

PP Cholera vaccines: grading of scientific evidence

II: Efficacy/effectiveness

Settings: Global

Question: What is the evidence for protective efficacy/effectiveness of currently licensed cholera vaccines (Dukoral™ and Shanchol™ /ORCVax™/) in endemic settings during the first two years following immunization?

Conclusion: High level of scientific evidence that the currently licensed cholera vaccines offer significant protection against cholera during the first two years after vaccination*.

*The ranges of protective efficacy 4-6 months, 1 year, and 2 years after vaccination are 86%-66%, 62%-45%, and 77%-58%, respectively. (With Dukoral, protection wanes more rapidly in children aged 2-5 years).

Quality assessment						Summary of Findings
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Quality
Efficacy/effectiveness of WC-rBS (Dukoral™)						
3	RCT	No serious	No serious	No serious	No serious	High
1	OBS**					
Efficacy/effectiveness of bivalent WC only vaccine (ORCVAX™/mORCVAX™/Shanchol™)						
1	RCT	No serious***	No serious	No serious	No serious	High

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*** An assessment based on one RCT only is a possible limitation. However, the scientific weight of these results were not downgraded due to the fact that the results are in agreement with those obtained with the related vaccines ORCVAX (see Trach DD et al 1997) and Dukoral.

Clemens JD et al (1990) published follow-up results of a randomized, placebo-controlled, double blinded study of WC-BS and WC-only vaccines. The study involved 62,285 children 2-15 years old and women 16 years and older in Matlab, Bangladesh who had completed 3 doses at 6 weeks' interval. For all ages (>2years), protective efficacy against El Tor/classical cholera, was 85% (95% CI 56-95) at 4-6 months; 62% (95% CI 46-74) at 1 year, and 58% (95% CI 40-71) at 2 years. For children 2-5 years of age, the corresponding efficacies were 100% (95% CI 80-100), 38% (95% CI 1-62), and 47% (95% CI 4-71). After 2 years, the respective protective efficacies waned rapidly (Table IV).

Sanchez JL (1994) conducted a randomized, placebo-controlled, double blinded study of the protective efficacy of WC/rBS cholera vaccine among Peruvian military recruits aged 16-45 years. After 4-5 months the protective efficacy against clinical cholera was 86% (95% CI 37-97) among the 1,426 individuals who had received 2 vaccine doses. Only El Tor cholera was detected.

In a randomized, double-blinded study Taylor DN et al (2000) assessed the efficacy of WC/rBS cholera vaccine against El Tor-cholera among 14,997 Peruvians aged 2-65 years who had received 2 doses of the vaccine and a booster dose 10 months later. After 2 years the protective efficacy against clinical cholera was 61% (95% CI 28-79). Vaccine efficacy was higher for persons >15 years old: 72% (95% CI 28-89). VE against illness requiring hospitalization was 82% (95% CI 27-96).

Lucas ME et al (2005) assessed the protective effectiveness against clinically significant cholera of two doses of the recombinant cholera-toxin B subunit, killed whole-cell (rBS-WC) oral cholera vaccine in a case-control study during the 2003-2004 outbreak of El Tor Ogawa cholera in Beira, Mozambique. The study included 43 persons with cholera and 172 controls. Receipt of one or more (usually 2) doses of rBS-WC vaccine was associated with 78% protection (95% CI 39- 92; P=0.004) 1-6 months after vaccination. The vaccine was equally effective in children < 5 years of age and in older persons. (In Beira, the seroprevalence of HIV is approximately 20 to 30 percent).

Sur D et al (2009) studied the efficacy and safety of a modified, killed whole-cell, oral cholera vaccine (Shanchol™ / mORCVAX™) among 31 932 participants > 1 year of age in Kolkata, India. An interim per-protocol analysis of this cluster-randomised, double-blind, placebo-controlled trial showed 45% protective efficacy of two doses of the vaccine against severe diarrhea after one year, 77% after 2 years, and a cumulative efficacy of 67% over 2 years. The protective efficacy did not differ significantly between age groups 1.0-<5 years, 5.0-<15 years, and 15 years and older.

Trach DD et al (1997) investigated the efficacy of 2 doses of a killed, oral cholera vaccine (ORCVAX, original vaccine) in a large-scale, open field trial in Hue, Vietnam. During an outbreak of El Tor cholera 8-10 months after vaccination, the protective efficacy among the 51,975 people who had received the complete two-dose vaccine regimen was 66% (95% CI 46-79) and this was similar for children aged 1-5 years (68%) and for older people (66%).

References on vaccine efficacy/effectiveness

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Sanchez JL, Vasquez B, Begue RE, et.al. Protective efficacy of oral whole-cell/recombinant-B-subunit cholera vaccine in Peruvian military recruits. *Lancet* 1994/ Nov 5;344(8932):1273-6.

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Sur D, Lopez AL, Kanungo S, et al. Efficacy and safety of a modified killed whole-cell oral cholera vaccine in India: an interim analysis of a cluster-randomised double-blind, placebo-controlled trial. *Lancet.* 2009 Nov 14;374(9702):1694-702.

Trach DD, Clemens JD, et al. Field trial of a locally produced, killed, oral cholera vaccine in Vietnam. *Lancet.* 1997 Jan 25;349(9047):231-5.