The Association between Vaccine Hesitancy and Pertussis: A Systematic Review and Meta-analysis

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Introduction

- Routine immunization with childhood pertussis-containing vaccines has been a long-standing vaccination program in many countries[1]. Since the resurgence of pertussis in the early 2010s, several countries have recommended Tdap/dTap to women between 28 and 38 weeks of pregnancy[2, 3]. However, pertussis outbreaks are still reported worldwide, with high incidence rates among fully vaccinated children[4].
- Vaccine hesitancy is a psychological state, a vaccination behavior, or a decision-making that is associated with pertussis-containing vaccine uptake[5].
- This study aimed to explore associations between vaccine hesitancy and pertussis in infants and children.

Methods

- We included primary studies that investigated the association between vaccine hesitancy and pertussis odds ratios (ORs), relative risks (RRs), or vaccine effectiveness (VE), published between 2012 and 2022 in English or Chinese. Infants, children ≤ 9 years old, and pregnant women were included and all pertussis-containing vaccines were measured.
- The qualities of studies were assessed according to the Newcastle-Ottawa Scale (NOS) to evaluate the risk of bias.
- Random-effects meta-analysis, cumulative meta-analysis, and subgroup analysis were used to generate estimated OR/VEs with 95% confidence intervals (CIs), where heterogeneity was assessed using I^2.

Results

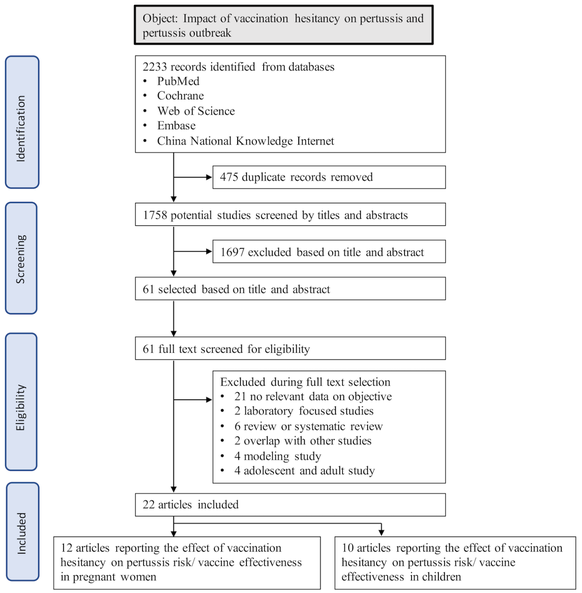

Fig. 1 The selection flowchart of the association between vaccine hesitancy and pertussis study

- 2233 publications were identified, 475 of which were excluded due to duplication. 1758 titles and abstracts were screened and 1697 were excluded according to the criteria. Of the remaining 61 studies, 22 were included in the meta-analysis (cohort study = 7, cross-sectional study = 1, case-control study = 14): 12 investigated the association between maternal vaccine hesitancy and pertussis in infants; 10 checked the effect of childhood vaccine hesitancy (Fig. 1).
- The studies were quality-appraised with a mean score of 7.0 (range 6.0-9.0).
- Meta-analysis of 18 studies generated a random-effects pooled OR of 4.12 (95% CI, 3.09-5.50; p < 0.01) in infants and children between the all doses vaccine-hesitant and the fully vaccinated.

Table 1 Pertussis Odds Ratio of Vaccine Hesitancy among Different Subgroups

Vaccine Population	Variable	No. of studies	Estimated OR and 95% CI	I^2
Children	Vaccine hesitancy status			
	Vaccine hesitant			
	Vaccine doses			
	All	7	2.85 (2.01, 4.03)	65%
	Unvaccinated			
	Vaccine doses			
	1	2	2.04 (0.76, 5.49)	87%
	2	2	3.79 (2.66, 5.40)	0%
	3	2	7.79 (6.82, 8.90)	6%
	4	2	14.26 (7.62, 26.70)	87%
	All	4	4.04 (3.10, 5.27)	0%
	Under-vaccinated			
	Vaccine doses			
	1	4	2.45 (1.69, 3.54)	29%
	2	3	2.45 (1.52, 3.94)	0%
	3	3	4.78 (2.19, 10.44)	51%
	4	2	8.21 (1.26, 53.49)	61%
	All	2	2.95 (1.61, 5.40)	63%
	Number of vaccine dose			
	Dose 1&2&3	2	3.44 (1.88, 6.29)	78%
	Dose 4&5	1	4.34 (2.17-8.68)	NA*
	Dose 4	2	2.09 (0.74, 5.90)	72%
	Dose 5	1	4.60 (2.59-8.17)	NA
	Vaccine delayed			
	Number of vaccine dose			
	All	2	1.40 (0.62, 3.16)	59%
	Dose 4	1	0.80 (0.48, 1.34)	NA
	Dose 5	1	1.30 (0.48, 3.49)	NA
Pregnant Women	Population age			
	All	10	5.63 (3.87, 8.18)	53%
	≤ 2 months	8	6.05 (4.31, 8.50)	12%
	≤ 3 months	4	5.14 (1.95, 13.52)	80%

Table 2 Vaccine Effectiveness of Vaccination among Different Subgroups

Vaccine Population	Variables	No. of studies	Estimated VE and 95% CI	I^2
Pregnant Women	Study Outcome			
	Pertussis case	12	89.83 (86.44, 93.35)	0%
	Hospitalization	2	80.60 (68.20, 95.26)	8%
	Timing of vaccine administration			
	The third trimester	7	89.56 (85.66, 93.64)	0%
	Any point during pregnancy	7	90.64 (83.99, 93.35)	0%
Children	Study Outcome			
	Pertussis case	6	86.45 (83.45, 89.55)	71%
	Hospitalization	1	92.04 (87.01, 97.36)	66%

*NA: Not Applicable

Conclusions

- Vaccine hesitancy increased pertussis risks in both infants and children.
- Ensuring that children receive all doses of pertussis-containing vaccine at the appropriate age is essential.
- Short delays in vaccine receipt may be unimportant.
- Maternal pertussis-containing vaccination is suggested to be encouraged.
- Limits: we mainly focused on the vaccination behavior aspect of vaccine hesitancy. The effects of psychological state or decision-making aspects of vaccine hesitancy on pertussis were not assessed because of limited studies.

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