**GRADE TABLE 4**
**Population:** Pregnant women and women of reproductive age.
**Intervention:** 2 or 3 doses of Tetanus Toxoid Containing Vaccine (TTCV).
**Comparison:** No vaccine or control.
**Outcome:** Neonatal tetanus deaths.

| **PICO Question:** *Are 2 or 3 doses of TTCV administered prior to and during pregnancy effective in protecting neonatal tetanus as compared to no vaccination?* | | | | |
|---|---|---|---|---|
| | | | Rating | Adjustment to rating |
| **Quality Assessment** | No. of studies/starting rating | | 2 RCT[1] | 4 |
| | Factors decreasing confidence | Limitation in study design | Serious[2] | -1 |
| | | Inconsistency | None serious | 0 |
| | | Indirectness | None serious | 0 |
| | | Imprecision | None serious | 0 |
| | | Publication bias | None serious | 0 |
| | Factors increasing confidence | Large effect | Applicable[3] | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of certainty of evidence** | | | 3 |
| **Summary of Findings** | **Statement on certainty of evidence** | | | Evidence supports a moderate degree of confidence that the true effect lies close to that of the estimate of effect on health outcome. This evidence is supported by several observational studies that demonstrated an effect of vaccinating pregnant women on preventing neonatal death. |
| | **Conclusion** | | | Tetanus toxoid is considered to be highly efficacious in pregnant women and women of reproductive age at preventing neonatal tetanus. These results are consistent across different populations and geographic location.[4] |

[1] From Demicheli et al. [1] 2 randomized controlled trial were identified[2,3] that evaluated the effectiveness of tetanus toxoid in comparison with another control vaccine during or prior to pregnancy in preventing neonatal tetanus deaths. Newell et al. [2] reported that 2-3 doses of TTCV provided protection against neonatal tetanus death (RR 0.02, 95% CI 0.00 to 0.30; 688 infants). No neonatal tetanus cases occurred in infants born to mothers that received 2 or 3 doses of TTCV for a period of more than 4 years post-vaccination. Black et al. [3] reported that neonatal mortality 4-14 days after birth was reduced in the tetanus-diphtheria vaccine group (RR 0.38, 95% CI 0.27 to 0.55).

[2] The quality of the body of evidence was downgraded for selection bias because the vials used for the intervention and control vaccine could have introduced a certain bias in selection

[3] The RCT [2,3] was not upgraded despite the strength of the association (2 or 3 doses provided high protection against neonatal tetanus (RR 0.02, 95% CI 0.00 to 0.30)) because downgrading had been applied for study design.

[4] Other supporting evidence from Blencowe et al. [4] includes a systematic review and meta-analysis which reviewed [2] 1 RCT and [5] 1 well-controlled cohort study. From the meta-analysis, the pooled risk ratio was (RR 0.06, 95% CI 0.02 to 0.20). Blencowe et al. reported that immunization of pregnant women or WRA with at least 2 properly spaced TT doses was estimated to reduce neonatal tetanus mortality by 94%.

References:

[1] Demicheli V, Barale A, Rivetti A. Vaccines for women for preventing neonatal tetanus 1. Cochrane Database Syst Rev 2015;(7):CD002959.

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[3] Black RE, Huber DH, Curlin GT. Reduction of neonatal tetanus by mass immunization of non-pregnant women: duration of protection provided by one or two doses of aluminium-adsorbed tetanus toxoid. Bulletin of the World Health Organization. 1980;58(6):927.

[4] Blencowe H, Lawn J, Vandelaer J, Roper M, Cousens S. Tetanus toxoid immunization to reduce mortality from neonatal tetanus. Int J Epidemiol. 2010 Apr;39 Suppl 1:i102–9.2015;(7):CD002959.

[5] Gupta SD, Keyl PM. Effectiveness of prenatal tetanus toxoid immunization against neonatal tetanus in a rural area in India. Pediatr Infect Dis J. 1998 Apr;17(4):316–21.