Costs of illness due to cholera, costs of immunization and cost-effectiveness of an oral cholera mass vaccination campaign in Zanzibar


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study objective was to assess the cost-effectiveness of an oral cholera mass vaccination (Dukoral) campaign conducted in Zanzibar in 2009. The authors concluded that the 2009 mass vaccination campaign was not cost-effective but mass vaccination campaigns may be cost-effective under circumstances of high prevalence and low oral cholera vaccine prices (<$1.3) and delivery costs. The study methods and the authors' conclusions appeared appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The study objective was to assess the cost-effectiveness of a mass oral vaccination (Dukoral) campaign conducted in Zanzibar in 2009 for the control of endemic cholera.

Interventions
Mass vaccination using Dukoral was compared to standard care. The authors stated that Dukoral had to be administered in two 3mL doses at least one week apart and required a temperature-controlled supply chain (2°C to 8°C).

Location/setting
Zanzibar/outpatient

Methods
Analytical approach:
A cost-effectiveness model was used to estimate costs and health effects of a mass vaccination campaign for a cohort of 50,000 individuals over three years. The time horizon and cohort size were chosen in line with the intervention/research project on which the analysis was modelled. The authors stated that the analysis was done from health care provider and societal perspectives.

Effectiveness data:
Effectiveness data included in the model consisted of the annual incidence of cholera, annual deaths from cholera, life expectancy and protective efficacy (herd protection). The baseline annual number of cholera cases for the no vaccination comparator arm was obtained using a published cholera incidence rate. Incidence of cholera was obtained from surveillance of diarrhoea cases with laboratory confirmation for cholera in the Zanzibar study area. The comparative number of cholera cases in the intervention arm was calculated by applying direct and indirect effects of the vaccination programme to the baseline value using data on protective efficacy among vaccinated and unvaccinated people. These data came from the Zanzibar mass vaccination campaign. Life expectancy was based on World Health Organisation (WHO) life tables for Tanzania.

Monetary benefit and utility valuations:
Disability-adjusted life-years (DALYs) for cholera were calculated according to a published method (Jeuland et al.) assuming no age weighting. The authors stated that no disability weights were available for cholera and so a disability weight of 0.11 for diarrhoeal diseases was used.
Three summary benefit measures were used: DALYs averted, deaths averted and cases averted. Future benefits were discounted at an annual rate of 3%.

Cost data:
Costs included public and private costs of illness due to endemic cholera and costs of the mass vaccination campaign. Public cost of illness included costs borne by the health care provider for setting up and running cholera treatment centres. Public cost of illness was estimated from three outbreaks of cholera that happened in 2009 outside the mass vaccination target communities. These costs were obtained from a range of sources that included interviews with local experts and patients, reports and record review. Private direct cost of illness included medical and non-medical expenses related to patient treatment. Indirect cost of illness included loss of income borne by patients and their families. Private (direct and indirect) cost of illness were elicited from a convenience sample of 95 patients admitted to cholera treatment centres during the 2009 outbreaks. Mass vaccination campaign costs were collected based on actual expenditure and planned budget data. Costs derived from the campaign project were adjusted to exclude costs related to research. Costs were reported in 2009 US dollars ($) and were based on mid-2009 exchange rates. Costs were not discounted.

Analysis of uncertainty:
One-way sensitivity analysis varied base-case key parameter values over plausible ranges to estimate the influence of parameter uncertainty and true variation on the incremental cost-effectiveness ratio (ICER) per DALY, death and cases averted. Plausible ranges were based on public health considerations (for vaccine purchase price and delivery costs, incidence), guidelines (for discount rate) and variation (local data for protective efficacy rates, case fatality rates, number of ill days and public and private cost of illness). Threshold analyses examined the vaccine purchase price at which the intervention would become cost-effective. Results of the analysis were reported in the text. Tornado diagrams for the sensitivity analysis were provided in a supporting document.

Results
Cost-effectiveness was examined according to WHO criteria which define an intervention as cost-effective if the given ICER is less than three times the per capita gross domestic product (GDP) per DALY averted. This was equivalent to $1,500/DALY in 2009.

Results were reported for the health care perspective analysis. Total mean public cost of illness was $61 across three treatment centres. Total direct and indirect mean private costs of illness was $43 for the 95 individuals interviewed. Total mass vaccination costs were $760,000. The estimated total cost per fully immunised individual was $30, which fell to $26 after exclusion of services from international consultants. Annual costs to immunise 50,000 people was $430,000 assuming one campaign per three years at a cost of $1.3 million. Annual public costs of illness averted by vaccination amounted to $4,000. Incremental costs (difference between total annual costs with and without vaccination) amounted to $430,000. The base-case ICERs were $750,000 per death averted, $6,000 per case averted and $30,000 per DALY averted. The authors stated that there were no differences between the two perspectives for the ICERs.

Sensitivity analysis showed that the most influential parameters on ICER per DALY averted were prevalence rate, case-fatality rates, discount rate and vaccine purchase price. Threshold analysis indicated that the purchase price per course would have to be $1.2 or below to make the mass vaccination campaign cost-effective from a health care provider perspective (societal perspective $1.3).

Authors' conclusions
The authors concluded that the 2009 mass vaccination campaign was not cost-effective but mass vaccination campaigns may be cost-effective under circumstances of high prevalence and low oral cholera vaccine prices (<$1.3) and delivery costs.

CRD commentary
Interventions:
The choice of interventions appeared appropriate: the proposed vaccine was stated to have been compared to standard practice. But standard practice was not defined so what the comparator was and whether it varied across treatment centres was unclear. The authors justified their choice of Dukoral as the intervention, stating that it was the only oral
cholera vaccine to have been pre-qualified by WHO in 2009. Details on administration of Dukoral were reported clearly.

**Effectiveness/benefits:**
Data on efficacy and benefits were reported clearly. Estimates for the protective effects of vaccination were obtained from a local study and should be applicable to this study setting. It would have been useful had the authors compared the protective effects with other published estimates. Limited details regarding the characteristics of the research/intervention project were reported. The disability weight used to calculate the DALY estimate was for diarrhoeal diseases rather than cholera and it was not clear how appropriate that was.

**Costs:**
Costs and methods used to derive them were reported clearly. The costs were relevant to the stated perspectives. The price year and source for the exchange rate were reported. The sources used to derive unit costs were specific to Zanzibar. The authors stated that campaign costs were not discounted as the mass campaign happened over one single year. If treatment of cholera is only short-term then that was appropriate.

**Analysis and results:**
Results of the base case and sensitivity analyses were reported clearly. The authors highlighted several limitations to their study. First, there was no probabilistic sensitivity analysis when such an analysis would have provided a more accurate account of the effect of parameter uncertainty on the results. Second, limited data availability meant the analysis was conducted for a population-wide campaign instead of a targeted approach towards high-risk or specific age groups, which might have made the intervention cost-effective. Third, usually only patients with diarrhoea were treated or admitted by their local public health care facility while it operated as a cholera treatment centre. People who sought treatment for non-diarrhoeal diseases (such as malaria) during an ongoing cholera outbreak would have to bear extra direct and indirect costs related to additional travel or potential serious complications due to delayed treatment. The authors suggested that future studies would be improved by collecting estimates on these costs.

**Concluding remarks:**
The study methods appeared adequate and the authors' conclusions appeared appropriate.

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