differences in antibody concentrations were reported in any of the other vaccine serotypes at either time point, nor were there any significant differences on the proportion achieving protective antibody thresholds for any pneumococcal vaccine serotype (2).

6. One study assessed the incidence of invasive pneumococcal disease in infants who were vaccinated with PCV10, PCV13 or a combination of PCV10 and PCV13 (4). The sub-analysis of a cohort of 82 infants who were vaccinated with PCV10 found that

maternal Tdap vaccination did not increase the odds of getting the disease caused by pneumococcal vaccine serotypes 19A or 19F (4). The overall analyses with the PCV types combined, found that for infants with invasive pneumococcal disease, maternal Tdap vaccination did not increase the odds of getting the disease caused by pneumococcal vaccine serotypes 19A or 19F (4).

7. No studies were identified that reported carriage of pneumococcal vaccine or non-vaccine serotypes, or incidence of non-invasive pneumococcal disease in infants who received any PCV type. No studies reported incidence of invasive pneumococcal disease in infants who received PCV13. No studies reported anti-PCV concentrations or proportion achieving protective antibody thresholds in infants who received mixed PCV types (PCV10, PCV13, or a combination of PCV10 and PCV13)

8. An assessment of the certainty of the evidence was completed using a modified Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach for each outcome (8). The evidence was rated very low to low certainty for serotypes across all evidence, mostly due to incomplete reporting of study details, and imprecision due to confidence intervals which crossed the line of no effect. There was one exception, with the anti-PCV antibody concentrations for one serotype rated as moderate certainty as the confidence interval did not cross the line of no effect.

9. The included studies differed from one another in terms of the schedules of when the PCV vaccines were given to infants, as well as the timing of outcome measurement. Evidence for most outcomes was limited to one study, and these factors limit the ability to draw firm conclusions from this evidence.

10. In conclusion, 7 studies were identified for inclusion that examined the effect of maternal Tdap vaccination on pneumococcal carriage and immune responses in infants who received a pneumococcal conjugate vaccination. The findings of the IPD meta-analysis suggested that maternal Tdap vaccination may lead to reduced anti-PCV antibody concentrations in infants vaccinated with PCV13, with significant reductions for 12 serotypes and significantly fewer infants achieving the protective antibody threshold for 5 serotypes compared to the infants whose mothers had not been given Tdap vaccine (1). However, no direct evidence was identified to determine whether maternal Tdap vaccination may also lead to increased pneumococcal carriage in infants. No evidence was found for vaccines other than PCV10 or PCV13. The evidence was mostly rated as low to very low certainty which, alongside the limited evidence, makes it difficult to draw any firm conclusions on the impact of maternal Tdap vaccination on pneumococcal carriage and immune responses of infants following PCV.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence that assessed whether maternal pertussis vaccination with Tdap (tetanus, diphtheria and acellular pertussis) vaccine given to mothers during pregnancy increased nasopharyngeal carriage of pneumococcal vaccine serotypes in infants who have received pneumococcal conjugate vaccination (PCV). Tdap vaccination may lead to increased pneumococcal carriage in infants due to higher levels of maternal antibodies in the infant following vaccination with Tdap vaccine, which in turn may suppress the immune response to PCV in infants and limit the effectiveness of vaccination.

The review question was:

1. Does maternal pertussis vaccination with Tdap vaccine (tetanus, diphtheria and acellular pertussis) during pregnancy lead to increased nasopharyngeal carriage of pneumococcal vaccine serotypes in infants?

This rapid systematic review was commissioned to support UKHSA's contribution to ongoing international discussions on pertussis vaccination policy, with a particular focus on the impact of maternal Tdap vaccination.

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process and provide a timely, evidence-informed answer to the review question without compromising the rigour of the review process. A literature search was undertaken to look for relevant experimental studies (randomised controlled trials, non-randomised controlled trials, quasi-experimental studies), observational studies (cohort studies), and systematic reviews, published or available as preprint, up to 4 June 2026. Three databases were searched: Ovid Medline, Ovid Embase, Web of Science Preprint Citation Index.

Studies in infants up to 3 years of age who had been partially or fully vaccinated with any routine infant PCV were included. Exposures of interest were maternal pertussis vaccination during pregnancy (vaccines: Tdap [also referred to as dTPa or DTaP], Adacel, Adacel-Polio, Boostrix, Boostrix-IPV, dTap/IPV and Repevax), compared to no maternal Tdap vaccine during pregnancy. The outcomes of interest were measures of carriage for both vaccine and non-vaccine pneumococcal serotypes, measures of anti-PCV protective antibody concentrations and incidence of both invasive and non-invasive pneumococcal disease.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are

provided in the protocol in Annexe A. The UKHSA health equity checklist for equity-focused reviews was implemented to ensure that health equity considerations were embedded throughout the review process, the full checklist is available in Annexe G (9).

The protocol stated that if there was insufficient comparative evidence identified then non-comparative evidence may also be included. All relevant evidence identified was comparative.

There were no deviations from the protocol.

There was one protocol clarification: indirect cohort studies, using a modified case-control approach ('the Broome method') were included if identified at the full text screening stage as they were designed to examine vaccine efficacy.

Screening on title and abstract was undertaken in duplicate by 3 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second.

Risk of bias assessment was conducted in duplicate by 2 reviewers using the appropriate JBI risk of bias checklist for the study design for primary studies (10 to 13) or AMSTAR-2 for systematic reviews (14). For the IPD meta-analysis, the risk of bias assessment was conducted using the AMSTAR-2 checklist (14). While the AMSTAR-2 checklist has not been specifically designed for IPD meta-analysis, it was considered the most appropriate for use in this review.

The certainty of evidence identified in this review was assessed across studies by outcome using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach (8). This process is described in detail in Annexe A and the summary findings tables in Annexe F. In brief, the certainty of evidence at the outcome level was assessed across 4 domains:

1. Risk of bias: where results may not represent the true effect because of limitations in the design or conduct of the study (assessed using the appropriate checklist).
2. Inconsistency: where studies show different effects for the same outcome.
3. Indirectness: where elements of the study differ from the review question.
4. Imprecision: a measure of how uncertain the result is.

Outcomes were given one of 4 ratings for certainty of evidence:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the true effect is similar to the estimated effect)

Where possible, evidence was combined but outcomes from studies that were not similar enough to combine were assessed individually. Where only one study was identified for an outcome, inconsistency was not assessed. To use GRADE, enough detail needed to be available for outcomes to be assessed across at least 3 of the 4 domains. Any outcomes that could not be assessed using GRADE have been reported without an assessment of the certainty of evidence.

Glossary of terms

This review includes specific terminology relating to study designs and measures of vaccine effectiveness. These terms are defined below in Table 1, with specific reference to PCV to help with interpretation of findings.

Table 1. Glossary of terms to support with interpretation of findings

Term	Meaning
Broome method	A modified case-control study design used to measure vaccine effectiveness by comparing the vaccination status of people who get vaccine-type infections with those who get non-vaccine-type infections.
Geometric mean concentration (GMC)	A statistical metric used to summarise antibody concentrations, used when data is not normally distributed.
Geometric mean ratio (GMR)	A statistical comparison between 2 sets of data (such as a treatment and control group) that shows the difference in effect size (for example, a geometric mean ratio of 1 would mean there was no difference between the 2 groups).
Individual participant data (IPD) meta-analysis	Quantitative evidence synthesis method that combines and analyses raw, original data from individual participants from within studies identified from a systematic review of the literature.
Protective antibody threshold	The minimum level of antibodies with which you would be protected from disease.

Evidence

In total, 2,164 studies were screened at title and abstract and 40 studies were screened at full text. Of these, 7 studies met the inclusion criteria. An additional study was included during screening but was subsequently retracted by the study authors and so is not included in this review.

A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded on full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D, risk of bias assessments in Annexe E, GRADE tables in Annexe F and health equity checklist in Annexe G.

One study was a systematic review with individual participant data (IPD) meta-analysis (1), one was a RCT (2), one was a non-randomised study (3) and 4 were cohort studies (5 to 7), including one indirect cohort study using the Broome method (4).

The IPD meta-analysis identified for inclusion in this review synthesised raw data from 4 primary studies (3, 5 to 7) which were also identified for inclusion in this review. In order not to double count results or misrepresent the extent of the evidence base, only the evidence from the IPD review is reported in the text and assessed with GRADE. Separate data extraction was completed for each primary study and is reported in Annexe D.

The IPD meta-analysis included 4 studies from multiple countries: Belgium, Canada, Czech Republic, Finland, Italy, Spain, Australia, and the United Kingdom (UK) (1). One study was conducted in the Netherlands (2), and one in Canada (4).

Evidence has been presented by pneumococcal vaccine type, with subheadings for each outcome for which data were available.

PCV13

One systematic review with an IPD meta-analysis of antibody responses following several childhood immunisations was identified for inclusion. One analysis within this examined the effect of maternal pertussis vaccination on anti-PCV antibody concentrations and the protective antibody thresholds for pneumococcal vaccine serotypes in infants vaccinated with PCV13 (1). Only the outcomes of the IPD meta-analysis of infants vaccinated with PCV13 was relevant to this review and reported here.

This IPD meta-analysis contained 4 studies (one non-randomised trial; 3 cohort studies) that were also identified within this rapid systematic review (3, 5 to 7). The results of the IPD meta-analysis have been reported in text, and individual details of the 4 studies as reported in their respective papers are included in Table D.2.

No studies were identified that looked at the effect on carriage of vaccine or non-vaccine pneumococcal serotypes, or incidence of invasive or non-invasive pneumococcal disease of infants vaccinated with PCV13. Anti-diphtheria toxoid antibodies were not reported in any studies of infants vaccinated with PCV13.

Anti-PCV antibody concentrations

The IPD meta-analysis examined the effect of maternal Tdap vaccination on infant antibody responses following PCV13 vaccination in infancy (1). Pregnant women were either given a dose of Tdap vaccine (Boostrix or Repevax) or were not. All infants received at least 2 doses of PCV13 (either 2 doses given at 2 and 4 months of age, or given 3 doses at 3 weeks, and 4 and 6 months of age).

The Geometric Mean Ratio (GMR) was calculated to compare the average anti-PCV antibody concentrations between infants whose mothers who had been given Tdap vaccine during pregnancy and infants whose mothers had not. For this outcome between 565 to 594 infants were included in the analysis, dependent on the pneumococcal vaccine serotype (age: 9 to 24 months, sex and ethnicity: not reported). Anti-*Streptococcus pneumoniae* Immunoglobulin G (IgG) concentrations were significantly lower in infants whose mothers had been given Tdap vaccine during pregnancy compared to those whose mothers had not (1). There were significant differences in all PCV13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 18C, 19A, 19F and 23F) except serotype 14, with differences ranging from 15% to 35% in infants whose mothers were given Tdap vaccine during pregnancy compared to infants whose mothers had not.

The certainty of evidence of the IPD meta-analysis for this outcome was assessed using GRADE for each pneumococcal vaccine serotype. The certainty of evidence for anti-PCV antibody concentrations in infants receiving PCV13 was rated as very low for 12 of 13 pneumococcal vaccine serotypes. GRADE assessment started at moderate as the study is an IPD meta-analysis of non-randomised studies and was further downgraded due to concerns about risk of bias. The systematic review lacked justification for the study designs included, did not provide a list of excluded studies or consistently report funding sources for included studies. They did not report some important study-level details (time between PCV vaccination and sample collection, and how maternal vaccination status was determined) for every serotype. For this outcome, evidence for serotype 14 was rated as low certainty. It was downgraded due to serious concerns with imprecision, with confidence intervals crossing the line of no effect. Inconsistency could not be assessed due to no there being no information reported to inform heterogeneity between studies. A summary of the risk of bias assessment is in Table E.1 and GRADE assessment is in Table F.1.

Achieving protective antibody threshold

The IPD meta-analysis (study previously described) analysed the number of infants achieving the protective antibody threshold for pneumococcal vaccine serotypes (antibody

concentrations against *Streptococcus pneumoniae* equal or greater than 0.35 µg per mL) following vaccination with PCV13 (n= between 583 and 613, depending on the pneumococcal vaccine serotype) (1). Numbers of those achieving the pneumococcal vaccine protective antibody threshold were significantly lower for 5 of the 13 vaccine serotypes (5, 6B, 9V, 19A, and 23F) in the infants whose mothers had been given Tdap vaccine during pregnancy compared to infants whose mothers had not (all $p<0.05$), with the number of infants who achieved the threshold was between 4% to 20% lower in infants whose mothers had been given Tdap vaccine during pregnancy. There were no significant differences by maternal Tdap vaccination status for any of the other 8 pneumococcal vaccine serotypes.

An assessment of the certainty of evidence using GRADE for this outcome was not conducted as 2 domains (inconsistency and imprecision) could not be assessed as the results for the individual studies and the variance data were not provided. A risk of bias assessment was conducted, as described previously. Overall risk of bias was assessed as moderate. The review lacked justification for the selected study designs, did not provide a list of excluded studies or consistently report funding sources for included studies, and omitted some important study-level details (time between PCV vaccination and sample collection, and how maternal vaccination status was determined). A summary of the risk of bias assessment is in Table E.1.

PCV10

Two studies were included which assessed the effect of maternal pertussis vaccination in infants vaccinated with PCV10 (2, 4). One RCT reported anti-PCV antibody concentrations and the proportion of infants achieving protective antibody thresholds (2), while an indirect cohort study reported on incidence of invasive pneumococcal disease in infants who were vaccinated with PCV10 (4). Anti-diphtheria toxoid antibody Geometric Mean Concentrations (GMCs) and the proportion who met anti-diphtheria toxoid antibody protective thresholds were reported for infants in one study (4), see Table D.2. No studies were identified that looked at the effect of maternal pertussis vaccination on carriage of pneumococcal vaccine or non-vaccine serotypes or incidence of non-invasive pneumococcal disease.

Anti-PCV antibody concentrations

Barug and others conducted a RCT in the Netherlands which examined the effect of maternal Tdap vaccination on anti-PCV antibody concentrations in infants vaccinated with PCV10 (2). Pregnant women were randomly allocated into 2 groups; 53 women were given Tdap vaccine during 30 to 32 weeks of pregnancy, and 50 women who were not vaccinated during pregnancy but were given Tdap vaccination 48 hours after giving birth. Infants were then followed up from birth to 12 months of age (n=103 infants, sex and ethnicity: not reported). All infants were given a dose of PCV10 at 3 and 5 months, as well as a booster at 11 months of age.

Anti-PCV antibody GMCs were calculated to estimate the antibody concentrations in infants whose mothers had been given Tdap vaccine during pregnancy compared with infants whose mothers had not, for vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F (2). Antibody concentrations were compared at both 6 and 12 months of age. There was a significant effect of maternal Tdap vaccination on the GMC ratios of vaccine serotype 19F at 6 months. It was significantly lower in the infants whose mothers had been given Tdap vaccine during pregnancy compared to infants whose mothers had not (GMC ratio: 0.4, 95% CI: 0.2 to 0.8, $p<0.05$), but this effect was no longer significant at 12 months (GMC ratio: 0.8, 95% CI: 0.5 to 1.2). There was no significant effect of maternal Tdap vaccination on any of the other vaccine serotypes (1, 4, 5, 6B, 7F, 9V, 14, 18C, and 23F) at either 6 or 12 months of age (all $p>0.05$).

For this outcome, the evidence was rated as low certainty for all vaccine serotypes at 6 and 12 months of age, except for serotype 19F which was rated as moderate certainty at 12 months of age. Evidence was downgraded for risk of bias as participants and investigators were not blinded and allocation concealment methods were not reported. Evidence was also downgraded for imprecision as there were confidence intervals crossing the line of no effect. Inconsistency was not assessed for this outcome, as there was only one included study. A summary of the risk of bias assessment is in Table E.2 and GRADE assessment is in Table F.2.

Antibody concentrations of 2 related non-vaccine serotypes (6A and 19A) were also reported (2). There was no significant effect of maternal Tdap vaccination on either serotype at 6 months or 12 months (both $p>0.05$). The evidence for these serotypes was rated as low certainty. It was downgraded for risk of bias and imprecision. Participants and staff were not blinded, and allocation concealment methods were not reported, and confidence intervals crossed the line of no effect. Inconsistency was not assessed for this outcome, as there was only one included study. A summary of the risk of bias assessment is in Table E.2 and GRADE assessment is in Table F.2.

The study reported anti-diphtheria toxoid antibody concentrations for each group, these are reported in Table D.2.

Achieving protective antibody threshold

Barug and others (study previously described) also reported the percentage of infants who met the protective antibody threshold for each pneumococcal vaccine serotype in infants whose mothers had been given Tdap vaccine during pregnancy and in infants whose mothers had not (2). There were no significant differences by maternal Tdap vaccination status on the percentages achieving protective antibody threshold at 6 or 12 months of age for any serotype (all $p>0.05$). The percentage achieving protective antibody threshold ranged from 54% to 98% at 6 months and from 98% to 100% at 12 months across both groups.

Certainty of evidence assessment was not conducted for this outcome as 2 of the GRADE domains (inconsistency and imprecision) could not be assessed as this was a single study with no variance data reported for each serotype at either time point. The risk of bias assessment was rated as moderate. There were concerns with limited details on allocation concealment, and a lack of blinding of participants and investigators to treatment assignment. A summary of the risk of bias is reported in Table E.2.

The study also reported the proportion of infants meeting the protective threshold for anti-diphtheria toxoid antibodies, see Table D.2.

Incidence of invasive pneumococcal disease

Thibault and others conducted a study in Canada using the 'Broome method', a modified case-control design or indirect cohort study, to examine whether maternal Tdap vaccination modified infant protection from pneumococcal disease through PCV (4). In this study, infants who had been vaccinated with PCV10 who had laboratory-confirmed invasive pneumococcal disease from vaccine serotypes 19A, 19F, or non-vaccine serotypes (including serotypes 15A, 15B, 22F, and 33F) were compared by maternal Tdap vaccination status (n=82, age range: 2 to 59 months, sex and ethnicity not reported). After adjusting for confounding factors (year of birth, age and vaccine schedule), maternal Tdap vaccination was not associated with increased odds of invasive pneumococcal disease from serotypes 19A or 19F in infants vaccinated with PCV10 (adjusted OR: 0.78, 95% CI: 0.28 to 2.11).

The evidence for the incidence of invasive pneumococcal disease following vaccination with PCV10 was rated as very low certainty. It was downgraded because of serious risk of bias, imprecision and indirectness. No detail was provided regarding the baseline characteristics of the subgroup vaccinated with PCV10, and there were wide confidence intervals that crossed the line of no effect. The indirect cohort study design used to estimate vaccine effectiveness does not directly measure invasive pneumococcal disease incidence. Inconsistency was not assessed for this outcome, as there was only one included study. A summary of the risk of bias assessment is in Table E.3 and GRADE assessment is in Table F.3.

Multiple or combined PCV

Thibault and others (study previously described) also assessed the effect of a combination of PCV10 and PCV13 on the incidence of invasive pneumococcal disease (4). Anti-diphtheria toxoid antibodies were not reported by this study. No studies were identified that reported outcomes on incidence of non-invasive pneumococcal disease, carriage of vaccine or non-vaccine serotypes, anti-PCV antibody concentrations or protective antibody thresholds for multiple or combined PCV vaccinations.

Incidence of invasive pneumococcal disease

As part of their indirect cohort study, Thibault and others compared the effect of maternal Tdap vaccination in infants diagnosed with laboratory-confirmed invasive pneumococcal disease from vaccine serotypes 19A and 19F or non-vaccine serotypes (4). Infants (n=127, age range: 2 to 59 months, sex and ethnicity: not reported) were vaccinated with either PCV10 (64.6%, 82 of 127), a mixed schedule of both PCV10 and PCV13 (30.7%, 39 of 127), or PCV13 (4.7%, 6 of 127). After adjusting for confounding factors (year of birth, age and vaccine schedule), maternal Tdap vaccination did not increase the odds of vaccinated infants developing invasive pneumococcal disease from serotype 19A or 19F (adjusted OR: 0.82, 95% CI: 0.32 to 2.07).

The evidence for the incidence of invasive pneumococcal disease following vaccination with PCV10, PCV13 or PCV10 and PCV13 was rated as very low certainty. It was downgraded because of serious risk of bias, indirectness, and imprecision. Baseline characteristics were not provided by maternal vaccination status and so it is unclear if any confounding factors were present. The indirect cohort study design used to estimate vaccine effectiveness does not directly measure invasive pneumococcal disease incidence. Imprecision was rated serious as there were wide confidence intervals that crossed the line of no effect. Inconsistency was not assessed for this outcome, as there was only one included study. A summary of the risk of bias assessment is in Table E.3 and GRADE assessment is in Table F.4.

Health inequalities

This review was focused on infants and pregnant mothers, population groups who are often considered at higher risk of health inequalities in general. Variations in health inequalities detailed in the protocol including socioeconomic status and deprivation were not reported in any of the included studies. It is therefore not possible to draw meaningful conclusions from the available evidence about the potential impact of socioeconomic status or deprivation in relation to this review question.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

Most studies in this review used different vaccination schedules, differing in the PCV type, the number of primary doses, the use of a booster dose, and the timing of administration. One study did not report timings that PCV doses were given (4).

Studies also used different time points for measuring the outcomes or did not specify the timing of outcome data collection following vaccination (1). Across primary studies, outcome data was collected at 10 days and over one month after PCV vaccination (2, 4). As measures of immunity are time-dependent, results may be influenced by the interval between vaccination and sample collection.

The certainty of evidence could not be completed using the modified GRADE assessment for the protective antibody threshold outcomes due to insufficient detail to assess inconsistency and imprecision. As a result, the overall confidence that can be placed in the findings is unclear. The other outcomes that were assessed with GRADE were unable to include the inconsistency domain within this which prevents evaluation of the extent to which findings are consistent across studies.

Limited evidence was identified for incidence of invasive pneumococcal disease, with the only included study employing an indirect cohort method whereby all participants had a diagnosis of invasive pneumococcal disease (4). As this study design is observational, maternal Tdap vaccination was not randomised. For this outcome, the risk of confounders may lead to systematic differences between mothers who had been given Tdap vaccine and those who had not (such as socioeconomic status, underlying health status, healthcare seeking behaviour).

Evidence gaps

There are several gaps in the evidence base. No evidence was identified relating to any outcome in infants receiving PCV7, PCV13, PCV14, PCV15, PCV20 or PCV20 vaccinations following a maternal vaccination of Tdap. No direct evidence was identified for carriage of pneumococcal vaccine or non-vaccine serotypes. No evidence was identified for the incidence of non-invasive pneumococcal disease in infants across all pneumococcal vaccine types.

Only one study was identified reporting the anti-PCV antibody concentrations in children vaccinated with PCV10. Only one study was identified reporting the incidence of invasive pneumococcal disease in children vaccinated with PCV10 or a mixed combination (PCV10, PCV13 or PCV10 and PCV13) (4). No evidence was identified for the incidence of invasive pneumococcal disease in children vaccinated with PCV13.

Conclusion

This rapid systematic review examined the impact of maternal pertussis Tdap vaccination during pregnancy on nasopharyngeal carriage of pneumococcal vaccine serotypes in infants. Seven studies were included in this review. There was limited evidence for incidence of invasive pneumococcal disease. There is no evidence for carriage of pneumococcal vaccine and non-vaccine serotypes or incidence of non-invasive pneumococcal disease.

One IPD meta-analysis synthesised evidence from 4 studies of infants who were vaccinated with PCV13 (1). This analysis found that infants of mothers who had been given Tdap vaccine during pregnancy had significantly lower antibody concentrations against 12 of 13 pneumococcal vaccine serotypes, and a lower percentage met protective antibody threshold for 5 pneumococcal vaccine serotypes, compared to those whose mothers were not given Tdap vaccine during pregnancy.

Two studies were included in infants vaccinated with PCV10, PCV13, or both PCV10 and PCV13. One study reported on incidence of invasive pneumococcal disease (4), and another reported on protective antibody thresholds of pneumococcal vaccine and non-vaccine serotypes (2). Evidence from these studies is too limited on which to draw conclusions on the effect of maternal pertussis vaccination on these outcomes.

The evidence was rated very low to low certainty for serotypes across all evidence. This was mostly due to risks of bias identified due to incomplete reporting of study details, and imprecision with confidence intervals crossing the line of no effect. There was one exception for anti-PCV antibody concentrations with one serotype rated as moderate certainty as the confidence interval did not cross the line of no effect. Studies had differences in vaccine schedules, PCV type given, and timing of outcome measurement. Low certainty of evidence and the differences between studies limit the conclusions that can be drawn.

In summary, although there is some evidence of lower anti-PCV antibody concentrations for PCV13 serotypes following maternal Tdap vaccination, no direct evidence was identified that assessed whether maternal Tdap vaccination increased pneumococcal carriage in infants. The limited evidence rated very low to low certainty means it is difficult to draw any firm conclusions on the impact of maternal Tdap vaccination on pneumococcal carriage of infants following PCV and the findings of this rapid review should be interpreted with caution. The clinical significance of these findings on infant health outcomes remains uncertain.

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Disclaimer

UKHSA's rapid systematic reviews and evidence summaries aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, and papers on preprint servers. Note that the reviews:

- use accelerated methods and may not be representative of the whole body of evidence publicly available
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- are only valid as of the date stated on the review

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11. Barker TH and others. 'The revised JBI critical appraisal tool for the assessment of risk of bias for quasi-experimental studies' JBI Evidence Synthesis 2024: volume 22, issue 3, pages 378 to 388
12. Barker TH and others. 'The revised JBI critical appraisal tool for the assessment of risk of bias for cohort studies' JBI Evidence Synthesis 2025: volume 23, issue 3, pages 441 to 453
13. JBI. Checklist for case-control studies 2017
14. Beverley JS and others. 'AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both' BMJ 2017: volume 358, j4008

Annexe A. Protocol

Review question

The review question is:

1. Does maternal pertussis vaccination with Tdap (tetanus, diphtheria and acellular pertussis) during pregnancy lead to increased nasopharyngeal carriage of pneumococcal vaccine serotypes in infants?

A search for primary evidence to answer this review question will be conducted up to 4 June 2026.

Eligibility criteria

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	Infants (0 to 3 years of age) who have been vaccinated (partially or fully) with a routine infant Pneumococcal Conjugate Vaccine (PCV) PCV includes: PCV7 (Prevnar 7) PCV10 (Synflorix) PCV13 (Prevnar 13) PCV14 (Pneubevax 14) PCV15 (Vaxneuvance) PCV20 (Prevnar 20) PCV21 (Capvaxive)	Children (aged 4 to 17 years) Adults (aged 18 years and over)
Context	Countries in which there's a routine infant PCV immunisation programme and a routine maternal Tdap vaccination programme in pregnancy	
Settings	Any	
Intervention or exposure	Maternal vaccination with Tetanus, diphtheria and acellular pertussis (Tdap) vaccine during pregnancy Vaccines include: Tdap (also referred to as dTPa or DTaP)	

	Included	Excluded
	Adacel Adacel-Polio Boostrix Boostrix-IPV dTap/IPV Repevax	
Comparator	No maternal vaccination with Tdap vaccine during pregnancy If insufficient evidence is available, evidence from studies with no comparator group will also be included	
Outcomes	• prevalence of Streptococcus pneumoniae nasopharyngeal carriage • carriage of non-vaccine serotypes (to detect any replacement) • anti-PCV antibody titres (IgG geometric mean concentrations) • proportion achieving protective antibody threshold of ≥0.35 µg per mL (or if alternative threshold is stated) per pneumococcal vaccine serotype • incidence of invasive pneumococcal disease • incidence of non-invasive pneumococcal disease	
Language	English	Any other language
Date of publication	Up to 4 June 2026	
Study design	Systematic reviews Experimental studies including randomised-controlled trials, non-randomised controlled trials, quasi-experimental studies Observational studies including cohort studies	Narrative reviews Cross-over designs Before-and-after studies Case-control studies Cross-sectional studies Descriptive studies including case series or case reports Modelling studies Qualitative studies Mixed methods
Publication type	Peer-reviewed published research Preprints	Conference abstracts Editorials

	Included	Excluded
		Letters News articles Grey literature Clinical trial registry records

Identification of studies

The following databases will be searched for studies published up to 4 June 2026: Ovid Medline, Ovid Embase, Web of Science Preprint Citation Index. The search strategy is presented below.

Screening

Title and abstract screening will be undertaken in duplicate by at least 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include participants (including formulation and schedule of PCV immunisation used), country, comparator, study period, study design, intervention (including formulation of Tdap vaccination), results, mediating variable of anti-diphtheria toxoid antibodies, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Data that is only available in graphs or figures and not in text will not be extracted.

Risk of bias assessment

Two reviewers will independently complete a risk of bias assessment for included studies, with disagreements resolved by discussion or with a third reviewer. Primary studies will be assessed using the relevant JBI checklist (10 to 13).

Systematic reviews will be assessed using the quality assessment tool AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both (14).

Certainty of evidence

If appropriate, the certainty of evidence identified within this review will be assessed using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (8). Certainty of evidence will be assessed at the outcome level, and be rated as one of 4 levels:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the authors are confident that the true effect is similar to the estimated effect)

The certainty of evidence will be assessed by one reviewer (and checked by a second) for each outcome across 4 domains:

1. Risk of bias: where results may not represent the true effect because of limitations in the design or conduct of the study.
2. Inconsistency: where studies show different effects for the same outcome of interest (only assessed where there are 2 or more studies measuring the same outcome). Inconsistency will be rated down if the point estimates are not similar, or the confidence intervals do not overlap.
3. Indirectness: where elements of the study differ from the intended elements in the review question (for example, the outcome of interest has not been directly measured). This will be rated down if the population, intervention, comparator, or outcome of interest have not been directly measured.
4. Imprecision: a measure of how uncertain the estimate is. Imprecision will be rated down if the confidence intervals cross the line of no effect, or if the reviewer judges that the confidence intervals are overly wide and so the true effect is likely to be different at the upper versus the lower end of the confidence interval.

Publication bias will not be used to assess the certainty of the evidence in this review.

Evidence may be downgraded one or 2 levels following the assessment of certainty or upgraded if there is a large magnitude of effect or clear dose-response gradient.

Synthesis

Where studies are similar enough to combine and present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of participants in each study, details on the formulation and schedule of PCV vaccination, effect size and variance and a summary of the risk of bias across studies reporting each outcome will be summarised and presented. Studies will be presented by vaccine and, where possible, by PCV serotype. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health equity

The UKHSA health equity checklist for equity focused reviews was used to draft this protocol (9). Variations across population groups by socioeconomic status and deprivation will be considered where evidence is available.

Search strategy

Ovid MEDLINE(R) ALL (1 January 1946 to 5 June 2026)

1. exp Pneumococcal Vaccines/ (10,000)
2. Bacterial Vaccines/ (20,312)
3. (pneumococc* adj2 (conjugate or vaccin* or immuni#ation*)).tw,kf. (13,202)
4. (PCV13 or PCV 13).tw,kf. (2,762)
5. (PCV7 or PCV 7).tw,kf. (1,716)
6. (PCV10 or PCV 10).tw,kf. (719)
7. (PCV14 or PCV 14).tw,kf. (12)
8. (PCV15 or PCV 15).tw,kf. (287)
9. (PCV20 or PCV 20).tw,kf. (386)
10. (PCV21 or PCV 21).tw,kf. (81)
11. (Prevnar13 or prevnar 13).tw,kf. (92)
12. Vaxneuvance.tw,kf. (21)
13. (Prevnar20 or prevnar 20).tw,kf. (14)
14. Capvaxive.tw,kf. (10)
15. Synflorix.tw,kf. (65)
16. (Prevnar7 or prevnar 7).tw,kf. (13)
17. Pneubevax 14.tw,kf. (3)
18. or/1-17 (34,696)
19. Child, Preschool/ (1,072,409)
20. exp Infant/ (1,346,221)
21. Infant Health/ (1,570)

22. Infant Welfare/ (2,788)
23. Infant Care/ or Perinatal Care/ (15,721)
24. exp Infant, Newborn/ (722,469)
25. (infant or infants or infantile or infancy or infantile).tw,kf. (601,462)
26. (premature or prematurity or preterm or pre-term or premie or premies or perinatal or peri-natal or perinat*).tw,kf. (362,930)
27. Postnatal Care/ (6,957)
28. (postnatal or post-natal or postnatal* or newborn or newborns or neonate or neonates or neonatal or neonatale or neonatales or neonatle or neonatles or neonatally or neonatorum).tw,kf. (620,124)
29. (baby or babies).tw,kf. (90,555)
30. (child or children or childhood or toddler*).tw,kf. (1,850,327)
31. "0 to 3 year*".tw,kf. (1,606)
32. "0 - 3 year*".tw,kf. (1,113)
33. under 3 year*.tw,kf. (1,496)
34. "0 to 2 year*".tw,kf. (1,638)
35. "0 - 2 year*".tw,kf. (1,125)
36. under 2 year*.tw,kf. (2,624)
37. or/19-36 (3,466,922)
38. 18 or 37 (3,491,216)
39. exp Pregnancy/ (1,089,014)
40. exp Pregnancy Trimesters/ (47,653)
41. Pregnant People/ (17,691)
42. pregnan*.tw,kf. (703,823)
43. Maternal Health/ (3,117)
44. Maternal Exposure/ (13,255)
45. exp Maternal Health Services/ (64,196)
46. maternal.tw,kf. (377,320)
47. maternity.tw,kf. (31,933)
48. mother*.tw,kf. (302,047)
49. (prenatal* or pre-natal*).tw,kf. (142,604)
50. exp Prenatal Exposure Delayed Effects/ (39,085)
51. gestation.tw,kf. (153,239)
52. or/39-51 (1,572,112)
53. Diphtheria-Tetanus-acellular Pertussis Vaccines/ (1,605)
54. Tetanus/ and Diphtheria/ and exp Bordetella Infections/ and exp Immunization/ (641)
55. (tetanus adj2 diphtheria adj2 pertussis).tw,kf. (3,482)
56. (tetanus adj2 diptheria adj2 pertussis).tw,kf. (41)
57. (pertussis adj2 diphtheria adj2 tetanus).tw,kf. (2,759)
58. (pertussis adj2 diptheria adj2 tetanus).tw,kf. (36)
59. acellular pertussis.tw,kf. (3,066)
60. DTAP.tw,kf. (1,111)
61. TDAP.tw,kf. (1,423)

62. dTPa.tw,kf. (14,816)
63. acel-imune.tw,kf. (7)
64. infanrix.tw,kf. (134)
65. tripedia.tw,kf. (12)
66. Adacel.tw,kf. (50)
67. Boostrix-IPV.tw,kf. (5)
68. Repevax.tw,kf. (12)
69. dTaPIPV.tw,kf. (4)
70. acel immune.tw,kf. (2)
71. acelluvax dpt.tw,kf. (0)
72. acelluvax DTP.tw,kf. (0)
73. adacel.tw,kf. (50)
74. adsorbed dt coq.tw,kf. (0)
75. anatoxal di te per berna.tw,kf. (0)
76. boostrix.tw,kf. (102)
77. certiva.tw,kf. (2)
78. covaxis.tw,kf. (4)
79. daptacel.tw,kf. (5)
80. diphtheria tetanus pertussis trivaccine.tw,kf. (5)
81. diptheria tetanus pertussis trivaccine.tw,kf. (0)
82. diteki booster.tw,kf. (0)
83. ditekibooster.tw,kf. (0)
84. DPT vaccine.tw,kf. (246)
85. DTP vaccine.tw,kf. (392)
86. infanrix.tw,kf. (134)
87. neodiftepertus.tw,kf. (0)
88. pertugen.tw,kf. (0)
89. tri immunol.tw,kf. (0)
90. triacelluvax.tw,kf. (2)
91. (triaxis or tribaccine or tripacel or tripedia or triplo vaccine or tripvac or tritanrix or trivax).tw,kf. (56)
92. or/53-91 (22003)
93. 38 and 52 and 92 (1,296)
94. limit 93 to (comment or editorial or letter or news or newspaper article) (23)
95. 93 not 94 (1,273)

Embase (1 January 1974 to 4 June 2026)

1. exp Pneumococcus vaccine/ (28,062)
2. (pneumococc* adj2 (conjugate or vaccin* or immuni#ation*)).tw,kf. (18,817)
3. (PCV13 or PCV 13).tw,kf. (4,250)
4. (PCV7 or PCV 7).tw,kf. (2,365)
5. (PCV10 or PCV 10).tw,kf. (951)
6. (PCV14 or PCV 14).tw,kf. (23)

7. (PCV15 or PCV 15).tw,kf. (429)
8. (PCV20 or PCV 20).tw,kf. (627)
9. (PCV21 or PCV 21).tw,kf. (131)
10. (Prevnar13 or prevnar 13).tw,kf. (498)
11. Vaxneuvance.tw,kf. (79)
12. (Prevnar20 or prevnar 20).tw,kf. (80)
13. Capvaxive.tw,kf. (21)
14. Synflorix.tw,kf. (386)
15. (prevnar 7 or prevnar7).tw,kf. (44)
16. pneubevax 14.tw,kf. (6)
17. or/1-16 (32,377)
18. exp child/ (3,621,422)
19. exp infant/ (1,293,466)
20. child health/ (42,180)
21. infant welfare/ (1,722)
22. infant care/ (2,433)
23. exp perinatal care/ (90,133)
24. (infant or infants or infantile or infancy or infantile).tw,kf. (675,558)
25. (premature or prematurity or preterm or pre-term or premie or premies or perinatal or peri-natal or perinat*).tw,kf. (506,379)
26. exp postnatal care/ (166,799)
27. (postnatal or post-natal or postnatal* or newborn or newborns or neonate or neonates or neonatal or neonatale or neonatales or neonatle or neonatles or neonatally or neonatorum).tw,kf. (791,806)
28. (baby or babies).tw,kf. (136,560)
29. (child or children or childhood or toddler*).tw,kf. (2,393,356)
30. "0 to 2 year*".tw,kf. (2,735)
31. "0 - 2 year*".tw,kf. (1,915)
32. under 2 year*.tw,kf. (3,763)
33. "0 to 3 year*".tw,kf. (2,535)
34. "0 - 3 year*".tw,kf. (1,772)
35. under 3 year*.tw,kf. (2,210)
36. or/18-35 (4,927,879)
37. 17 or 36 (4,945,726)
38. exp pregnancy/ (894,159)
39. exp named groups by pregnancy/ (197,116)
40. pregnan*.tw,kf. (933,070)
41. maternal welfare/ (23,170)
42. maternal exposure/ (6,124)
43. maternal health service/ (4,216)
44. maternal.tw,kf. (495,540)
45. maternity.tw,kf. (41,621)
46. mother*.tw,kf. (398,970)

47. (prenatal* or pre-natal*).tw,kf. (188,295)
48. exp prenatal care/ (209,424)
49. exp prenatal exposure/ (45,647)
50. exp perinatal exposure/ (3,547)
51. gestation.tw,kf. (217,245)
52. or/38-51 (1,782,345)
53. diphtheria pertussis tetanus vaccine/ (10,713)
54. exp tetanus/ and pertussis/ and diphtheria/ and exp immunization/ (4,279)
55. (tetanus adj2 diphtheria adj2 pertussis).tw,kf. (4,115)
56. (tetanus adj2 diptheria adj2 pertussis).tw,kf. (65)
57. (pertussis adj2 diphtheria adj2 tetanus).tw,kf. (3,206)
58. (pertussis adj2 diptheria adj2 tetanus).tw,kf. (56)
59. acellular pertussis.tw,kf. (3,822)
60. DTAP.tw,kf. (1,550)
61. TDAP.tw,kf. (2,123)
62. dTPa.tw,kf. (20,015)
63. acel-imune.tw,kf. (50)
64. infanrix.tw,kf. (986)
65. tripedia.tw,kf. (143)
66. Adacel.tw,kf. (383)
67. Boostrix-IPV.tw,kf. (29)
68. Repevax.tw,kf. (116)
69. dTaPIPV.tw,kf. (7)
70. acel immune.tw,kf. (37)
71. acelluvax dpt.tw,kf. (0)
72. acelluvax DTP.tw,kf. (2)
73. adacel.tw,kf. (383)
74. adsorbed dt coq.tw,kf. (0)
75. anatoxal di te per berna.tw,kf. (0)
76. boostrix.tw,kf. (587)
77. certiva.tw,kf. (34)
78. covaxis.tw,kf. (25)
79. daptacel.tw,kf. (146)
80. diphtheria tetanus pertussis trivaccine.tw,kf. (2)
81. diptheria tetanus pertussis trivaccine.tw,kf. (0)
82. diteki booster.tw,kf. (1)
83. ditekibooster.tw,kf. (2)
84. DPT vaccine.tw,kf. (287)
85. DTP vaccine.tw,kf. (473)
86. infanrix.tw,kf. (986)
87. neodiftepertus.tw,kf. (1)
88. pertugen.tw,kf. (1)
89. tri immunol.tw,kf. (27)

90. triacelluvax.tw,kf. (7)
91. (triaxis or tribaccine or tripacel or tripedia or triplo vaccine or tripvac or tritanrix or trivax).tw,kf. (365)
92. or/53-91 (36,325)
93. 37 and 52 and 92 (2,525)
94. limit 93 to (conference abstract or conference paper or "conference review" or editorial or letter) (330)
95. 93 not 94 (2,195)
96. limit 95 to "clinical trial (clinicaltrials.gov)" (99)
97. 95 not 96 (2,096)

Web of Science Preprint Citation Index (1990 to current)

Date of search: 9 June 2026

TS=(pneumococc* NEAR/2 (conjugate OR vaccin* OR immuni?ation*)) OR TS=(PCV13 OR "PCV 13") OR TS=(PCV7 OR "PCV 7") OR TS=(PCV10 OR "PCV 10") OR TS=(PCV14 OR "PCV 14") OR TS=(PCV15 OR "PCV 15") OR TS=(PCV20 OR "PCV 20") OR TS=(PCV21 OR "PCV 21") OR TS=(Prevnar13 OR "prevnar 13") OR TS=(Vaxneuvance) OR TS=(Prevnar20 OR "prevnar 20") OR TS=(Capvaxive) OR TS=(Synflorix) OR TS=(prevnar7 OR “prevnar 7” OR “Pneubevax 14”) OR TS=(infant OR infants OR infantile OR infancy OR infantile) OR TS=(premature OR prematurity OR preterm OR pre-term OR premie OR premies OR perinatal OR peri-natal OR perinat*) OR TS=(postnatal OR post-natal OR postnatal* OR newborn OR newborns OR neonate OR neonates OR neonatal OR neonatale OR neonatales OR neonatle OR neonatles OR neonatally OR neonatorum) OR TS=(baby OR babies) OR TS=("0 to 2 year*") OR TS=("0 - 2 year*") OR TS=("under 2 year*") OR TS=("0 to 3 year*") OR TS=("0 - 3 year*") OR TS=("under 3 year*") OR TS=(child or children or childhood or toddler*).

AND

TS=(pregnan*) OR TS=(maternal) OR TS=(maternity) OR TS=(mother* or gestation)

AND

TS=((tetanus NEAR/1 diphtheria NEAR/1 pertussis)) OR TS=((tetanus NEAR/1 diptheria NEAR/1 pertussis)) OR TS=((pertussis NEAR/1 diphtheria NEAR/1 tetanus)) OR TS=((pertussis NEAR/1 diptheria NEAR/1 tetanus)) OR TS=("acellular pertussis") OR TS=(DTAP) OR TS=(TDAP OR dTPa) OR TS=(acel-imune) OR TS=(infanrix) OR TS=(tripedia) OR TS=(Adacel) OR TS=(Boostrix-IPV) OR TS=(Repevax) OR TS=(dTaPIPV) OR TS=("acel immune") OR TS=("acelluvax dpt") OR TS=("acelluvax DTP") OR TS=(adacel) OR TS=("adsorbed dt coq") OR TS=("anatoxal di te per berna") OR TS=(boostrix) OR TS=(certiva) OR TS=(covaxis) OR TS=(daptacel) OR TS=("diphtheria tetanus pertussis trivaccine") OR TS=("diptheria tetanus pertussis trivaccine") OR TS=("diteki booster") OR

TS=(ditekibooster) OR TS=("DPT vaccine") OR TS=("DTP vaccine") OR TS=(infanrix) OR TS=(neodiftepertus) OR TS=(pertugen) OR TS=("tri immunol") OR TS=(triacelluvax) OR (TS=((triaxis OR tribaccine OR tripacel OR tripedia OR "triplo vaccine" OR tripvac OR tritanrix OR trivax)))

12 results.

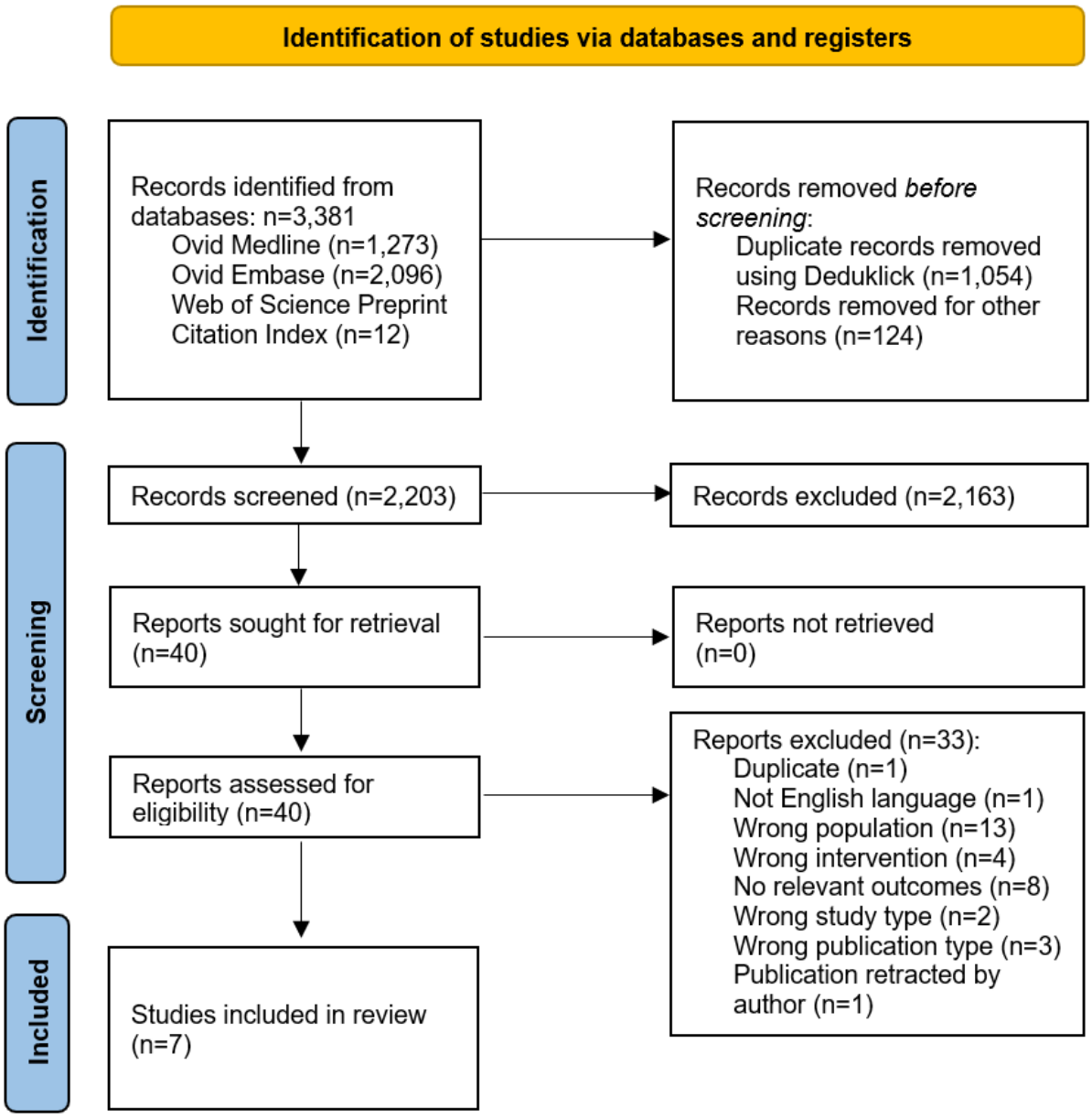
Deviations

There were no deviations from the protocol.

There was one protocol clarification: indirect cohort studies, using a modified case-control approach (‘the Broome method’) were included if identified at the full text screening stage as they have been designed to examine vaccine efficacy.

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 7 studies.

From identification of studies via databases and registers, n=3,381 records identified from databases:

- Ovid Medline (n=1,273)
- Ovid Embase (n=2,096)
- Web of Science Preprint Citation Index (n=12)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=1,054)
- records removed for other reasons (n=124)

n=2,203 records screened, of which n=2,163 were excluded, leaving n=40 papers sought for retrieval, of which n=0 were not retrieved.

Of the n=40 papers assessed for eligibility, n=33 reports were excluded:

- not English language (n=1)
- duplicate (n=1)
- wrong population (n=13)
- wrong intervention (n=4)
- no relevant outcomes (n=8)
- wrong study type (n=2)
- wrong publication type (n=3)
- publication retracted by author (n=1)

n=7 papers included in the review

Annexe C. Excluded full texts

Not English language (1 study)

Miranda Quintero J and others. 'Expert consensus on vaccination as a primary prevention strategy for women of reproductive age, pregnant, or adulthood' Revista Colombiana de Obstetricia y Ginecologia 2025: volume 76, issue 2, page 20

Duplicate (1 study)

Anonymous. 'Erratum: Pneumococcal Immune Response in Infants Whose Mothers Received Tetanus, Diphtheria and Acellular Pertussis Vaccination During Pregnancy' Paediatric Infectious Disease Journal 2018: volume 37, issue 5, page 450

Wrong population (13 studies)

Bjorkholm B and others. 'Influence of high titers of maternal antibody on the serologic response of infants to diphtheria vaccination at three, five and twelve months of age' Pediatric Infectious Disease Journal 1995: volume 14, issue 10, pages 846 to 850

Cates KL and others. 'Longitudinal development of specific and functional antibody in very low birth weight premature infants' Pediatric Research 1988: volume 23(1), issue, pages 14 to 22

Fallo AA and others. 'Prevalence of Pertussis Antibodies in Maternal Blood, Cord Serum, and Infants From Mothers With and Those Without Tdap Booster Vaccination During Pregnancy in Argentina' Journal of the Pediatric Infectious Diseases Society 2018: volume 7, issue 1, pages 11 to 17

Gall SA and others. 'Maternal immunization with tetanus-diphtheria-pertussis vaccine: effect on maternal and neonatal serum antibody levels' American Journal of Obstetrics and Gynecology 2011: volume 204, issue 4, pages 334.e1 to e5

Hardy-Fairbanks AJ and others. 'Immune responses in infants whose mothers received Tdap vaccine during pregnancy' Pediatric Infectious Disease Journal 2013: volume 32, issue 11, pages 1,257 to 1,260

Kaur I and others. 'Association of postpartum maternal tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine administration and timeliness of infant immunization' Pediatric Infectious Disease Journal 2013: volume 32, issue 11, pages 1,287 to 1,289

Maertens K and others. 'Pertussis vaccination during pregnancy in Belgium: Results of a prospective controlled cohort study' Vaccine 2016: volume 34, issue 1, pages 142 to 150

Maertens K and others. 'Breastfeeding after maternal immunisation during pregnancy: Providing immunological protection to the newborn: A review' Vaccine 2014: volume 32, issue 16, pages 1,786 to 1,792

Munoz FM and others. 'Safety and immunogenicity of tetanus, diphtheria, and acellular pertussis immunization during pregnancy in mothers and infants: A randomized clinical trial' Obstetrical and Gynecological Survey 2014: volume 69, issue 9, pages 517 to 519

Ozdil M and others. 'Pertussis antibody levels in infants and their mothers receiving combined tetanus-diphtheria toxoid and acellular pertussis vaccine during pregnancy in Turkey' European Journal of Obstetrics, Gynecology, and Reproductive Biology 2021: volume 265, issue, pages 212 to 216

Radia K and others. 'An observational, cohort, multi-centre, open label phase IV extension study comparing IPV immune responses to preschool dTaP-IPV booster vaccines in children whose mothers received or did not receive an IPV-containing pertussis vaccine during pregnancy in England' Vaccine 2026: volume 76, page 128306

Rice TF and others. 'Modification of innate immune responses to Bordetella pertussis in babies from pertussis vaccinated pregnancies' EBioMedicine 2021: volume 72, issue, 103612

Saso A and others. 'Mucosal immune responses to Bordetella pertussis in Gambian infants after maternal and primary vaccination: an immunological substudy of a single-centre, randomised, controlled, double-blind, phase 4 trial' The Lancet. Microbe 2026: volume 7, issue 1, 101219

Wrong intervention (4 studies)

Ginda T and others. 'Evaluation of the Development of Post-Vaccination Immunity against Selected Bacterial Diseases in Children of Post-Solid-Organ-Transplant Mothers' Vaccines 2024: volume 12, issue 6, page 22

Madhi SA and others. 'Antibody Kinetics and Response to Routine Vaccinations in Infants Born to Women Who Received an Investigational Trivalent Group B Streptococcus Polysaccharide CRM197-Conjugate Vaccine During Pregnancy' Clinical Infectious Diseases 2017: volume 65, issue 11, pages 1,897 to 1,904

McKittrick ND and others. 'Parasitic infections during pregnancy need not affect infant antibody responses to early vaccination against Streptococcus pneumoniae, diphtheria, or Haemophilus influenzae type B' PLoS Neglected Tropical Diseases [electronic resource] 2019: volume 13, issue 2, e0007172

Puumalainen T and others. 'Greater antibody responses to an eleven valent mixed carrier diphtheria- or tetanus-conjugated pneumococcal vaccine in Filipino than in Finnish or Israeli infants' Pediatric Infectious Disease Journal 2003: volume 22, issue 2, pages 141 to 149

No relevant outcomes (8 studies)

Abu-Raya B and others. 'Factors affecting antibody responses to immunizations in infants born to women immunized against pertussis in pregnancy and unimmunized women: Individual-Participant Data Meta-analysis' Vaccine 2021: volume 39, issue 44, pages 6,545 to 6,552

Andersen AR and others. 'Systematic review and meta-analysis of the effect of pertussis vaccine in pregnancy on the risk of chorioamnionitis, non-pertussis infectious diseases and other adverse pregnancy outcomes' Vaccine 2022: volume 40, issue 11, pages 1,572 to 1,582

Anonymous. 'Pneumococcal Immune Response in Infants Whose Mothers Received Tetanus, Diphtheria and Acellular Pertussis Vaccination During Pregnancy: ERRATUM' Paediatric Infectious Disease Journal 2018: volume 37, issue 5, page 450

Barug D and others. 'Maternal pertussis vaccination and its effects on the immune response of infants aged up to 12 months in the Netherlands: an open-label, parallel, randomised controlled trial' The Lancet Infectious Diseases 2019: volume 19, issue 4, pages 392 to 401

de Bruin O and others. 'Are maternal vaccines effective and safe for mothers and infants? A systematic review and meta-analysis of randomised controlled trials' BMJ Global Health 2023: volume 8, issue 10, page 10

Furuta M and others. 'Efficacy and safety of pertussis vaccination for pregnant women - a systematic review of randomised controlled trials and observational studies' BMC Pregnancy and Childbirth 2017: volume 17, issue 1, page 390

Holland C and others. 'Systematic review and meta-analysis of the non-specific and broader impact of respiratory vaccines on acute lower respiratory infections in young children' BMJ Open 2025: volume 15, issue 12

Jones CE and others. 'A phase IV, multi-centre, randomized clinical trial comparing two pertussis-containing vaccines in pregnant women in England and vaccine responses in their infants' BMC Medicine 2021: volume 19, issue 1, page 138

Wrong study type (2 studies)

Francois W and others. 'Nasopharyngeal Carriage of Streptococcus pneumoniae Among Young Children in Haiti Before Pneumococcal Conjugate Vaccine Introduction' Journal of Infectious Diseases 2021: volume 224, issue 12 Supplement 2, pages S248 to S257

Ladhani SN and others. 'Antibody responses after primary immunization in infants born to women receiving a pertussis-containing vaccine during pregnancy: single arm observational study with a historical comparator' Clinical Infectious Diseases 2015: volume 61, issue 11, pages 1,637 to 1,644

Wrong publication type (3 studies)

Broderick D. 'The association between third-trimester tdap immunization and neonatal pertussis antibody concentration' Irish Medical Journal 2019: volume 112, issue 8

Edwards KM. 'Impact of Vaccination During Pregnancy on Infant Pertussis Disease' Pediatrics 2023: volume 152, issue 5

Levy C and others. 'Is the interplay between maternal Tdap and pneumococcal conjugate vaccines relevant to infant pneumococcal carriage?' The Journal of infectious diseases. 2026: volume 6

Publication retracted by author (1 study)

Van den Bosch E and others. 'Interplay between Tetanus, Diphtheria, Acellular Pertussis Vaccination in Pregnancy and Infant Pneumococcal Vaccination in Shaping Infant Pneumococcal Vaccine Serotype Carriage' Journal of Infectious Diseases 2026: volume 233, issue 2, pages 298 to 306

Annexe D. Data extraction tables

Table D.1. Summary of individual participant data meta-analysis on effect of maternal Tdap vaccination during pregnancy on infant immune responses following PCV13 vaccination
Abbreviations: GMR: Geometric mean ratio, IgG: Immunoglobulin G, Tdap: tetanus, diphtheria and acellular pertussis vaccine, PCV: pneumococcal conjugate vaccine

Study, country, search period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMRs)	Proportion achieving threshold of protection (equal to or greater than 0.35 µg per mL)	Narrative results
Abu-Raya B and others, 2021(1) [A] Systematic review of 14 papers, of 10 studies. An individual participant data meta-analysis was conducted on 4 papers relevant to this review and reported. 1 January 1990 to 6 January 2020	Total: n=between 565 and 613 depending on serotype and outcome measured (n=565 to 594 for GMR antibody concentrations, n=583 to 613 for protective antibody thresholds) Age: 9 to 24 months Sex: not reported Ethnicity: not reported	Maternal Tdap vaccination: • Boostrix, 22 to 33 weeks of pregnancy • Boostrix, 27 to 36 weeks of pregnancy • Repevax (prior to July 2014) and Boostrix-IPV (after July 2014) • Boostrix, timing not reported	No maternal Tdap vaccination during pregnancy	Included infants who were post-primary vaccination or post-booster vaccination Formulation: 13-valent pneumococcal conjugate vaccine (Prevenar 13) Schedule: • Prevenar 13 at 2 and 4 months, with booster at 12 months • Prevenar 13 at 2 and 4 months, or 3 and 5 months, or 2,4 and 6 months, or 2, 3 and 4 months (dependent on countries' routine primary immunisation schedules), no booster dose • Prevenar 13 at 2 and 4 months, no booster dose • Prevenar 13 at 6 weeks, 4 months	Meta analysis model: mixed effects models Serotype 1: n=594, GMR: 0.8 (0.6 to 0.9) Serotype 3: n=565, GMR: 0.9 (0.8 to 1.0) Serotype 4: n=594, GMR: 0.8 (0.6 to 0.9) Serotype 5: n=584, GMR: 0.8 (0.6 to 0.9) Serotype 6A: n=568, GMR: 0.7 (0.6 to 0.9) Serotype 6B: n=594, GMR: 0.8 (0.6 to 1.0) Serotype 7F: n=593, GMR: 0.7 (0.5 to 1.0) Serotype 9V: n=594, GMR: 0.7 (0.5 to 0.8) Serotype 14: n=593, GMR: 0.8 (0.58 to 1.1)	Meta analysis model: mixed effects models Serotype 1: Tdap vaccinated: 94.7% (306 of 322); unvaccinated: 95.9% (278 of 290), p=0.642 Serotype 3: Tdap vaccinated: 76.6% (233 of 303); unvaccinated: 82.1% (229 of 279), p=0.13 Serotype 4: Tdap vaccinated: 87.0% (281 of 323); unvaccinated: 92.1% (267 of 290), p=0.057 Serotype 5: Tdap vaccinated: 84.8% (268 of 316); unvaccinated: 92.7% (266 of 287), p=0.004 Serotype 6A: Tdap vaccinated: 92.8% (284 of 305); unvaccinated: 96.4% (271 of 282), p=0.079 Serotype 6B: Tdap vaccinated: 72.5% (234 of 323); unvaccinated: 81.7% (237 of 290), p=0.009 Serotype 7F: Tdap vaccinated: 98.1% (316 of 322); unvaccinated: 99.0% (287 of 290), p=0.607	Infants born to women who received the Tdap vaccination in pregnancy had significantly lower anti-PCV IgG levels for serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 18C, 19A, 19F, 23F, with a reduction ranging from 15% to 35%, compared to infants whose mothers who were unvaccinated. There was not a significant difference for serotype 14. Number of infants achieving the threshold for protection against PCV13 serotypes 5, 6B, 9V, 19A, 23F were significantly lower in infants born to women who received the Tdap vaccination during pregnancy compared to infants whose mothers were unvaccinated (all p<0.05). The differences for each serotype ranged between 4% and 20%. Other serotypes measured (1, 3, 4, 6A, 7F, 14, 18C, 19F) were

Study, country, search period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMRs)	Proportion achieving threshold of protection (equal to or greater than 0.35 µg per mL)	Narrative results
				and 6 months, no booster dose	Serotype 18C: n=594, GMR: 0.8 (0.7 to 1.0) Serotype 19A: n=568, GMR: 0.8 (0.6 to 0.9) Serotype 19F: n=592, GMR: 0.8 (0.7 to 0.9) Serotype 23F: n=591, GMR: 0.7 (0.6 to 0.9)	Serotype 9V: Tdap vaccinated: 88.2% (285 of 323); unvaccinated: 94.1% (273 of 290), p=0.016 Serotype 14: Tdap vaccinated: 97.2% (314 of 324); unvaccinated: 95.5% (276 of 288), p=0.358 Serotype 18C: Tdap vaccinated: 92.6% (299 of 322); unvaccinated: 93.8% (272 of 289), p=0.661 Serotype 19A: Tdap vaccinated: 91.8% (281 of 306); unvaccinated: 96.1% (270 of 281), p=0.048 Serotype 19F: Tdap vaccinated: 99.4% (319 of 322); unvaccinated: 99.3% (288 of 291), p=0.1 Serotype 23F: Tdap vaccinated: 75.7% (243 of 321); unvaccinated: 85.5% (247 of 289), p=0.003	not statistically significantly different (all p>0.05)

[A] Includes data from 4 studies included in this report. These are reported separately in Table D.2 (3, 5 to 7).

Table D.2. Summary of effect of maternal Tdap vaccination during pregnancy on infant immune responses following PCV vaccination

Abbreviations: CI: confidence interval, DT: diphtheria toxoid, GMC: geometric mean concentration, GMR: geometric mean ratio, IgG: immunoglobulin G, IU per mL: international units per millilitre, p: p-value, PCV: pneumococcal conjugate vaccine, Tdap: tetanus, diphtheria and acellular pertussis vaccine, µg: micrograms, mL: millilitre, UK: United Kingdom

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
Barug D and others, 2020 (2) Netherlands Randomised controlled trial January 2014 to February 2016	Overall: n=103 mother-infant pairs Age: infants were followed from birth to 12 months of age Sex: not reported Ethnicity: not reported Infants in maternal Tdap during pregnancy group (n=53 mother-infant pairs) [At birth, n=58 were enrolled (5 withdrew for prematurity, severe disease or voluntary withdrawal during study): Sex: Male: 41% (24 of 58), Female: 59% (34 of 58)]	Maternal Tdap vaccination (Boostrix) Timing: 30 to 32 weeks of pregnancy	No maternal Tdap vaccination during pregnancy	Formulation: 10-valent pneumococcal conjugate vaccine (Synflorix, PHiD-CV10) PCV schedule: 2 primary doses: 3 and 5 months Booster dose: 11 months	At 6 months of age: At 6 months of age, PCV10 serotype 19F between the maternally Tdap vaccinated (n=52) and the unvaccinated group (n=50) were significantly different (p<0.05), all other PCV10 serotypes were non-significant (p>0.05). Serotype 1: Tdap vaccinated: 2.5 (1.7 to 3.5); unvaccinated: 3.0 (2.1 to 4.2); GMC ratio: 0.8 (0.5 to 1.4) Serotype 4: Tdap vaccinated: 0.6 (0.4 to 0.8); unvaccinated: 0.7 (0.5 to 0.9); GMC ratio: 0.9 (0.6 to 1.3) Serotype 5: Tdap vaccinated: 1.6 (1.2 to 2.3); unvaccinated: 1.6 (1.2 to 2.1); GMC ratio: 1.1 (0.7 to 1.6) Serotype 6B: Tdap vaccinated: 0.3 (0.2 to 0.6); unvaccinated: 0.3 (0.2 to 0.5); GMC ratio: 1.1 (0.5 to 2.2) Serotype 7F: Tdap vaccinated: 4.0 (3.0 to 5.3); unvaccinated: 3.6 (2.8 to 4.8); GMC ratio: 1.1 (0.7 to 1.6) Serotype 9V: Tdap vaccinated: 1.4 (1.1 to 2.0); unvaccinated: 1.7 (1.3 to 2.2); GMC ratio: 0.8 (0.6 to 1.2)	There were no statistically significant differences between the maternal Tdap and control groups at either time point for any PCV10 serotype (all p>0.05). In both maternal Tdap and control groups, between 54% and 98% of infants met the threshold of protection for PCV10 serotypes after primary vaccination. Following booster vaccination, between 98% and 100% of infants met the threshold for protection for all PCV10 serotypes. At 6 months of age: Serotype 1: Tdap vaccinated: 92% (48 of 52); unvaccinated: 94% (47 of 50) Serotype 4: Tdap vaccinated: 71% (37 of 52); unvaccinated: 74% (37 of 50) Serotype 5: Tdap vaccinated: 90% (47 of 52); unvaccinated: 90% (45 of 50) Serotype 6B: Tdap vaccinated: 67% (35 of 52); unvaccinated: 54% (30 of 50)	IgG GMCs for Diphtheria toxoid (IU per ml): Cord blood (at birth or within 48h of birth): Tdap vaccinated: 0.6 (0.5 to 0.9); unvaccinated: not reported (0.1 to 0.2); GMC ratio: 5.5 (3.5 to 8.7), p<0.001 At 2 months of age: Tdap vaccinated: 0.1 (0.1 to 0.17); unvaccinated: 0.03 (0.02 to 0.04); GMC ratio: 4.9 (3.1 to 7.7), p<0.001 At 3 months of age: Tdap vaccinated: 0.07 (0.06 to 0.10); unvaccinated: 0.01 (0.01 to 0.02); GMC ratio: 4.9 (3.1 to 7.8), p<0.001 At 6 months of age (post-primary PCV vaccination): Tdap vaccinated: 0.1 (0.1 to 0.2); unvaccinated: 0.4 (0.3 to 0.5); GMC ratio: 0.4 (0.3 to 0.6), p<0.001	Not reported

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
	Infants in control group- maternal Tdap after delivery (n=50) [At birth, n=60 were enrolled (10 withdrew for prematurity, voluntary withdrawal, severe disease or poor neonate condition or lost to follow up): Male: 37% (22 of 60) Female: 63% (38 of 60)]				Serotype 14: Tdap vaccinated: 2.7 (2.0 to 3.7); unvaccinated: 2.9 (2.1 to 3.9); GMC ratio: 0.9 (0.6 to 1.5) Serotype 18C: Tdap vaccinated: 0.9 (0.6 to 1.4); unvaccinated: 1.0 (0.7 to 1.5); GMC ratio: 0.9 (0.5 to 1.6) Serotype 19F: Tdap vaccinated: 4.8 (3.0 to 7.6); unvaccinated: 11.5 (7.2 to 8.2); GMC ratio: 0.4 (0.2 to 0.8); p<0.05 Serotype 23F: Tdap vaccinated: 0.6 (0.4 to 0.9); unvaccinated: 0.5 (0.3 to 0.8); GMC ratio: 1.1 (0.6 to 2.1) Related serotypes not included in PHiD-CV10 vaccine remained low after primary vaccines in both groups: Serotype 6A: Tdap vaccinated: 0.04 (0.03 to 0.07); unvaccinated: 0.05 (0.03 to 0.08); GMC ratio: 0.9 (0.4 to 1.8) Serotype 19A: Tdap vaccinated: 0.07 (0.04 to 0.10); unvaccinated: 0.12 (0.08 to 0.17); GMC ratio: 0.6 (0.3 to 1.0) At 12 months of age: At 12 months of age, there were no statistically significant differences between the	Serotype 7F: Tdap vaccinated: 98% (51 of 52); unvaccinated: 98% (49 of 50) Serotype 9V: Tdap vaccinated: 88% (46 of 52); unvaccinated: 94% (47 of 50) Serotype 14: Tdap vaccinated: 96% (50 of 52); unvaccinated: 94% (47 of 50) Serotype 18C: Tdap vaccinated: 71% (37 of 52); unvaccinated: 80% (40 of 50) Serotype 19F: Tdap vaccinated: 90% (47 of 52); unvaccinated: 96% (48 of 50) Serotype 23F: Tdap vaccinated: 73% (38 of 52); unvaccinated: 66% (33 of 50) Cross reactive serotypes not included in PHiD-CV10 vaccine: Serotype 6A: Tdap vaccinated: 13% (7 of 52); unvaccinated: 14% (7 of 50) Serotype 19A: Tdap vaccinated: 8% (4 of 52); unvaccinated: 18% (9 of 50) At 12 months of age:	At 11 months of age (pre-booster): Tdap vaccinated: 0.04 (0.03 to 0.05); unvaccinated: 0.07 (0.05 to 0.09); GMC ratio: 0.5 (0.4 to 0.8), p<0.001 At 12 months of age (post-booster): Tdap vaccinated: 0.8 (0.7 to 1.0); unvaccinated: 1.2 (1.0 to 1.6); GMC ratio: 0.7 (0.5 to 0.9), p<0.001 Proportion achieving basic (0.01IU/ml) or full (0.1IU/ml) level of protection: Cord blood (at birth or within 48h of birth): Basic protection: Tdap vaccinated: 100% (54 of 54); unvaccinated: 100% (53 of 53), p>0.05 Full protection: Tdap vaccinated: 96% (52 of 54); unvaccinated: 57% (30 of 53), p<0.05 At 2 months of age: Basic protection:	

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					maternally Tdap vaccinated group (n=51) compared to the control (n=47) for any serotype (p>0.05) Serotype 1: Tdap vaccinated: 9.1 (7.0 to 11.8); unvaccinated: 10.4 (7.8 to 13.7); GMC ratio: 0.9 (0.6 to 1.3) Serotype 4: Tdap vaccinated: 1.8 (1.5 to 2.2); unvaccinated: 1.8 (1.5 to 2.3); GMC ratio: 1.0 (0.7 to 1.3) Serotype 5: Tdap vaccinated: 5.3 (4.1 to 6.8); unvaccinated: 5.7 (4.3 to 7.6); GMC ratio: 0.9 (0.6 to 1.3) Serotype 6B: Tdap vaccinated: 5.5 (4.3 to 7.0); unvaccinated: 4.8 (3.7 to 6.2); GMC ratio: 1.2 (0.8 to 1.6) Serotype 7F: Tdap vaccinated: 10.4 (8.2 to 13.0); unvaccinated: 9.3 (7.5 to 11.6); GMC ratio: 1.1 (0.8 to 1.5) Serotype 9V: Tdap vaccinated: 5.6 (4.6 to 6.7); unvaccinated: 6.1 (4.9 to 7.7); GMC ratio: 0.9 (0.7 to 1.2) Serotype 14: Tdap vaccinated: 4.7 (3.5 to 6.1); unvaccinated: 4.9 (3.6 to 6.5); GMC ratio: 1.0 (0.7 to 1.4) Serotype 18C: Tdap vaccinated: 8.2 (6.5 to 10.5); unvaccinated: 7.4 (5.6 to 9.9); GMC ratio: 1.1 (0.8 to 1.6)	Serotype 1: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 4: Tdap vaccinated: 100% (51 of 51); unvaccinated: 98% (46 of 47) Serotype 5: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 6B: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 7F: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 9V: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 14: Tdap vaccinated: 98% (50 of 51); unvaccinated: 98% (46 of 47) Serotype 18C: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47) Serotype 19F: Tdap vaccinated: 100% (51 of 51); unvaccinated: 100% (47 of 47)	Tdap vaccinated: 100% (55 of 55); unvaccinated: 74% (39 of 53), p<0.05 Full protection: Tdap vaccinated: 67% (37/ of 55); unvaccinated: 23% (12 of 53), p<0.05 At 3 months of age: Basic protection: Tdap vaccinated: 94% (51/ of 54); unvaccinated: 64% (32 of 50), p<0.05 Full protection: Tdap vaccinated: 41% (22 of 54); unvaccinated: 8% (4 of 50), p<0.05 At 6 months of age (post-primary PCV vaccination): Basic protection: Tdap vaccinated: 100% (53 of 53); unvaccinated: 100% (50 of 50), p>0.05 Full protection: Tdap vaccinated: 59% (31 of 53); unvaccinated: 84% (42 of 50), p<0.05 At 11 months of age (pre-booster): Basic protection:	

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 19F: Tdap vaccinated: 32.4 (25.2 to 41.6); unvaccinated: 40.6 (30.0 to 54.9); GMC ratio: 0.8 (0.5 to 1.2) Serotype 23F: Tdap vaccinated: 4.1 (3.3 to 5.3); unvaccinated: 3.7 (3.0 to 4.7); GMC ratio: 0.1 (0.8 to 1.5) Related serotypes not included in PHiD-CV10 vaccine: Serotype 6A: Tdap vaccinated: 0.6 (0.3 to 1.0); unvaccinated: 0.5 (0.3 to 0.9); GMC ratio: 1.1 (0.5 to 2.3) Serotype 19A: Tdap vaccinated: 0.5 (0.3 to 0.7); unvaccinated: 0.7 (0.5 to 1.1); GMC ratio: 0.6 (0.3 to 1.1)	Serotype 23F: Tdap vaccinated: 98% (50 of 51); unvaccinated: 100% (47 of 47) Cross reactive serotypes not included in PHiD-CV10 vaccine: Serotype 6A: Tdap vaccinated: 67% (34 of 51); unvaccinated: 74% (35 of 47) Serotype 19A: Tdap vaccinated: 65% (33 of 51); unvaccinated: 70% (33 of 47)	Tdap vaccinated: 92% (47 of 51); unvaccinated: 96% (45 of 47), p>0.05 Full protection: Tdap vaccinated: 16% (8 of 51); unvaccinated: 40% (19 of 47), p<0.05 At 12 months of age (post-booster): Basic protection: Tdap vaccinated: 100% (53 of 53); unvaccinated: 100% (50 of 50), p>0.05 Full protection: Tdap vaccinated: 98% (52 of 53); unvaccinated: 100% (50 of 50), p>0.05	
Maertens K and others, 2017 (5) Prospective cohort study Belgium 2011 to 2015	Total: n=77 mother-infant pairs (77 mothers, 79 children [2 sets of twins]) Age: 0 to 15 months Sex: Male: 48.1% (38 of 77) Female: 52.9% (41 of 77)	Maternal Tdap vaccination (Boostrix) Timing: between week 18 to 34 of pregnancy	No maternal vaccination with a pertussis-containing vaccine for at least 10 years	13-valent pneumococcal vaccine (Prevenar 13) Schedule: 3 doses: 8 weeks,16 weeks and 12 months All infants were vaccinated at the respective	At 5 months of age (one month after second vaccine): Maternally Tdap vaccinated infants had significantly lower antibody GMCs for PCV13 serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 19A than the control (all<0.05). Serotype 1 (n=49): Tdap vaccinated: 1.0 (0.8 to 1.3); control (n=24): 1.0 (1.3 to 3.0); GMC ratio: 0.5; p=0.004 Serotype 3 (n=44): Tdap vaccinated: 0.5 (0.4 to 0.7); control	At 5 months of age (one month after second vaccine): At month 5, maternally Tdap vaccinated infants had statistically significant lower percentage reaching the protective antibody threshold for PCV13 serotype 3 compared to the control. Serotype 1: Tdap vaccinated: 95.6% (89.4 to 100%); unvaccinated: 91.7% (80.5 to 100%); p=0.606 Serotype 3: Tdap vaccinated: 73.8% (60.4 to 87.2%);	Not reported	Several influencing factors were identified, but these differed per serotype and group. The following factors were identified as having an effect on serotypes for at least one vaccine or control group were gender (serotype 7F),

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
	Ethnicity: Caucasian mother: 98.7% (76 of 77), other: 1.3% (1 of 77) Maternal Tdap vaccination (n=54): Sex: Male: 48.2% (26 of 54) Female: 51.9% (28 of 54) Ethnicity: born to a Caucasian mother: 98.1% (51 of 54), born to a mother of another race: 1.9% (1 of 54) Unvaccinated (n=25): Sex: Males: 48.0% (12 of 25) Females: 52.0% (13 of 25) Ethnicity: born to a Caucasian mother: 100%			immunisation visits	(n=22): 0.9 (0.6 to 1.1); GMC ratio: 0.6; p=0.044 Serotype 4 (n=49): Tdap vaccinated: 1.0 (0.8 to 1.2); control (n=24): 1.5 (1.0 to 2.3); GMC ratio: 0.6; p=0.024 Serotype 5 (n=46): Tdap vaccinated: 0.5 (0.4 to 0.6); control (n=24): 0.9 (0.7 to 1.3); GMC ratio: 0.5; p=0.003 Serotype 6A (n=46): Tdap vaccinated: 0.8 (0.6 to 1.1); control (n=24): 1.5 (1.0 to 2.3); GMC ratio: 0.5; p=0.025 Serotype 6B (n=49): Tdap vaccinated: 0.2 (0.2 to 0.3); control (n=24): 0.3 (0.2 to 0.5); GMC ratio: 0.8; p=0.528 Serotype 7F (n=46): Tdap vaccinated: 1.7 (1.4 to 2.0); control (n=24): 2.7 (1.8 to 4.2); GMC ratio: 0.6; p=0.027 Serotype 9V (n=49): Tdap vaccinated: 0.5 (0.4 to 0.7); control (n=24): 1.9 (0.8 to 1.8); GMC ratio: 0.5; p=0.001 Serotype 14 (n=49): Tdap vaccinated: 3.4 (2.5 to 4.7); control (n=23): 7.4 (4.4 to 12.4); GMC ratio: 0.5; p=0.011	unvaccinated: 95.6% (86.8 to 100%); p=0.045 Serotype 4: Tdap vaccinated: 97.8% (93.3 to 100%); unvaccinated: 91.7% (80.5 to 100%); p=0.276 Serotype 5: Tdap vaccinated: 65.9% (51.8 to 80.0%); unvaccinated: 87.5% (74.2 to 100%); p=0.083 Serotype 6A: Tdap vaccinated: 84.1% (73.2 to 95.0%); unvaccinated: 91.7% (80.5 to 100%); p=0.476 Serotype 6B: Tdap vaccinated: 37.8% (23.5 to 52.1%); unvaccinated: 41.7% (21.9 to 61.5%); p=0.475 Serotype 7F: Tdap vaccinated: 97.7% (93.2 to 100%); unvaccinated: 95.8% (87.7 to 100%); p=1.00 Serotype 9V: Tdap vaccinated: 77.8% (65.5 to 90.0%); unvaccinated: 87.5% (74.2 to 100%); p=0.519 Serotype 14: Tdap vaccinated: 95.6% (89.4 to 100%); unvaccinated: 95.7% (87.2 to 100%); p=1.0 Serotype 18C: Tdap vaccinated: 88.9% (79.6 to 98.2%);		nutrition (serotype 5), age at blood sampling (5, 6B, 14, 18C), infant vaccination timing (serotype 5, 6A ,14, 18c), Weight (6B), gestational age at delivery (serotype 4), interval between vaccine and sample (5, 6A, 6B, 13, 18C)

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
	(25 of 25), born to a mother of another race: 0.0% (0 of 25)				Serotype 18C (n=49): Tdap vaccinated: 0.9 (0.7 to 1.1); control (n=24): 1.1 (0.7 to 1.7); GMC ratio: 0.8; p=0.270 Serotype 19A (n=46): Tdap vaccinated: 1.2 (0.9 to 1.5); control (n=24): 2.2 (1.6 to 3.1); GMC ratio: 0.5; p=0.005 Serotype 19F (n=45): Tdap vaccinated: 3.3 (2.5 to 4.4); control (n=24): 4.9 (3.1 to 7.7); GMC ratio: 0.7; p=0.136 Serotype 23F (n=49): Tdap vaccinated: 0.4 (0.3 to 0.6); control (n=24): 0.6 (0.4 to 1.0); GMC ratio: 0.7; p=0.214 At 15 months of age (2.5 months after third [booster] vaccine): At month 15, maternally Tdap vaccinated infants had significantly lower antibody GMCs for PCV13 serotypes 1 and 4 compared to the control (p<0.05). Serotype 1 (n=49): Tdap vaccinated: 1.2 (0.9 to 1.4); control (n=24): 1.9 (1.3 to 2.8); GMC ratio: 0.6; p=0.025 Serotype 3 (n=38): Tdap vaccinated: 0.7 (0.6 to 0.9); control (n=19): 0.7 (0.5 to 1.0); GMC ratio: 1.0; p=0.902	unvaccinated: 91.7% (80.5 to 100%); p=1.0 Serotype 19A: Tdap vaccinated: 88.6% (79.2 to 98.1%); unvaccinated: 100%; p=0.153 Serotype 19F: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 23F: Tdap vaccinated: 57.8% (43.3 to 72.3%); unvaccinated: 62.5% (43.0 to 82.0%); p=0.799 At 15 months of age (2.5 months after third [booster] vaccine): At month 15, maternally Tdap vaccinated infants had no statistically significant differences in the percentage reaching the protective antibody threshold for PCV13 serotypes compared to the control (all p>0.05). Serotype 1: Tdap vaccinated: 95.92% (90.3 to 100%); unvaccinated: 95.5% (86.7 to 100%); p=1.0 Serotype 3: Tdap vaccinated: 94.7% (87.8 to 100%); unvaccinated: 83.3% (66.0 to 100%); p=0.314 Serotype 4: Tdap vaccinated: 87.8% (78.5 to 97.1%); unvaccinated: 100%; p=0.167		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 4 (n=49): Tdap vaccinated: 0.8 (0.7 to 1.0); control (n=24): 1.4 (1.0 to 1.9); GMC ratio: 0.6; p=0.008 Serotype 5 (n=49): Tdap vaccinated: 0.9 (0.8 to 1.1); control (n=24): 1.0 (0.8 to 1.3); GMC ratio: 0.9; p=0.659 Serotype 6A (n=49): Tdap vaccinated: 5.3 (4.3 to 6.7); control (n=24): 7.7 (5.4 to 11.0); GMC ratio: 0.7; p=0.084 Serotype 6B (n=49): Tdap vaccinated: 2.6 (2.0 to 3.4); control (n=24): 3.9 (2.7 to 5.6); GMC ratio: 0.7; p=0.095 Serotype 7F (n=49): Tdap vaccinated: 1.9 (1.5 to 2.2); control (n=24): 2.6 (1.9 to 3.4); GMC ratio: 0.7; p=0.062 Serotype 9V (n=49): Tdap vaccinated: 0.8 (0.7 to 0.9); control (n=24): 1.0 (0.7 to 1.4); GMC ratio: 0.8; p=0.192 Serotype 14 (n=49): Tdap vaccinated: 5.1 (4.0 to 6.6); control (n=24): 7.7 (4.9 to 12.0); GMC ratio: 0.7; p=0.108 Serotype 18C (n=49): Tdap vaccinated: 0.6 (0.5 to 0.8); control (n=24): 0.8 (0.5 to 1.2); GMC ratio: 0.8; p=0.289	Serotype 5: Tdap vaccinated: 95.9% (90.3 to 100%); unvaccinated: 90.9% (78.8 to 100%); p=0.583 Serotype 6A: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 6B: Tdap vaccinated: 95.9% (90.3 to 100%); unvaccinated: 100%; p=0.566 Serotype 7F: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 9V: Tdap vaccinated: 91.8% (84.1 to 99.6%); unvaccinated: 95.5% (86.7 to 100%); p=0.673 Serotype 14: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 18C: Tdap vaccinated: 81.6% (70.7 to 92.6%); unvaccinated: 77.3% (59.7 to 94.9%); p=0.750 Serotype 19A: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 19F: Tdap vaccinated: 100%; unvaccinated: 100%; p=N/A Serotype 23F: Tdap vaccinated: 87.8% (78.5 to 97.1%); unvaccinated: 100%; p=0.167		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 19A (n=49): Tdap vaccinated: 3.6 (2.9 to 4.6); control (n=24): 3.6 (2.4 to 5.4); GMC ratio: 1.0; p=0.985 Serotype 19F (n=49): Tdap vaccinated: 3.8 (3.1 to 4.7); control (n=24): 3.8 (2.7 to 5.3); GMC ratio: 1.0; p=0.966 Serotype 23F (n=49): Tdap vaccinated: 1.1 (0.8 to 1.4); control (n=24): 1.7 (1.2 to 2.4); GMC ratio: 0.7; p=0.073			
Rice TF and others, 2019 (6) Cohort UK May 2014 to September 2016	Total: n=31 mother infant pairs Age: 0 to 5 months Tdap vaccinated (n=16): Sex: Male: 50.0% (8 of 16) Female: 50.0% (8 of 16) Ethnicity of mother: Asian 13.3% (2 of 16) Black 13.3% (2 of 16)	Maternal Tdap vaccination (Repevax or Boostrix-IPV) Timing: not reported	No maternal Tdap vaccination	13-valent pneumococcal conjugate vaccine (Prevenar13) Dose: 2 doses Timing: 8 and 16 weeks	At 5 months, maternally Tdap vaccinated infants had significantly lower antibody concentrations for PCV13 serotypes 7F and 14 compared to the control. Post-vaccination (5 months) pneumococcal IgG antibody concentrations (IU per mL) in infants: Serotype 1: Tdap vaccinated: 6.4 (2.5 to 10.4); unvaccinated: 6.7 (1.8 to 11.5); p=0.64 Serotype 4: Tdap vaccinated: 0.5 (0.3 to 0.8); unvaccinated: 0.7 (0.3 to 1.1); p=0.38 Serotype 5: Tdap vaccinated: 3.4 (0.4 to 6.4); unvaccinated: 3.0 (0.8 to 5.2); p=0.6	Not reported	Not reported	Parity (previous births)

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
	White 60.0% (9 of 16) Other: 13.3% (2 of 16) Unvaccinated (n=15): Sex: Male: 46.7% (7 of 15) Female: 53.3% (8 of 15) Ethnicity of mother: Asian: 6.3% (1 of 15) Black 0.0% (0 of 15) White: 87.5% (14 of 15) Other: 6.3% (1 of 15)				Serotype 6B: Tdap vaccinated: 0.8 (0.1 to 1.6); unvaccinated: 0.4 (-0.1 to 1.0); p=0.43 Serotype 7F: Tdap vaccinated: 5.2 (2.4 to 8.0); unvaccinated: 8.7 (5.0 to 12.3); p=0.002 Serotype 9V: Tdap vaccinated: 1.4 (0.6 to 2.1); unvaccinated: 2.7 (0.8 to 4.6); p=0.11 Serotype 14: Tdap vaccinated: 4.6 (1.3 to 7.9); unvaccinated: 1.7 (0.2 to 3.1); p=0.04 Serotype 18C: Tdap vaccinated: 2.6 (0.4 to 4.9); unvaccinated: 3.0 (0.9 to 5.1); p=0.56 Serotype 19F: Tdap vaccinated: 20.9 (7.0 to 34.9); unvaccinated: 20.1 (7.6 to 32.5); p=0.72 Serotype 23F: Tdap vaccinated: 1.0 (-0.1 to 2.1); unvaccinated: 1.9 (-0.0 to 3.8); p=0.16			
Perrett KP and others, 2020 (3) Non-randomised study Global (Australia, Canada, Czech Republic, Finland, Italy and Spain)	Healthy infants (n=601; 542 included in final analysis) Age: up to 7 months Tdap vaccinated (n=296; 268	Maternal Tdap vaccination (Boostrix) Timing: 27 to 37 weeks of pregnancy	No maternal Tdap vaccination Placebo given during pregnancy and Tdap vaccination 72 hours post-partum.	13-valent pneumococcal vaccine (Prevnar 13) and DTaP-HBV/Hib Schedule: 2 or 3 doses (dependent on countries	One month after primary PCV13 vaccination, maternally Tdap vaccinated infants had significantly lower antibody GMCs for PCV13 serotypes 4 and 19F compared to the unvaccinated control. Serotype 1: Tdap vaccinated: 1.6 (1.4 to 1.8); unvaccinated: 1.9 (1.7 to 2.1)	One month after primary PCV13 vaccination, maternally Tdap vaccinated infants had no statistically significant differences in the percentage reaching the protective antibody threshold for PCV13 serotypes compared to the unvaccinated infants (all p>0.05). Serotype 1: Tdap vaccinated: 95.7% (92.2 to 97.9%);	Not reported	Analysis not adjusted

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
22 January 2016 to 7 March 2018	included in final analysis): Sex: Female: 47.6% (141 of 296) Ethnicity: White: 90.8% (269 of 296), Asian: 1.7% (5 of 296), African/African American: 1.4% (4 of 296), Other: 6.1% (18 of 296) Tdap unvaccinated: Sex: Female: 47.2% (144 of 305) Ethnicity: White: 94.4% (288 of 305), Asian: 0.0% (0 of 305), African/African American: 3.0% (9 of 305), Other: 2.6% (8 of 305)			routine vaccine schedules) Timing: 2 dose schedule: either 2 months and 4-month vaccines (2-4 schedule) and blood sampling at 5 months or 3 months and 5-month vaccines (3-5 schedule) and blood sampling at 6 months. 3 dose schedule: either 2-, 3- and 4-month vaccine (2-3-4) with blood sampling at 5 months or 2-, 4-, and 6-month (2-4-6 schedule) vaccines with blood sampling at 7.	Serotype 3: Tdap vaccinated: 0.5 (0.5 to 0.6); unvaccinated: 0.6 (0.6 to 0.7) Serotype 4: Tdap vaccinated: 1.2 (1.1 to 1.4); unvaccinated: 1.6 (1.4 to 1.8) Serotype 5: Tdap vaccinated: 1.1 (1.0 to 1.2); unvaccinated: 1.3 (1.1 to 1.4) Serotype 6A: Tdap vaccinated: 2.2 (1.9 to 2.5); unvaccinated: 2.6 (2.3 to 3.0) Serotype 6B: Tdap vaccinated: 1.4 (1.1 to 1.7); unvaccinated: 1.4 (1.2 to 1.7) Serotype 7F: Tdap vaccinated: 2.4 (2.2 to 2.7); unvaccinated: 2.7 (2.4 to 2.9) Serotype 9V: Tdap vaccinated: 1.3 (1.2 to 1.5); unvaccinated: 1.6 (1.5 to 1.8) Serotype 14: Tdap vaccinated: 5.7 (5.0 to 6.5); unvaccinated: 6.6 (5.7 to 7.6) Serotype 18C: Tdap vaccinated: 1.6 (1.4 to 1.8); unvaccinated: 1.8 (1.6 to 2.0)	unvaccinated: 95.8% (92.4 to 98.0%) Serotype 3: Tdap vaccinated: 74.6% (68.5 to 80.0%); unvaccinated: 76.4% (70.4 to 81.6%) Serotype 4: Tdap vaccinated: 92.2% (88.0 to 95.3%); unvaccinated: 96.2% (92.9 to 98.2%) Serotype 5: Tdap vaccinated: 88.1% (83.1 to 92.0%); unvaccinated: 91.5% (87.1 to 94.7%) Serotype 6A: Tdap vaccinated: 95.3% (91.7 to 97.6%); unvaccinated: 95.4% (91.8 to 97.7%) Serotype 6B: Tdap vaccinated: 79.7% (74.0 to 84.7%); unvaccinated: 84.4% (79.1 to 88.8%) Serotype 7F: Tdap vaccinated: 98.7% (96.3 to 99.7%); unvaccinated: 99.6% (97.7 to 100%) Serotype 9V: Tdap vaccinated: 91.4% (87.0 to 94.7%); unvaccinated: 95.8% (92.4 to 98.0%)		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 19A: Tdap vaccinated: 1.6 (1.4 to 1.8); unvaccinated: 2.0 (1.8 to 2.3) Serotype 19F: Tdap vaccinated: 2.6 (2.4 to 2.8); unvaccinated: 3.2 (2.9 to 3.6) Serotype 23F: Tdap vaccinated: 0.9 (0.7 to 1.0); unvaccinated: 1.0 (0.9 to 1.2) Subgroup analyses: When analysed by dosing schedule, one month after primary PCV13 vaccination, maternally Tdap vaccinated infants had significantly lower antibody GMCs for PCV13 serotypes 4 and 19F compared to the control. Serotype 1: 2-dose: Tdap vaccinated: 1.5 (1.1 to 2.1) (n=21); unvaccinated: 2.0 (1.4 to 2.7) (n=32) 3-dose: Tdap vaccinated: 1.6 (1.4 to 1.8) (n=211); unvaccinated: 1.9 (1.7 to 2.1) (n=205) Serotype 3: 2-dose: Tdap vaccinated: 0.6 (0.4 to 0.7) (n=21); unvaccinated: 0.7 (0.5 to 0.8) (n=32) 3-dose: Tdap vaccinated: 0.5 (0.5 to 0.6) (n=211); unvaccinated: 0.6 (0.5 to 0.7) (n=205)	Serotype 14: Tdap vaccinated: 98.7% (96.3 to 99.7%); unvaccinated: 98.3% (95.7 to 99.5%) Serotype 18C: Tdap vaccinated: 94.8% (91.1 to 97.3%); unvaccinated: 94.1% (90.3 to 96.7%) Serotype 19A: Tdap vaccinated: 93.1% (89.0 to 96.0%); unvaccinated: 95.8% (92.4 to 98.0%) Serotype 19F: Tdap vaccinated: 99.1% (96.9 to 99.9%); unvaccinated: 98.3% (95.7 to 99.5%) Serotype 23F: Tdap vaccinated: 79.1% (73.3 to 84.2%); unvaccinated: 86.0% (80.9 to 90.2%) Subgroup analyses: When analysed by dosing schedule, maternally Tdap vaccinated infants had no statistically significant differences in the percentage reaching the protective antibody threshold for PCV13 serotypes compared to the unvaccinated control (all p>0.05). Serotype1:		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 4: 2-dose: Tdap vaccinated: 1.2 (0.8 to 1.8) (n=21); unvaccinated: 2.1 (1.5 to 2.8) (n=32) 3-dose: Tdap vaccinated: 1.2 (1.1 to 1.4) (n=211); unvaccinated: 1.5 (1.3 to 1.7) (n=205) Serotype 5: 2-dose: Tdap vaccinated: 0.8 (0.6 to 1.2) (n=20); unvaccinated: 1.0 (0.7 to 1.5) (n=32) 3-dose: Tdap vaccinated: 1.1 (1.0 to 1.3) (n=206); unvaccinated: 1.3 (1.2 to 1.5) (n=202) Serotype 6A: 2-dose: Tdap vaccinated: 1.5 (0.9 to 2.4) (n=21); unvaccinated: 1.9 (1.2 to 3.0) (n=32) 3-dose: Tdap vaccinated: 2.2 (2.0 to 2.6) (n=211); unvaccinated: 2.7 (2.4 to 3.1) (n=205) Serotype 6B: 2-dose: Tdap vaccinated: 0.3 (0.2 to 0.5) (n=21); unvaccinated: 0.4 (0.3 to 0.7) (n=32) 3-dose: Tdap vaccinated: 1.6 (1.3 to 2.0) (n=211); unvaccinated: 1.7 (1.4 to 2.1) (n=205) Serotype 7F: 2-dose: Tdap vaccinated: 1.9 (1.4 to 2.6) (n=21); unvaccinated: 2.2 (1.7 to 2.8) (n=32)	2-dose: Tdap vaccinated: 95.2% (76.2 to 99.9%) (n=21); unvaccinated: 96.9% (83.8 to 99.9%) (n=32) 3-dose: Tdap vaccinated: 95.7% (92.1 to 98.0%) (n=211); unvaccinated: 95.6% (91.8 to 98.0%) (n=205) Serotype 3: 2-dose: Tdap vaccinated: 81.0% (58.1 to 94.6%) (n=21); unvaccinated: 87.5% (71.0 to 96.5%) (n=32) 3-dose: Tdap vaccinated: 73.9 (67.5 to 79.7%) (n=211); unvaccinated: 74.6% (68.1 to 80.4%) (n=205) Serotype 4: 2-dose: Tdap vaccinated: 90.5% (69.6 to 98.8%) (n=21); unvaccinated: 96.9% (83.8 to 99.9%) (n=32) 3-dose: Tdap vaccinated: 92.4% (88.0 to 95.6%) (n=211); unvaccinated: 96.1% (92.5 to 98.3%) (n=205) Serotype 5: 2-dose: Tdap vaccinated: 85.0% (62.1 to 96.8%) (n=20); unvaccinated: 84.4% (67.2 to 94.7%) (n=32) 3-dose: Tdap vaccinated: 88.3% (83.2 to 92.4%) (n=206); unvaccinated: 92.6% (88.0 to 95.8%) (n=202)		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					3-dose: Tdap vaccinated: 2.5 (2.2 to 2.7) (n=211); unvaccinated: 2.8 (2.5 to 3.1) (n=205) Serotype 9V: 2-dose: Tdap vaccinated: 1.1 (0.7 to 1.8) (n=21); unvaccinated: 1.8 (1.2 to 2.7) (n=32) 3-dose: Tdap vaccinated: 1.4 (1.2 to 1.5) (n=211); unvaccinated: 1.6 (1.4 to 1.8) (n=205) Serotype 14: 2-dose: Tdap: 3.4 (2.1 to 5.7) (n=21); unvaccinated: 4.7 (2.7 to 7.7) (n=32) 3-dose: Tdap vaccinated: 6.0 (5.2 to 6.9) (n=211); unvaccinated: 6.9 (6.0 to 8.0) (n=205) Serotype 18C: 2-dose: Tdap vaccinated: 1.1 (0.7 to 1.6) (n=21); unvaccinated: 1.57 (1.1 to 2.3) (n=32) 3-dose: Tdap vaccinated: 1.7 (1.5 to 1.9) (n=211); unvaccinated: 1.8 (1.6 to 2.1) (n=205) Serotype 19A: 2-dose: Tdap vaccinated: 2.0 (1.3 to 3.2) (n=21); unvaccinated: 3.1 (2.0 to 4.8) (n=32) 3-dose: Tdap vaccinated: 1.6 (1.4 to 1.8) (n=211); unvaccinated: 1.9 (1.7 to 2.1) (n=205) Serotype 19F:	Serotype 6A: 2-dose: Tdap vaccinated: 90.5% (69.6 to 98.8%) (n=21); unvaccinated: 87.5% (71.0 to 96.5%) (n=32) 3-dose: Tdap vaccinated: 95.7% (92.1 to 98.0%) (n=211); unvaccinated: 96.6% (93.1 to 98.6%) (n=205) Serotype 6B: 2-dose: Tdap vaccinated: 33.3% (14.6 to 57.0%) (n=21); unvaccinated: 62.5% (43.7 to 78.9%) (n=32) 3-dose: Tdap vaccinated: 84.4% (78.7 to 89.0%) (n=211); unvaccinated: 87.8% (82.5 to 92.0%) (n=205) Serotype 7F: 2-dose: Tdap vaccinated: 100% (83.9 to 100%) (n=21); unvaccinated: 100% (89.1 to 100%) (n=32) 3-dose: Tdap vaccinated: 98.6% (95.9 to 99.7%) (n=211); unvaccinated: 99.5% (97.3 to 100%) (n=205) Serotype 9V: 2-dose: Tdap vaccinated: 90.5% (69.6 to 98.8%) (n=21); unvaccinated: 93.8% (79.2 to 99.2%) (n=32) 3-dose: Tdap vaccinated: 91.5% (86.9 to 94.9%) (n=211);		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					2-dose: Tdap vaccinated: 4.6 (3.4 to 6.2) (n=21); unvaccinated: 5.9 (4.0 to 8.8) (n=32) 3-dose: Tdap vaccinated: 2.4 (2.2 to 2.7) (n=211); unvaccinated: 3.0 (2.7 to 3.3) (n=205)	unvaccinated: 96.1% (92.5 to 98.3%) (n=205) Serotype 14: 2-dose: Tdap vaccinated: 100% (83.9 to 100%) (n=21); unvaccinated: 96.9% (83.8 to 99.9%) (n=32) 3-dose: Tdap vaccinated: 98.6% (95.9 to 99.7%) (n=211); unvaccinated: 98.5% (95.8 to 99.7%) (n=205) Serotype 18C: 2-dose: Tdap vaccinated: 95.2% (76.2 to 99.9%) (n=21); unvaccinated: 87.5% (71.0 to 96.5%) (n=32) 3-dose: Tdap vaccinated: 94.8% (90.9 to 97.4%) (n=211); unvaccinated: 95.1% (91.2 to 97.6%) (n=205) Serotype 19A: 2-dose: Tdap vaccinated: 90.5% (69.6 to 98.8%) (n=21); unvaccinated: 93.8% (79.2 to 99.2%) (n=32) 3-dose: Tdap vaccinated: 93.4% (89.1 to 96.3%) (n=211); unvaccinated: 96.1% (92.5 to 98.3%) (n=205) Serotype 19F: 2-dose: Tdap vaccinated: 100% (83.9 to 100%) (n=21); unvaccinated: 96.9% (83.8 to 99.9%) (n=32)		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
						3-dose: Tdap vaccinated: 99.1% (96.6 to 99.9%) (n=211); unvaccinated: 98.5% (95.8 to 99.7%) (n=205)		
Zimmermann P and others, 2019(7) Cohort Australia 2013 to 2016	Total: n=369 Age: up to 13 months of age Ethnicity: not reported Tdap vaccinated: Collection at 7 months of age: Sex: Male: 43.5% (20 of 46) Collection at 13 months of age: Sex: Male: 37.7% (55 of 146) Tdap unvaccinated: Collection at 7 months of age: Sex: Male: 51.1% (23 of 45)	Maternal Tdap vaccination (Boostrix) Timing: not reported	No maternal Tdap vaccination	13-valent pneumococcal vaccine (Prevnar13) Dose: not reported Timing: 6 weeks, 4 and 6 months of age	At 7 months: At 7 months of age, infants who had the maternal Tdap vaccine had lower average antibody concentrations (adjusted GMRs below 1 in all except for serotypes 3 and 4) compared to those who did not have a maternal Tdap vaccination. No comparisons reached statistical significance (p>0.05) GMC (95% CI): Serotype 1: Tdap vaccinated: 3.8 (2.8 to 5.3); unvaccinated: 5.0 (3.8 to 6.6) Serotype 3: Tdap vaccinated: 1.4 (1.2 to 1.8); unvaccinated: 1.4 (1.2 to 1.7) Serotype 4: Tdap vaccinated: 0.5 (0.4 to 0.7); unvaccinated: 0.5 (0.4 to 0.6) Serotype 5: Tdap vaccinated: 2.8 (2.1 to 3.8); unvaccinated: 3.6 (2.8 to 4.6) Serotype 6A: Tdap vaccinated: 4.0 (3.0 to 5.3); unvaccinated: 5.9 (4.7 to 7.3)	At 7 months: At 7 months of age, infants maternally vaccinated with Tdap (n=46) achieved the standard protective correlate value of 95% for serotypes 1, 3, 5, 6A, 7F, 9V, 18C, 19F, but not for 4, 6B, 14, 19A, 23F. Infants not maternally vaccinated with Tdap achieved the standard protective correlate value of 95% for serotypes PCV 1, 3, 5, 6A, 7F, 9V, 18C, 19A, 19F but not for PCV 4, 6B, 14, or 23F. The number achieving the protective antibody threshold were generally lower for infants with maternal Tdap vaccination, with the largest difference observed for serotype 4 (Tdap vaccinated: 63%, unvaccinated: 75.6%, -12.5% difference, p=0.26), although there were no statistically significant differences between those achieving the standard protective correlate in those vaccinated maternally versus those who were not in any of the pneumococcal serotypes (all p>0.05). Serotype 1: Tdap vaccinated 95.7% (85.2 to 99.5%);	Not reported	Analyses of GMR by serotype could be adjusted for at least one of the following variables: maternal influenza immunisation during pregnancy, gestational age, delivery mode, sex, birth weight, BCG immunisation, age as first Tdap/PCV13 immunisation, age at blood sampling, time between immunisation and blood sample, MMR/HiB-MenC immunisation. Variables adjusted for varied by sample time and serotype,

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
	Collection at 13 months of age: Sex: Male: 52.1% (86 of 165) 33 infants had blood collected at both 7 months and 13 months				Serotype 6B: Tdap vaccinated: 1.5 (1.0 to 2.3); unvaccinated: 2.4 (1.5 to 4.0) Serotype 7F: Tdap vaccinated: 5.4 (4.1 to 7.0); unvaccinated: 7.0 (5.8 to 8.5) Serotype 9V: Tdap vaccinated: 2.2 (1.6 to 2.9); unvaccinated: 2.82 (2.3 to 3.5) Serotype 14: Tdap vaccinated: 2.5 (1.7 to 3.5); unvaccinated: 2.9 (2.0 to 4.3) Serotype 18C: Tdap vaccinated: 2.8 (2.1 to 3.8); unvaccinated: 3.1 (2.4 to 4.0) Serotype 19A: Tdap vaccinated: 1.5 (1.1 to 1.9); unvaccinated: 2.0 (1.5 to 2.7) Serotype 19F: Tdap vaccinated: 9.6 (7.3 to 12.8); unvaccinated: 13.9 (11.0 to 17.6) Serotype 23F: Tdap vaccinated: 2.1 (1.5 to 3.0); unvaccinated: 2.6 (1.8 to 3.7) Adjusted GMR (95% CI): Serotype 1: 0.9 (0.6 to 1.3), p=0.56	unvaccinated: 97.8% (88.2 to 99.9%); difference −2.1% (−12.7 to 7.8%), p=1. Serotype 3: Tdap vaccinated 97.8% (88.5 to 99.9%); unvaccinated: 100% (92.1 to 100%); difference −2.2% (−11.4 to 5.9%), p=1. Serotype 4: Tdap vaccinated 63.0% (47.5 to 76.8%); unvaccinated: 75.6% (60.4 to 87.1%); difference −12.5% (−30.8 to 6.7%), p=0.26. Serotype 5: Tdap vaccinated 95.7% (85.2 to 99.5%); unvaccinated: 100% (92.1 to 100%); difference −4.3% (−14.6 to 3.8%), p=0.49. Serotype 6A: Tdap vaccinated 95.7% (85.2 to 99.5%); unvaccinated: 100% (92.1 to 100%); difference −4.3% (−14.6 to 3.8%), p=0.49. Serotype 6B: Tdap vaccinated 87.0% (73.7 to 95.1%); unvaccinated: 91.1% (78.8 to 97.5%); difference −4.2% (−18.3 to 9.7%), p=0.74. Serotype 7F: Tdap vaccinated 100% (92.3 to 100%); unvaccinated: 100% (92.1 to 100%); difference 0% (−7.8 to 7.9%), p=N/A		full details in original paper.

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 3: 1.1 (0.8 to 1.4), p=0.70 Serotype 4: 1.1 (0.8 to 1.6), p=0.49 Serotype 5: 0.9 (0.6 to 1.3), p=0.59 Serotype 6A: 0.8 (0.6 to 1.1), p=0.19 Serotype 6B: 0.8 (0.4 to 1.5), p=0.41 Serotype 7F: 0.8 (0.6 to 1.1), p=0.17 Serotype 9V: 0.9 (0.7 to 1.3), p=0.61 Serotype 14: 0.9 (0.5 to 1.4), p=0.55 Serotype 18C: 1.0 (0.7 to 1.4), p=0.86 Serotype 19A: 0.8 (0.5 to 1.1), p=0.18 Serotype 19F: 0.7 (0.5 to 1.1), p=0.09 Serotype 23F: 0.9 (0.6 to 1.5), p=0.78 Unadjusted GMR (95% CI):	Serotype 9V: Tdap vaccinated 95.7% (85.2 to 99.5%); unvaccinated: 100% (92.1 to 100%); difference −4.3% (−14.6 to 3.8%), p=0.49 Serotype 14: Tdap vaccinated 93.5% (82.1 to 98.6%); unvaccinated: 88.9% (75.9 to 96.3%); difference 4.6% (−8.1 to 18.1%), p=0.49 Serotype 18C: Tdap vaccinated 95.7% (85.2 to 99.5%); unvaccinated: 95.6% (85.9 to 99.5%); difference 0% (−10.8 to 11.2%), p=1. Serotype 19A: Tdap vaccinated 89.1% (76.4 to 96.4%); unvaccinated: 97.8% (88.2 to 99.9%); difference −8.6% (−21.3 to 2.1%), p=0.20 Serotype 19F: Tdap vaccinated 100% (92.3 to 100%); unvaccinated: 100% (92.1 to 100%); difference 0% (−7.8 to 7.9%), p= N/A Serotype 23F: Tdap vaccinated 93.5% (82.1 to 98.6%); unvaccinated: 93.3% (81.7 to 98.6%); difference 0.1% (−11.9 to 12.4%), p=1.0 At 13 months:		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 1: 0.8 (0.5 to 1.2), p=0.22 Serotype 3: 1.0 (0.6 to 1.3), p=0.94 Serotype 4: 1.0 (0.7 to 1.5), p=0.81 Serotype 5: 0.8 (0.5 to 1.2), p=0.22 Serotype 6A: 0.7 (0.5 to 1.0), p=0.03 Serotype 6B: 0.6 (0.3 to 1.2), p=0.13 Serotype 7F: 0.8 (0.6 to 1.1), p=0.10 Serotype 9V: 0.8 (0.5 to 1.1), p=0.12 Serotype 14: 0.9 (0.5 to 1.4), p=0.55 Serotype 18C: 0.9 (0.6 to 1.3), p=0.63 Serotype 19A: 0.7 (0.5 to 1.1), p=0.09 Serotype 19F: 0.7 (0.5 to 1.0), p=0.05	At 13 months of age, infants maternally vaccinated with Tdap achieved the standard protective correlate value of 95% for serotypes 7F and 19F, but not for 1, 3, 4, 5, 6A, 6B, 9V, 14, 18C, 19A, 23F Infants not maternally vaccinated with Tdap achieved the standard protective correlate value of 95% for serotypes 1, 7F, 19F, but not for 3, 4, 5, 6A, 6B, 9V, 14, 18C, 19A, 23F Numbers of those achieving the protective antibody thresholds were generally lower at 13 months compared to 7 months for all infants (Tdap or unvaccinated infants). However, numbers were generally lower for infants with maternal Tdap vaccination compared to those without the maternal vaccination, with statistically significant differences for PCV serotype 1, 6A and 6B (p<0.01, p<0.01 and p=0.02, respectively). There were no significant differences for serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 23F (all p>0.05) Serotype 1: Tdap vaccinated 89.0% (82.8 to 93.6%); unvaccinated: 97.6% (93.9 to 99.3%); difference −8.5% (−14.9 to 3.3%), p<0.01		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 23F: 0.8 (0.5 to 1.3), p=0.39 At 13 months: At 13 months of age, infants who had the maternal Tdap vaccine had lower average antibody concentrations (adjusted GMRs below 1 in all serotypes) compared to those who did not have a maternal Tdap vaccination. This was statistically significant for PCV serotypes 1, 4, 5, 6A, 6B, 7F, 18C and 23F (all p<0.05), but not for PCV serotypes 3, 9V, 14, 19A, 19F (all p>0.05) GMC (95% CI): Serotype 1: Tdap vaccinated 1.0 (0.9 to 1.2); unvaccinated: 1.3 (1.2 to 1.5) Serotype 3: Tdap vaccinated 0.5 (0.4 to 0.6); unvaccinated: 0.6 (0.5 to 0.7) Serotype 4: Tdap vaccinated 0.2 (0.2 to 0.2); unvaccinated: 0.2 (0.2 to 0.3) Serotype 5: Tdap vaccinated 0.8 (0.7 to 0.9); unvaccinated: 1.1 (0.9 to 1.2)	Serotype 3: Tdap vaccinated 67.8% (59.6 to 75.3%); unvaccinated: 71.5% (64.0 to 78.3%); difference −3.7% (−14.0 to 6.5%), p=0.54 Serotype 4: Tdap vaccinated 19.2% (13.1 to 26.5%); unvaccinated: 27.3% (20.6 to 34.7%); difference −8.1% (−17.4 to 1.4%), p=0.11 Serotype 5: Tdap vaccinated 84.9% (78.1 to 90.3%); unvaccinated: 89.1% (83.3 to 93.4%); difference −4.2% (−12.0 to 3.3%), p=0.31 Serotype 6A: Tdap vaccinated 80.1% (72.7 to 86.3%); unvaccinated: 92.1% (86.9 to 95.7%); difference −12.0% (−20.0 to 4.4%), p<0.01 Serotype 6B: Tdap vaccinated 57.5% (49.1 to 65.7%); unvaccinated: 70.3% (62.7 to 77.2%); difference −12.8% (−23.3 to 2.1%), p=0.02 Serotype 7F: Tdap vaccinated 99.3% (96.2 to 100%); unvaccinated: 99.4% (96.7 to 100%); difference −0.1% (−3.2 to 2.7%), p=1.00 Serotype 9V: Tdap vaccinated 73.3% (65.3 to 80.3%); unvaccinated: 78.2% (71.1 to		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 6A: Tdap vaccinated 0.8 (0.7 to 1.0); unvaccinated: 1.2 (1.1 to 1.4) Serotype 6B: Tdap vaccinated 0.4 (0.4 to 0.5); unvaccinated: 0.6 (0.5 to 0.7) Serotype 7F: Tdap vaccinated 1.7 (1.5 to 1.9); unvaccinated: 2.1 (1.8 to 2.3) Serotype 9V: Tdap vaccinated 0.6 (0.5 to 0.6); unvaccinated: 0.6 (0.6 to 0.7) Serotype 14: Tdap vaccinated 1.0 (0.9 to 1.2); unvaccinated: 1.1 (0.9 to 1.3) Serotype 18C: Tdap vaccinated 0.6 (0.5 to 0.7); unvaccinated: 0.7 (0.6 to 0.8) Serotype 19A: Tdap vaccinated 0.5 (0.4 to 0.6); unvaccinated: 0.5 (0.4 to 0.6) Serotype 19F: Tdap vaccinated 3.0 (2.5 to 3.6); unvaccinated: 3.2 (2.8 to 3.7) Serotype 23F: Tdap vaccinated 0.5 (0.4 to 0.6); unvaccinated: 0.7 (0.5 to 0.8) Adjusted GMR (95% CI):	84.2%); difference −4.9% (−14.5 to 4.6%), p=0.35 Serotype 14: Tdap vaccinated 84.2% (77.3 to 89.7%); unvaccinated: 88.5% (82.6 to 92.9%); difference −4.2% (−12.2 to 3.4%), p=0.32 Serotype 18C: Tdap vaccinated 72.6% (64.6 to 79.7%); unvaccinated: 80.6% (73.7 to 86.3%); difference −8.0% (−17.6 to 1.4%), p=0.11 Serotype 19A: Tdap vaccinated 47.3% (38.9 to 55.7%); unvaccinated: 52.1% (44.2 to 59.9%); difference −4.9% (−15.9 to 6.3%), p=0.43 Serotype 19F: Tdap vaccinated 98.6% (95.1 to 99.8%); unvaccinated: 100% (97.8 to 100%); difference −1.4% (−4.9 to 0.9%), p=0.22 Serotype 23F: Tdap vaccinated 56.2% (47.7 to 64.4%); unvaccinated: 66.1% (58.3 to 73.2%); difference −9.9% (−20.6 to 1.0%), p=0.08		

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Serotype 1: 0.8 (0.7 to 1.0), p=0.02 Serotype 3: 0.9 (0.7 to 1.0), p=0.11 Serotype 4: 0.8 (0.7 to 1.0), p=0.01 Serotype 5: 0.8 (0.6 to 1.0), p=0.01 Serotype 6A: 0.7 (0.6 to 0.9), p<0.01 Serotype 6B: 0.7 (0.5 to 0.9), p<0.01 Serotype 7F: 0.8 (0.7 to 1.0), p=0.03 Serotype 9V: 0.9 (0.7 to 1.1), p=0.17 Serotype 14: 0.9 (0.8 to 1.2), p=0.59 Serotype 18C: 0.8 (0.7 to 1.0), p=0.02 Serotype 19A: 1.0 (0.8 to 1.3), p=0.99 Serotype 19F: 1.0 (0.8 to 1.2), p=0.73 Serotype 23F: 0.7 (0.6 to 0.9), p=0.01			

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Anti-PCV antibody concentrations (IgG GMCs) µg per mL (95% CI)	Proportion achieving antibody threshold of protection (95% CI)	Anti-Diphtheria toxoid antibodies (95% CI)	Confounders
					Unadjusted GMR (95% CI): Serotype 1: 0.8 (0.7 to 1.0), p=0.02 Serotype 3: 0.9 (0.7 to 1.0), p=0.11 Serotype 4: 0.8 (0.7 to 1.0), p<0.01 Serotype 5: 0.8 (0.6 to 0.9), p<0.01 Serotype 6A: 0.7 (0.5 to 0.9), p<0.01 Serotype 6B: 0.7 (0.5 to 0.9), p<0.01 Serotype 7F: 0.8 (0.7 to 1.0), p=0.02 Serotype 9V: 0.9 (0.7 to 1.0), p=0.12 Serotype 14: 0.9 (0.8 to 1.2), p=0.62 Serotype 18C: 0.8 (0.7 to 1.0), p=0.01 Serotype 19A: 1.0 (0.7 to 1.3), p=0.81 Serotype 19F: 0.9 (0.7 to 1.2), p=0.56 Serotype 23F: 0.7 (0.6 to 1.0), p=0.03			

Table D.3. Summary of effect of maternal Tdap vaccination during pregnancy on invasive pneumococcal disease incidence following PCV vaccination
Abbreviations: Tdap: tetanus, diphtheria and acellular pertussis vaccine, PCV: pneumococcal conjugate vaccine

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Incidence of invasive pneumococcal disease	Anti-Diphtheria toxoid antibodies	Confounders
Thibault and others, 2024 (4) Indirect cohort or modified case control using the Broome method Canada 1 January 2018 to 29 May 2023	Total n=127 cases with invasive pneumococcal disease caused by either 19A or 19F or non-vaccine serotypes (including serotype 22F, 15B, 15A and 33F) Maternal Tdap vaccination: n=71; Unvaccinated: n=56 Age: 2 to 59 months Sex: not reported Ethnicity: not reported	Maternal Tdap vaccination (product undefined) Timing: between 3 and 36 weeks before delivery	No maternal Tdap vaccination	10-valent pneumococcal vaccine (PCV10), 13-valent pneumococcal vaccine (PCV13) or a mixed schedule of PCV10 and PCV13 PCV10: n=82 (64.6%) (33 cases with 19A or 19F invasive pneumococcal disease, 49 cases with non-vaccine serotype invasive pneumococcal disease) PCV13: n=6 (4.7%) (1 cases with 19A or 19F invasive pneumococcal disease, 5 cases with non-vaccine serotype invasive pneumococcal disease) Mixed (PCV10 and PCV13): n=39 (30.7%) (3 cases with 19A or 19F invasive pneumococcal disease, 36 cases with non-vaccine serotype invasive pneumococcal disease) Dose: all had at least one dose of PCV10 or PCV13 (100%) One dose: n=11 (8.7%) (6 cases with 19A or 19F invasive pneumococcal disease, 5 cases with non-vaccine serotype invasive pneumococcal disease)	37 infants had invasive pneumococcal disease serotypes 19A or 19F whereas 97 had non-vaccine serotype invasive pneumococcal disease, including serotypes 22F, 15B, 15A, and 33F. 22 (59.5%) cases with 19A or 19F invasive pneumococcal disease had maternal Tdap vaccination during pregnancy, 15 (40.5%) did not. Forty-nine (54.4%) with non-vaccine serotype invasive pneumococcal disease had maternal Tdap vaccination during pregnancy, 41 (45.6%) did not. Following multivariable logistic regression analysis, the odds of cases having been exposed to maternal Tdap vaccination during pregnancy was 0.8 (95% CI: 0.3 to 2.1; adjusted). Sub-analyses of those only with a PCV10 vaccine showed the odds of cases with 19A or 19F invasive pneumococcal disease being exposed to maternal Tdap vaccination during pregnancy of 0.8 (95% CI: 0.3 to 2.1; adjusted). No analyses were conducted restricted to those on a PCV13 or mixed vaccine schedule due to small sample sizes. 33 (89.2%) of cases with 19A or 19F invasive pneumococcal disease received only PCV10 during infancy, one (2.7%) received PCV13, and 3 (8.1%) had a mixed schedule, compared to 54.8% and 40.0% of those with non-vaccine serotype invasive pneumococcal disease respectively. A higher proportion of cases with 19A or 19F invasive pneumococcal disease than those with	Not reported	Age category (2 to 11 months, 12 to 23 months, 24 to 59 months), year of birth (2018 to 2019, 2020, 2021, 2022, 2023), type of vaccine received (PCV10-only, PCV13-only, mixed schedule).

Study, country and time period	Population characteristics	Intervention (dose and timing)	Comparator	PCV formulation and schedule	Incidence of invasive pneumococcal disease	Anti-Diphtheria toxoid antibodies	Confounders
				2 doses: n=51 (40.2%) (21 cases with 19A or 19F invasive pneumococcal disease, 30 cases with non-vaccine serotype invasive pneumococcal disease) 3 doses: n=62 (48.8%) (10 cases with 19A or 19F invasive pneumococcal disease, 52 cases with non-vaccine serotype invasive pneumococcal disease) 4 doses: n=3 (2.4%) (0 cases with 19A or 19F invasive pneumococcal disease, 3 cases with non-vaccine serotype invasive pneumococcal disease) Timing: PCV dose given 10 days or greater before specimen collection	non-vaccine serotype invasive pneumococcal disease received 2 or more doses of PCV (73.0% compared to 38.9%).		

Annexe E. Risk of bias assessment

Table E.1. Risk of bias assessment for systematic reviews [A]

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Comments (including reason for no)
Abu-Raya B and others, 2021 (1)	Yes	Yes	No	No	Yes	N/A	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	N/A	Yes	Q3 - Review does not explicitly justify why RCTs, and observational study designs were selected Q4 - Full search strategy across each database is not provided Q6 - Not applicable for an IPD meta-analysis where data extraction is not required Q7 - Review does not provide a full list of excluded studies with reasons for exclusion Q8 - Included studies are well described in terms of vaccines, population and outcomes, but some details like comparator and setting are incomplete Q10 - Funding sources of the individual included studies are not consistently reported in the review Q15 - Not enough studies included in the IPD for adequate investigation of publication bias to take place

[A] While AMSTAR-2 is not specifically designed for systematic reviews with meta-analysis of IPD but was still considered the most appropriate appraisal tool within this review.

Critical appraisal was done using the AMSTAR-2 checklist for systematic reviews (14)

List of questions:
Q1: Did the research questions and inclusion criteria for the review include the components of Population, Intervention, Comparator, Outcome (PICO)?
Q2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
Q3: Did the review authors explain their selection of the study designs for inclusion in the review?
Q4: Did the review authors use a comprehensive literature search strategy?
Q5: Did the review authors perform study selection in duplicate?
Q6: Did the review authors perform data extraction in duplicate?
Q7: Did the review authors provide a list of excluded studies and justify the exclusions?
Q8: Did the review authors describe the included studies in adequate detail?
Q9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
Q10: Did the review authors report on the sources of funding for the studies included in the review?
Q11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
Q12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
Q13: Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
Q14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
Q15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
Q16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

Table E.2. Risk of bias assessment for randomised controlled trials

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Comments (including reason for no)
Barug D and others, 2020 (2)	Yes	Unclear	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Q2 - Participants were randomised but authors do not describe allocation concealment methods Q4 - Open-label trial, participants were not blinded Q5 - Clinical trial staff were not blinded

Critical appraisal was done using the JBI checklist for randomised controlled trials (10)

List of questions:
Q1: Was true randomisation used for assignment of participants to treatment groups?
Q2: Was allocation to treatment groups concealed?
Q3: Were treatment groups similar at the baseline?
Q4: Were participants blind to treatment assignment?
Q5: Were those delivering treatment blind to treatment assignment?
Q6: Were outcome assessors blind to treatment assignment?
Q7: Were treatment groups treated identically other than the intervention of interest?
Q8: Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analysed?
Q9: Were participants analysed in the groups to which they were randomised?
Q10: Were outcomes measured in the same way for treatment groups?
Q11: Were outcomes measured in a reliable way?
Q12: Was appropriate statistical analysis used?
Q13: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?

Table E.3. Risk of bias assessment for case-control studies [A]

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comments (including reason for no)
Thibault M and others, 2024 (4)	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Q1: Groups come from the same invasive pneumococcal disease surveillance system but baseline characteristics not reported by maternal Tdap status. Q2: No matching was done; groups were selected based on whether their mothers had received a Tdap vaccination during pregnancy

[A] While case-control studies were excluded from this review, this checklist was the most appropriate to apply to the indirect cohort study, as this is a modified case-control method

Critical appraisal was done using the JBI checklist for case-control studies (13)

List of questions:
Question 1: Were the groups comparable other than presence of disease in cases or absence of disease in controls?
Question 2: Were cases and controls matched appropriately?
Question 3: Were the same criteria used for identification of cases and controls?
Question 4: Was exposure measured in a standard, valid and reliable way?

Question 5: Was exposure measured in the same way for cases and controls?
Question 6: Were confounding factors identified?
Question 7: Were strategies to deal with confounding factors stated?
Question 8: Were outcomes assessed in a standard, valid and reliable way for cases and controls?
Question 9: Was the exposure period of interest long enough to be meaningful?
Question 10: Was appropriate statistical analysis used?

Annexe F. GRADE Summary of findings

Abbreviations: CI: confidence interval, IgG: Immunoglobulin G, GRADE: Grading of recommendations, assessment, development and evaluations framework, GMC: Geometric mean concentration, GMR: Geometric mean ratio, OR: odds ratio, PCV: Pneumococcal vaccine, RCT: Randomised controlled trial.

Table F.1. GRADE assessment of antibody concentrations by maternal Tdap vaccination status in infants vaccinated with PCV13

Certainty assessment							Effect	Certainty
Number of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative effect (95% CI)**	
Antibody concentrations of pneumococcal serotype 1 (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.75 (0.63 to 0.90)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 3 (assessed with: GMR of anti-PCV IgG)								
3 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.85 (0.76 to 0.96)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 4 (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.77 (0.64 to 0.93)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 5 (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.75 (0.63 to 0.89)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 6A (assessed with: GMR of anti-PCV IgG)								
3 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.71 (0.60 to 0.85)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 6B (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.79 (0.64 to 0.98)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 7F (assessed with: GMR of anti-PCV IgG)								

Certainty assessment							Effect	Certainty
Number of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative effect (95% CI)**	
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.70 (0.49 to 0.99)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 9V (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.65 (0.52 to 0.80)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 14 (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMR: 0.81 (0.58 to 1.12)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 18C (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.84 (0.72 to 0.99)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 19A (assessed with: GMR of anti-PCV IgG)								
3 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.76 (0.64 to 0.90)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 19F (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.76 (0.66 to 0.87)	⨁◯◯◯ Very low [note 1, 2]
Antibody concentrations of pneumococcal serotype 23F (assessed with: GMR of anti-PCV IgG)								
4 (1)	non-randomised studies	very serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMR: 0.73 (0.60 to 0.90)	⨁◯◯◯ Very low [note 1, 2]

Notes

[note 1]: The review lacked justification for the selected study designs, did not provide a list of excluded studies or consistently report funding sources for included studies, and omitted some important study-level details (time between PCV vaccination and sample collection, and how maternal vaccination status was determined)

[note 2]: The individual participant data meta-analysis and did not report I^2, Chi^2, or study-specific effect estimates, or provide a forest plot. No evidence of between-study heterogeneity could be identified from the available information.

[note 3]: The confidence interval crosses the crossed the line of no effect.

Table F.2. GRADE assessment of anti-PCV antibody concentrations at 6 and 12 months by maternal Tdap vaccination status in infants vaccinated with PCV10

Certainty assessment							Effect	Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative effect (95% CI)	
Serotype 1 at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.8 (0.5 to 1.4)	⊕⊕◯◯ Low [note 1, 2]
Serotype 1 at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.6 to 1.3)	⊕⊕◯◯ Low [note 1, 2]
Serotype 4 at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.6 to 1.3)	⊕⊕◯◯ Low [note 1, 2]
Serotype 4 at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.0 (0.7 to 1.3)	⊕⊕◯◯ Low [note 1, 2]
Serotype 5 at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.7 to 1.6)	⊕⊕◯◯ Low [note 1, 2]
Serotype 5 at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.6 to 1.3)	⊕⊕◯◯ Low [note 1, 2]
Serotype 6B at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.5 to 2.2)	⊕⊕◯◯ Low [note 1, 2]
Serotype 6B at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.2 (0.8 to 1.6)	⊕⊕◯◯ Low [note 1, 2]
Serotype 7F at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.7 to 1.6)	⊕⊕◯◯ Low [note 1, 2]

Certainty assessment							Effect	Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative effect (95% CI)	
Serotype 7F at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.8 to 1.5)	⊕⊕◯◯ Low [note 1, 2]
Serotype 9V at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.8 (0.6 to 1.2)	⊕⊕◯◯ Low [note 1, 2]
Serotype 9V at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.7 to 1.2)	⊕⊕◯◯ Low [note 1, 2]
Serotype 14 at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.6 to 1.5)	⊕⊕◯◯ Low [note 1, 2]
Serotype 14 at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.0 (0.7 to 1.4)	⊕⊕◯◯ Low [note 1, 2]
Serotype 18C at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.5 to 1.6)	⊕⊕◯◯ Low [note 1, 2]
Serotype 18C at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.8 to 1.6)	⊕⊕◯◯ Low [note 1, 2]
Serotype 19F at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	not serious	none	GMC ratio: 0.4 (0.2 to 0.8)	⊕⊕⊕◯ Moderate [note 1, 2]
Serotype 19F at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.8 (0.5 to 1.2)	⊕⊕◯◯ Low [note 1, 2]
Serotype 23F at 6 months (assessed with: GMC ratio of anti-PCV IgG)								

Certainty assessment							Effect	Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative effect (95% CI)	
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.6 to 2.1)	⊕⊕◯◯ Low [note 1, 2]
Serotype 23F at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.1 (0.8 to 1.5)	⊕⊕◯◯ Low [note 1, 2]
Non-vaccine pneumococcal serotype 6A at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.9 (0.4 to 1.8)	⊕⊕◯◯ Low [note 1, 2]
Non-vaccine pneumococcal serotype 6A at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 1.1 (0.5 to 2.3)	⊕⊕◯◯ Low [note 1, 2]
Non-vaccine pneumococcal serotype 19A at 6 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.6 (0.3 to 1.0)	⊕⊕◯◯ Low [note 1, 2]
Non-vaccine pneumococcal serotype 19A at 12 months (assessed with: GMC ratio of anti-PCV IgG)								
1 (2)	RCT	serious [note 1]	not assessed [note 2]	not serious	serious [note 3]	none	GMC ratio: 0.6 (0.3 to 1.1)	⊕⊕◯◯ Low [note 1, 2]

Notes

[note 1]: Participants and investigators were not blinded, allocation concealment methods were not reported.
[note 2]: Only one study, not possible to assess inconsistency.
[note 3]: Confidence interval crosses line of no effect.

Table F.3. GRADE assessment of invasive pneumococcal disease incidence by maternal Tdap vaccination status in infants vaccinated with PCV10

Certainty assessment							Effect		Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative effect (95% CI)	Absolute effect (95% CI)	
Incidence of invasive pneumococcal disease (caused by serotypes 19A or 19F)									
1 (4)	Indirect cohort	serious [note 1]	not assessed [note 2]	serious [note 3]	serious [note 4]	none	OR 0.78 (0.28 to 2.11)	1 fewer per 1,000 (from 2 fewer to 0 fewer)	⊕◯◯◯ Very low [note 1, 2, 3, 4]

Notes

[note 1]: Baseline characteristics not described by maternal Tdap vaccination status in infants receiving PCV10.
[note 2]: Only one study, not possible to assess inconsistency.
[note 3]: Indirect cohort design used to estimate vaccine effectiveness against invasive pneumococcal disease where cases are retrospectively identified and compared. The study does not directly measure invasive pneumococcal disease incidence in the target population.
[note 4]: The confidence interval crossed the line of no effect and wide confidence interval around the point estimate of effect.

Table F.4. GRADE assessment of invasive pneumococcal disease incidence by maternal Tdap vaccination status in infants following PCV vaccination

Certainty assessment							Number of patients		Effect		Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Maternal Tdap vaccination	No maternal vaccination	Relative effect (95% CI)	Absolute effect (95% CI)	
Incidence of invasive pneumococcal disease (caused by serotypes 19A or 19F)											
1 (4)	Indirect cohort	very serious [note 1]	not assessed [note 2]	serious [note 3]	serious [note 4]	none	22 of 37 (59.5%)	15 of 37 (40.7%)	OR 0.82 (0.32 to 2.07)	50 fewer per 1,000 (from 250 fewer to 222 more)	⨁◯◯◯ Very low [note 1, 2, 3, 4]

Notes

[note 1]: Baseline characteristics were not reported by maternal Tdap vaccination status; it is unclear if groups differed for key characteristics.

[note 2]: Only one study, not possible to assess inconsistency.

[note 3]: Indirect cohort design used to estimate vaccine effectiveness against invasive pneumococcal disease, where cases are retrospectively identified and compared. The study does not directly measure invasive pneumococcal disease incidence in the target population. Invasive pneumococcal disease cases were retrospectively identified and compared.

[note 4]: The confidence interval crossed the line of no effect and wide confidence interval around the point estimate of effect.

Annexe G. Health Equity Checklist

Table G.1. UKHSA Evidence Network health equity checklist for equity focused reviews (9)

Checklist step	Criterion questions	Yes/No/NA	Notes
1. Equity framing and population groups	Q1.1 Have you identified the population groups that may be at risk of experiencing health inequalities in relation to the review question using the CORE20PLUS framework, and have you considered how these health inequalities might impact the results?	Yes	Protocol specified that variations across population groups by socioeconomic status and deprivation would be considered where evidence was available. Relevant CORE20PLUS groups may include infants and pregnant women experiencing socioeconomic deprivation, ethnic minority populations and other underserved groups who may have differential access to maternal vaccination programmes or healthcare services.
	Q1.2 Have you included equity-specific objectives that aim to assess the differential impacts of exposures or interventions across CORE20PLUS population groups?	Yes	Protocol specified that variations across population groups by socioeconomic status and deprivation would be considered where evidence was available.
	Q1.3 Have you considered the potential mediating and moderating factors, as well as the pathways through which the intervention or exposure is expected to impact health equity, ensuring this understanding is informed by topic expert input?	Yes	Protocol specified that variations across population groups by socioeconomic status and deprivation would be considered where evidence was available.

Checklist step	Criterion questions	Yes/No/NA	Notes
2. Study design (eligibility criteria)	Q2.1 Are the criteria for study design selection appropriate given the focus on equity?	Yes	A broad range of study designs were included: systematic reviews, RCTs, non-randomised studies and cohort studies, allowing inclusion of evidence relevant to different study settings.
3. Outcomes (eligibility criteria)	Q3. Have you included relevant and important outcomes (for example, self-reported or patient-reported outcome measures) to address equity questions and to assess impacts in CORE20PLUS population groups?	NA	Outcomes included carriage, antibody responses and pneumococcal disease outcomes
4. Publication type (eligibility criteria) and information sources (search strategy)	Q4.1 Are the criteria for publication type selection appropriate given the focus on equity (for example, are you including grey literature such as government reports and community-based organisation publications)?	Yes	Review included peer-reviewed research and preprints. Grey literature was not included in search sources due to rapid turnaround required for the review.
	Q4.2 Have you included any grey literature sources or equity-focused databases to ensure adequate coverage of health equity considerations?	No	Applicability of equity focused databases was considered by reviewers and information scientists, but was determined not relevant for this review.
5. Search terms (search strategy)	Q5. Are the search terms and concepts in your search strategy aligned to address the health equity questions of the review?	Yes	Search terms include detailed terms for both relevant population groups of infants and pregnant women. Search was peer reviewed by a second information specialist as a further check on terms.
6. Data extraction	Q6.1 Is the data extraction template designed to collect information on	Yes	Data extraction template was designed to capture relevant

Checklist step	Criterion questions	Yes/No/NA	Notes
	sociodemographic categories (for example, socioeconomic status, sex, race or ethnicity) and data relevant to the specific population groups identified at step 1?		information on health inequalities.
	Q6.2 Is the data extraction template designed to collect contextual information on the mechanisms and pathways, or wider determinants of health that may be impacting health equity in the CORE20PLUS population groups identified at step 1?	No	Data extraction template included participant characteristics, outcomes and other relevant contextual information. Socioeconomic status and deprivation were identified as factors of interest where reported, although collection of wider determinants of health and other CORE20PLUS characteristics were not specified in the protocol and so not extracted.
7. Evidence synthesis, including applicability of findings and identification of evidence gaps	Q7.1 Where relevant, have you planned analyses to assess differences in effects for CORE20PLUS population groups?	Yes	Protocol states that variations by socioeconomic status and deprivation would be considered where evidence was available.
	Q7.2 Where relevant, did you plan to synthesise findings on health equity and present both relative and absolute differences?	No	No formal synthesis of health equity findings was planned because the review was not designed to compare outcomes across CORE20PLUS groups and relevant data were anticipated to be limited.
	Q7.3 Where relevant, have you discussed the implications of differences in	NA	No evidence on differential effects across CORE20PLUS groups was identified, hence

Checklist step	Criterion questions	Yes/No/NA	Notes
	absolute or relative effects for the CORE20PLUS population groups identified at step 1?		discussion of relative or absolute differences was not possible.
	Q7.4 Have you considered the eligibility criteria of the primary studies, and how that affects generalisability?	Yes	Review discusses limitations related to study populations, vaccination schedules, sample sizes and outcome measurement.
	Q7.5 Where relevant, have you identified evidence gaps and discussed their implications, for instance in terms of research recommendations?	Yes	Evidence gaps were identified, including limited evidence on carriage outcomes, invasive pneumococcal disease outcomes, non-invasive disease, non-vaccine serotypes and newer PCV formulations.
8. Conclusions	Q8.1 Have you summarised the evidence related to the groups identified, within the conclusions, including evidence gaps?	NA	No evidence specific to CORE20PLUS population groups was identified or reported.
	Q8.2 Have you provided appropriate research recommendations?	NA	

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