GRADE TABLE 1b
Population: Children and adolescents.
Intervention: Tetanus Toxoid Containing Vaccine (TTCV) booster dose administered during the second year of life.
Comparison: TTCV booster dose administered at 4-7 years.
Outcome: Tetanus cases between priming doses until second (intervention group) or first (control group) booster given at 4-7 years of age.

<table>
<tr><td colspan="5">PICO Question: Will a booster dose during the second year of life confer better protection from tetanus until school-age as compared to 3 priming doses only?</td></tr>
<tr><td></td><td colspan="2"></td><td>Rating</td><td>Adjustment to rating</td></tr>
<tr><td rowspan="10">Quality Assessment</td><td colspan="2">No. of studies/starting rating</td><td>3 RCT[1]</td><td>4</td></tr>
<tr><td rowspan="5">Factors decreasing confidence</td><td>Limitation in study design</td><td>None serious</td><td>0</td></tr>
<tr><td>Inconsistency</td><td>None serious</td><td>0</td></tr>
<tr><td>Indirectness</td><td>Serious[2]</td><td>-1</td></tr>
<tr><td>Imprecision</td><td>None Serious</td><td>0</td></tr>
<tr><td>Publication bias</td><td>None serious</td><td>0</td></tr>
<tr><td rowspan="3">Factors increasing confidence</td><td>Large effect</td><td>Not applicable</td><td>0</td></tr>
<tr><td>Dose-response</td><td>Not applicable</td><td>0</td></tr>
<tr><td>Antagonistic bias and confounding</td><td>Not applicable</td><td>0</td></tr>
<tr><td colspan="3">Final numerical rating of certainty of evidence</td><td>3</td></tr>
<tr><td rowspan="2">Summary of Findings</td><td colspan="3">Statement on certainty of evidence</td><td>Evidence supports a moderate degree of confidence that the true effect lies close to that of the estimate of effect on health outcome.</td></tr>
<tr><td colspan="3">Conclusion</td><td>A booster dose during the second year of life provides better protection from tetanus until school entry age as compared to no booster.[3]</td></tr>
</table>

[1] From Mueller et al. [1] 1 study was identified [2] that evaluated delaying the first booster vaccination to age 18 months compared to 12 or 15 months. They reported that delaying may yield higher antitoxin concentrations. Another study was identified [3] that evaluated the effect of boosting at 18 months following a 3-dose primary series. The results suggest substantial increase in tetanus antibody. From Dhillon et al. [4] 1 study was identified [5] that evaluated a booster vaccination during the second year of life. 100% seroprotection was achieved by boosting at 12-19 months. At 4-6 years of age following 4 doses of TTCV, approximately 3.5 years after boosting, 75% of children, continued to have seroprotective antibody levels against tetanus. At 7 to 9 years of age, 65% of children who were not further vaccinated had protective tetanus-specific antibody levels compared to 100% for those boosted at age 5-6 years.

[2] Protective antibody levels ≥ 0.01 IU/ml were used as a proxy to indirectly measure tetanus cases. Even though antibody levels were significantly lower in those with 3 priming doses only, it remains uncertain if this will also translate in a lower protection against clinical disease.

[3] Other supporting evidence includes [3] 1 open-label booster study that evaluated a booster dose during the second year of life. All participant (100% seroconverted by boosting at 12-19 months. At 4-6 years of age following 4 doses of TTCV, approximately 3.5 years after boosting, 76% of children, continued to have seroprotective antibody levels against tetanus.

References:

[1]Mueller J. Part 1. Diphtheria and tetanus vaccines. Comparative efficacy/effectiveness of schedules in infant immunization against pertussis, diphtheria and tetanus: systematic review and meta-analysis. 13-08-2014. Available from http://www.who.int/immunization/sage/meetings/2015/april/5_Report_D_T_140812.pdf; accessed Nov 2016.

[2]Scheifele DW, Guasparini R, Lavigne P. A comparative study of PENTA™ vaccine booster doses given at 12, 15 or 18 months of age. 1999 Vaccine;17:543-550.

[3] Conway S, James J, Balfour A, Smithells R. Immunisation of the preterm baby. J Infect. 1993 Sep;27(2):143–50.

[4] Dhillon S. DTPa-HBV-IPV/Hib Vaccine (Infanrix hexa): A Review of its Use as Primary and Booster Vaccination. Drugs 2010 May 28;70(8):1021-58.

[5] Tichmann I, Preidel H, Grunert D, et al. Comparison of the immunogenicity and reactogenicity of two commercially available hexavalent vaccines administered as a primary vaccination course at 2, 4 and 6 months of age. Vaccine 2005 May 9;23(25):3272-9.

[6] Heininger U, Sanger R, Jacquet JM, Schuerman L. Booster immunization with a hexavalent diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliovirus vaccine and Haemophilus influenzae type b conjugate combination vaccine in the second year of life: safety, immunogenicity and persistence of antibody responses. Vaccine 2007 Jan 22;25(6):1055-63.