

Grade Table 7: Is it safe to administer the first dose of vaccine at different ages?ⁱ

PICO question: Is it safe to administer the first dose of vaccine at different ages?				
			Rating	Adjustment to score
Quality Assessment	No of studies/starting score		<ul style="list-style-type: none"> ● 1 RCT direct comparison (RV1), ● 37 RCTs indirect comparisons (27 RV1, 10 RV5)ⁱⁱ 	4
	Factors decreasing confidence	Limitation in study design	Serious ⁱⁱⁱ	-1
		Inconsistency	None serious	0
		Indirectness	Serious ^{iv}	-1
		Imprecision	Serious ^v	-1
		Publication bias	Serious ^{vi}	-1
	Factors increasing confidence	Strength of association	No large effect	0
		Dose-response	No	0
		Mitigated bias and confounding	No	0
	Final numerical score of quality of evidence			1
Summary of findings	Statement on quality of evidence		We are very uncertain about the estimate of effect	
	Conclusion		There is insufficient evidence to determine the effect on safety of administering the first vaccine dose at different ages.	

Note:

- We have no data indicating whether or not lifting the currently recommended age window for rotavirus vaccination is safe
- No RCTs or observational studies reported on safety outside the currently recommended age window, thus there is no evidence on whether lifting the currently recommended age window for rotavirus vaccine administration is safe.
- Weak evidence from RCTs has not shown an increase risk of intussusception 1-7 or 1-42 days after vaccination.
- Weak evidence from observational studies showed an excess of intussusception cases after rotavirus vaccine doses were given in Brazil, Mexico and Australia.
- Weak evidence from RCTs administering the first and last dose at different ages (all inside the recommended age window) has not shown any impact of age on serious adverse events or intussusception.

ⁱ Adapted from Soares-Weiser K et al: Rotavirus vaccine schedules: a systematic review of safety and efficacy from RCTs and observational studies of childhood schedules using RV1 and RV5 vaccines. Report to WHO/IVR 2012.

ⁱⁱ Only one RCT reporting safety outcomes, *South Africa3 RV1*, directly compared different ages at first rotavirus vaccine dose. No observational studies reporting safety outcomes compared different age at vaccine administration.

ⁱⁱⁱ Risk of bias, mainly no report of allocation concealment but also risk of blinding and attrition bias, was found for 27 of the 37 included RCTs.

^{iv} Only *South Africa3 RV1* directly compared serious adverse events for different ages (6 or 10 weeks) at first vaccine dose. The remaining RCTs were stratified according to age at first vaccine dose and can therefore only provide indirect comparisons.

^v The direct comparison of different age at first vaccine dose have wide 95% confidence intervals, as do 3 of the 11 indirect comparisons.

^{vi} Publication bias is likely as only one study was found that directly compared vaccine safety for different ages at first vaccine dose.