TCV vaccines indicator

Benefits of the intervention

Serogroup or serotype coverage by vaccines considered (for serogroup- or serotype-specific vaccines)

TCVs conjugate the Vi capsular polysaccharide to a carrier protein (tetanus toxoid, CRM197 or diphtheria toxoid); product differences relate mainly to carrier protein, presentation, licensed age range and manufacturer rather than antigenic breadth (see indicator 1.3 for antigen/serovar coverage). Rare Vi-negative *S*. Typhi variants were first described among patients with typhoid fever in the Faisalabad region of Pakistan.[1] These variants are clinically indistinguishable from Vi-positive infection and would not be targeted by current TCVs. Available genomic surveillance has not demonstrated vaccine-driven selection for Vi loss, although continued surveillance after national introduction is recommended.[2] Effectiveness also appears preserved against antimicrobial-resistant strains: in Hyderabad, Pakistan, effectiveness was 97% (95% CI: 95–98) against XDR *S*. Typhi specifically, comparable to 95% (95% CI: 93–96) against culture-confirmed *S*. Typhi overall in the same cohort.[3] Current studies are not powered to compare effectiveness by genotype, and there is no evidence as yet that vaccine-induced pressure is changing circulating bacterial populations.

Efficacy and effectiveness estimates (e.g. against infection, disease, hospitalization, death), including in different populations

Three randomized controlled trials of Vi-TT in children nine months–16 years of age reported 79% efficacy in Nepal (95% CI: 61.9–88.5), 83.7% in Malawi in the per-protocol analysis (95% CI: 68.1–91.6) and 85% total protection (97.5% CI: 76–91) in the Bangladesh cluster-randomized trial against blood culture-confirmed typhoid over 18–24 months.[4, 5, 6, 7] The Bangladesh trial also estimated overall cluster-level protection of 57%; indirect protection among unvaccinated residents was imprecise and not statistically significant.[6] Observational studies following campaigns or programme introduction in India, Pakistan and Zimbabwe generally reported effectiveness of approximately 70% to >90% against culture-confirmed disease.[8, 9, 10, 11] Effectiveness was also high against extensively drug-resistant *S.* Typhi in Pakistan.[3]

Duration of protection and waning of immunity in general and risk groups

Extended follow-up indicates that protection after a single TCV dose persists for several years, but the pattern of waning differs across settings.

In Malawi, cumulative efficacy was 83.4% at one year, 80.7% at two years, 80.1% at three years, 77.1% at four years and 78.3% through a maximum follow-up of 4.6 years; interval-specific analyses found no statistically significant decline, although later estimates were imprecise.[12] Over the full 4.61 year follow-up period, efficacy was 70.6% among children vaccinated before two years of age, 79.6% among those vaccinated at two to four years and 79.3% among those vaccinated at five to 12 years of age.[12]

Preliminary extended follow-up in Nepal found protection of 77% at one to five years among more recently vaccinated children and 53% at four to eight years among earlier vaccinees, with greater decline among children vaccinated at younger ages.[13]

Preliminary findings from Bangladesh suggested a decline from 91% in year one and 86% in year two to 50% in year five; estimates in years 6–7 were imprecise, and waning was most pronounced among children vaccinated before two years of age.[14]

Collectively, these findings suggest more evident waning in the very-high-incidence Nepal and Bangladesh settings than in Malawi, potentially reflecting differences in transmission intensity, age at vaccination, study design and follow-up.

No clinical efficacy or effectiveness data are available for a booster dose; current evidence is limited to immunogenicity studies showing a boosting response, with longer intervals generally producing stronger responses.[15, 7]

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