

Table 1b: TIV in pregnant women, infant outcomes

Is inactivated influenza vaccine versus no intervention or non-influenza vaccine in pregnant women effective to prevent influenza infection and severe outcomes of infection in infants below 6 months of age?				
		Rating	Adjustment to rating	
Quality Assessment	No of studies/starting rating		1 RCT ^{1, 2, 3}	4
	Factors decreasing confidence	Limitation in study design	None serious ⁴	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious ⁵	0
		Publication bias	None serious	0
	Factors increasing confidence	Strength of association/ large effect	Large effect, strong evidence ⁶	+1
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable ⁷	0
	Final numerical rating of quality of evidence			4 (numerical rating 5 but value cannot be >4)
Summary of Findings	Statement on quality of evidence		Our confidence in the estimate of effect of maternal influenza vaccine on infants is high.	
	Conclusion		Influenza vaccination of pregnant women is efficacious against laboratory-confirmed influenza in their infants and indicates an efficacy of 63% (95% CI: 5 to 85) in newborns . Maternal influenza vaccination is also significantly effective against respiratory illness with fever (28.9%; 95% CI: 6.9 to 45.7) as well as against clinical visits for respiratory illness with fever (42%; 95% CI: 18.2 to 58.8). The rate of clinician testing for influenza (=confirmation of ILI by a clinician) was also significantly reduced in newborn receiving influenza vaccine (49%; 95% CI: 25.4 to 64.7).	

NOTES

¹ Zaman et al. 2008, RCT conducted in Bangladesh in 2004-05, included 340 pregnant women in the 3rd trimester that were follow-up until 6 months after delivery together with and their newborns (follow-up of mothers for effectiveness measures such as respiratory illness and clinical visits: until infants were 24 weeks old). 159 infants followed-up received TIV and 157 infants received pneumococcal polysaccharide vaccine.

² In addition to immunogenicity data from Zaman et al. (2008), there was another RCT assessing immunogenicity and safety of TIV in pregnant women and their infants (Englund et al. 1993, see table 1a, note 2).

³ Regarding the evidence on immunogenicity, findings from observational studies on infant outcomes confirm those from RCTs (e.g. Englund et al. 1993), which implies significantly higher protective antibody

titre/seroprotection among newborn of vaccinated mothers versus unvaccinated mothers/controls (Eick et al. 2011, Puleston et al. 2010). The prospective controlled observational study by Eick et al. (2011) showed significantly higher protective antibody titers against all vaccine strains in the TIV for maternal–infant pairs at delivery, in cord blood and for their infants at 2–3 months of age, but no significant differences at 6 months of age.

Five observational studies also assessed the effectiveness of influenza vaccination in infants of vaccinated versus unvaccinated mothers using different outcomes. Vaccine effectiveness against laboratory-confirmed influenza in children of vaccinated mothers was assessed in one of those observational studies (Eick et al. 2011), and showed a 41% decrease in laboratory-confirmed influenza in infants of vaccinated mothers versus infants of unvaccinated mothers (RR 0.59; 95% CI: 0.37 to 0.93) as well as a 39% decrease in hospitalization due to ILI (RR 0.61; 95% CI: 0.45 to 0.84). Another observational study (Benowitz et al. 2010) found vaccine effectiveness (91.5%) against laboratory-confirmed influenza hospitalization in children of vaccinated mothers. However, in this study, the control group was recruited from infants that were hospitalized for other causes, which may have overestimated the effectiveness measure.

Poehling et al. 2011 showed a fully adjusted OR of 0.52 (95% CI: 0.30 to 0.91) for influenza-positive, hospitalized infants among vaccinated mothers versus unvaccinated mothers, implying that infants of vaccinated mothers were 45-48% (depending on model) less likely to be hospitalized for laboratory-confirmed influenza infection than those of unvaccinated mothers. However, these results are subject to bias since influenza vaccination was self-reported, data used were of surveillance nature, or findings are not generalizable to outpatient settings.

Several infant outcomes were considered in an observational cohort study by Omer et al. (2011) who compared TIV vaccinated pregnant women and their infants to unvaccinated pregnant women and to reference values from time periods in which no virus circulation was measured. Birth weight of newborns of vaccinated women were significantly higher (on average 96.7 g) than that of newborns of unvaccinated women (3,348 g versus 3,251 g; $p=0.002$). During the putative influenza season, the difference between the two groups increased but no significant differences in birth weights were seen outside the putative influenza season. During periods of widespread influenza activity, vaccination in pregnancy had a beneficial impact on the likelihood of prematurity and the likelihood of small for gestational age birth. The odds for prematurity were approximately 70% lower among the newborns of the vaccinated mothers compared to mothers not receiving the influenza vaccine (OR adjusted: 0.28; 95% CI: 0.11 to 0.74). The likelihood of small for gestational age birth was reduced by 69% in infants born to vaccinated women (OR adjusted: 0.31; 95% CI: 0.13 to 0.75).

Another observational study (France et al. 2006) did not find a benefit of maternal influenza immunization on neonatal acute respiratory illness visits among their newborns.

⁴ Adequate blinding, masking, and allocation sequence concealment. Small loss to follow-up (93% followed up until week 24).

⁵ Availability of tests and shortage of supply is mentioned as well as the fact that not all laboratory-confirmed cases were detected. However, illnesses were recorded in detail throughout the project, resulting in a low risk of bias.

⁶ Vaccine efficacy result suggests a high magnitude of the effect.

⁷ There is a potential for underestimating the true effect of maternal influenza vaccination on infant outcomes (related to the control vaccine used), implying an independent positive effect of influenza vaccine. However, no upgrading was applied since the availability of tests may have impacted on detection of laboratory-confirmed cases.

References

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