Protection against cholera from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis

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Background

- Killed whole-cell oral cholera vaccines (kOCVs) are becoming a standard cholera control and prevention tool.
- However, vaccine efficacy and direct effectiveness estimates have varied, with differences in study design, location, follow-up duration, and vaccine composition posing challenges for public health decision making.
- We did a systematic review and meta-analysis to generate average estimates of kOCV efficacy and direct effectiveness from the available literature.

Methods

- **Design**
  - For this systematic review and meta-analysis, we searched PubMed, Embase, Scopus, and the Cochrane Review Library on July 9, 2016, and ISI Web of Science on July 11, 2016,
  - We included randomized controlled trials and observational studies that reported estimates of direct protection against medically attended confirmed cholera conferred by kOCVs.
  - We included studies published on any date in English, Spanish, French, or Chinese.
  - This study is registered with PROSPERO, number CRD42016048232.
- **Data extraction**
  - We extracted from the published reports the primary efficacy and effectiveness estimates from each study and also estimates according to number of vaccine doses, duration, and age group.
- **Study outcomes**
  - The main study outcome was average efficacy and direct effectiveness of two kOCV doses.
- **Data analysis**
  - We conduct the meta-analysis using a random-effect models.

Results

–Seven trials (with 695 patients with cholera) and six observational studies (217 patients with cholera) met the inclusion criteria.

–The average two-dose efficacy of 58% (95% CI 42-69, I^2=58%) and effectiveness of 76% (62-85, I^2=0). (Figure 2).

–Two-dose efficacy estimates of kOCV were similar during the first 2 years after vaccination, with estimates of 56% (95% CI 42-66, I^2=45%) in the first year and 59% (49-67, I^2=0) in the second year. (Figure 3).

–The efficacy reduced to 39% (13 to 57, I^2=48%) in the third year, and 26% (-46 to 63, I^2=74%) in the fourth year.

–Average two-dose efficacy in children younger than 5 years (30% [95% CI 15-42], I^2=0%) was lower than in those 5 years or older (64% [58-70], I^2=0%; p<0·0001). (Figure 5).

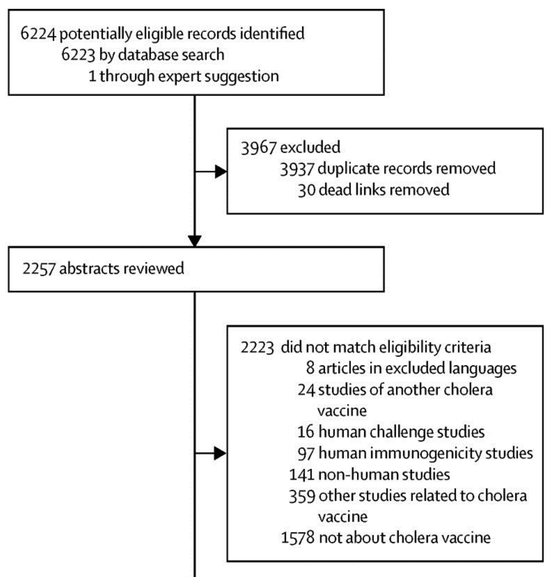

Figure 1. PRISMA flow chart highlighting details of the systematic review and data abstraction process

Results - Figures

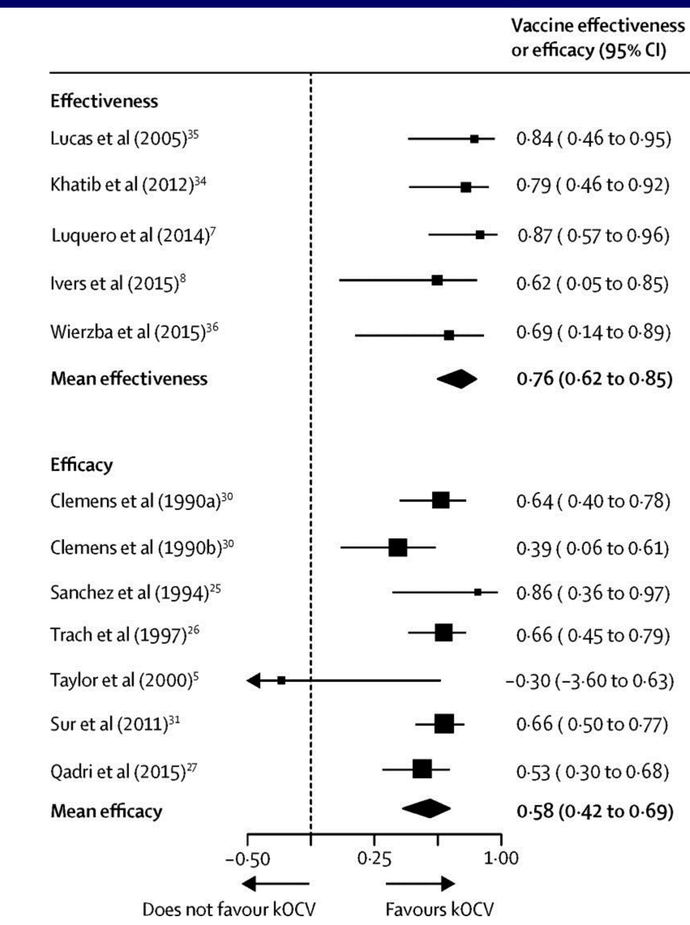

Figure 2. Effectiveness and efficacy main pooled analyses for two-dose killed whole-cell oral cholera vaccine

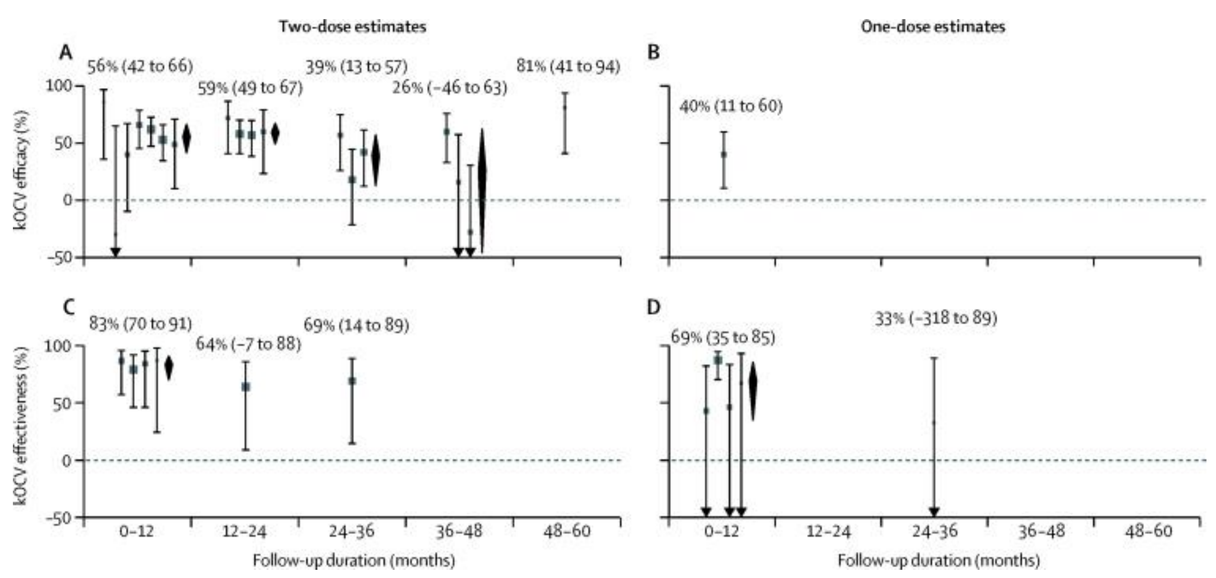

Figure 3. Efficacy and effectiveness by time since vaccination and number of doses

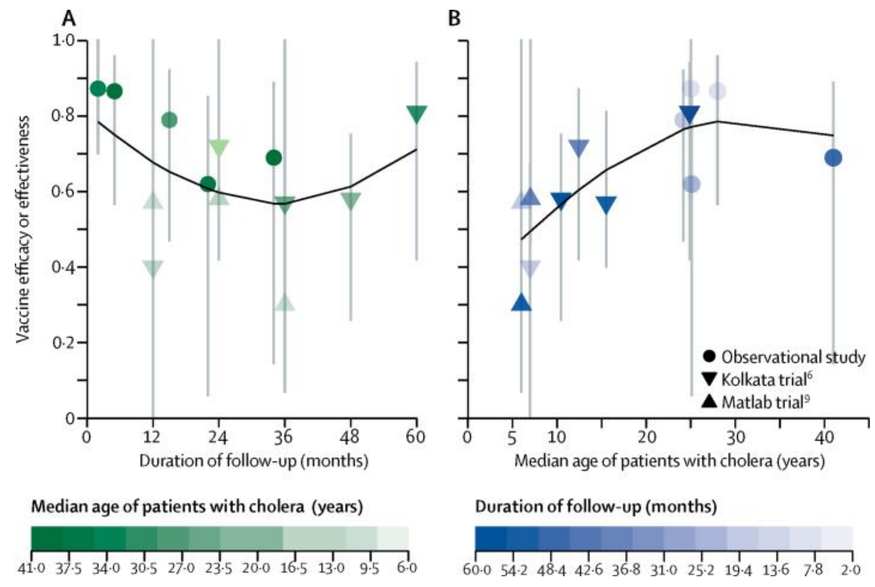

Figure 4. Relationship between protection by vaccine, duration of follow-up, and median age of patients with cholera. (A) Relationship between protection and months of follow-up. Shading shows median age of patients with cholera. (B) Relationship between protection and the median age of patients with cholera measured in years. Shading shows duration of follow-up.

Conclusion

- Two kOCV doses provide protection against cholera for at least 3 years. One kOCV dose provides at least short-term protection, which has important implications for outbreak management. kOCVs are effective tools for cholera control.

Acknowledgments

We would like to thank the study investigators who provided supplemental data for these analyses and participants from all kOCV studies who together have made possible this new understanding of kOCVs.