GRADE Table. Duration of protection conferred by diphtheria vaccination.

- Population : Immunocompetent children and adults
- Intervention : Vaccination with diphtheria toxoid (-containing) vaccination
- Comparison : No vaccine or control
- Outcome : Diphtheria serum antibody levels/ seroprevalence

What is the duration of continued seroprotection of diphtheria vaccination ( $\geq$ 10 years) conveyed by a specific schedule of diphtheria toxoid (- containing) vaccination which is comprised of at least 3 vaccine doses (primary series) and 3 booster doses until adulthood?

|                     |   |                                   | Rating   | Adjustment to rating  |
|---------------------|---|-----------------------------------|--|---|
| Quality Assessment  | No. of studies/starting rating                |                                   | 1 observational <sup>1</sup>   | 2   |
|                     | Factors<br>decreasing<br>confidence           | Limitation in study design        | None serious   | 0   |
|                     |   | Inconsistency                     | None serious   | 0   |
|                     |   | Indirectness                      | None serious   | 0   |
|                     |   | Imprecision                       | None serious   | 0   |
|                     |   | Publication Bias                  | None serious   | 0   |
|                     | Factors<br>increasing<br>confidence           | Large effect <sup>2</sup>         | Applicable   | +2  |
|                     |   | Dose-response                     | Not applicable   | 0   |
|                     |   | Antagonistic bias and confounding | Not applicable   | 0   |
|                     | Final numerical rating of quality of evidence |                                   |  | 4   |
| Summary of findings | Statement on quality of evidence              |                                   |  | Evidence supports a high level of confidence that<br>the true effect lies close to that of the estimate of<br>the effect on the health outcome. |
|                     | Conclusion                                    |                                   | Evidence supports a high degree of confidence that<br>3 primary doses and 3 booster doses until<br>adulthood confer high levels of seroprotection, at<br>least up to age 39 and likely longer. These data<br>suggest, that the immediate administration of<br>decennial booster doses following a 3<br>dose primary and 3 dose booster schedule may not<br>be needed, however this needs to be monitored in<br>the long-term with increasing life expectancy in<br>large parts of the world. |   |

## References

1. Swart et al. Long-Term Protection against Diphtheria in the Netherlands after 50 Years of Vaccination: Results from a Seroepidemiological Study. PLoS ONE 11(2): e0148605

<sup>1</sup> This grading is based on evidence retrieved from a systematic review of literature (<u>http://www.who.int/immunization/sage/meetings/2017/april/2 Review Diphtheria results April2017 final clean.pdf?ua=1</u>, accessed April 2017). The literature review retrieved one large population-based cross-sectional representative seroepidemiological study (Swart et al. 2016) which suggests that 95% of the oldest age group included in the trial (35-39 years) continue to have diphtheria seroprevalence above the protective threshold (≥0.01 IU/mI).

<sup>&</sup>lt;sup>2</sup> Quality rating was upgraded by two levels as there is strong evidence of high levels of seroprotection, even in the older agegroups (up to 39 years of age).