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Report on the WHO Quantitative Immunization and Vaccines Related Research (QUIVER)

Advisory Committee Meeting
Geneva, 4-6 October 2011

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World Health Organization
Department of Immunization, Vaccines and Biologicals
CH-1211 Geneva 27, Switzerland
• *Fax:* + 41 22 791 4227 • *Email:* vaccines@who.int •

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Contents

1. Executive Summary

- The fifth meeting of the QUIVER advisory committee was held October 4-6, 2011 in Geneva, Switzerland. Briefly, QUIVER was set up as a technical committee advising the Strategic Advisory Group of Experts (SAGE) due to increasing demand for the use quantitative methods in evaluating vaccines.
- WHO and UNICEF have developed an approach to formalising the rules for vaccine coverage estimation within a computational logic framework. The approach was found to be reasonable. Linguistic grading of the robustness of evidence was preferred as numerical uncertainty intervals may not be justifiable.
- An exercise has been completed using the Cooke method to elicit parameters for pertussis natural history models from eight experts. The uncertainty in model results highlights the importance of more field studies, both for informing the parameters in a more robust way, as well as for external validation of the elicited values. The use of unweighted responses from the experts was encouraged, as was consideration of different ways to combine results from each expert.
- An agent-based polio model has been developed by Intellectual Ventures. It offers a good approach to guiding policy about polio vaccination and identifying knowledge gaps. However, the model may need greater transparency around its input parameter and the way it calculates R0, as well as better sensitivity and uncertainty analysis. QUIVER advised against making it widely available to policy makers without sufficient guidance about interpreting the results.
- Malaria vaccine models have been developed by groups at the Swiss Tropical and Public Health Institute, Imperial College, Intellectual Ventures and GlaxoSmithKline. Publication of the first of three sets of phase III trial results of the most advanced malaria candidate vaccine may stimulate further work. Some of these models suggest that vaccination will only reduce transmission if the target age range includes older children and adults, as the human infectious reservoir extends well beyond the age of five years. QUIVER felt that modellers should inform the design of phase IV trials in order to obtain more robust population-level data about indirect vaccine effects. Substantial gaps in data and the need for further model fitting were highlighted.
- PAHO's TriVac tool was developed in response to requests for technical support for economic evaluation by PAHO countries. It allows economic evaluation of pneumococcal, HiB and rotavirus vaccination. QUIVER members were appreciative of the model, but there were concerns about the comparability with non-vaccine interventions.

- The Lives Saved Tool (LiST) is a proportionate mortality model that allows evaluation of the impact of about 80 childhood interventions, including pneumococcal, rotavirus, DTP, measles and meningitis vaccination. The tool offers many possibilities, but at present did not seem well suited to model for measles and perhaps other epidemic diseases. There are more specific tools that should be used for that purpose.
- A model for Generalised cost-effectiveness analysis (G-CEA) of vaccination has been developed as part of the WHO-CHOICE collaboration.
- QUIVER members encouraged comparisons between TriVac, LiST, G-CEA, and real-world data. They were interested in collaborating with TriVac, LiST and G-CEA tool developers in order to incorporate transmission dynamic effects into these models.
- The ProVac initiative is useful for encouraging an approach to vaccine decision-making which incorporates evidence, good studies and economic modelling. However, it is important for results from the TriVac model to be compared to other models to avoid over-reliance on a single tool.
- QUIVER members were encouraged that work is being conducted to investigate the case for measles eradication, well before the measles end game has been reached. There are a number of complex issues that need to be considered, so the present work may be a means of highlighting key research priorities for the next decade rather than an end in itself.
- Reliable estimates of dengue disease burden are important to inform decision-making on vaccine introduction. Multi-country studies by the Pediatric Dengue Vaccine Initiative suggest substantial under-reporting by routine surveillance and provide methodological approaches for improving disease burden estiamtes. Similar studies are needed in other countries.
- An ad hoc WHO consultation was held to discuss ways of capturing the full economic impact of vaccination beyond what is evaluated in traditional cost-effectiveness methods. This is a useful approach, and development of guidelines would be helpful to ensure that work in this area is informed by robust evidence.
- WHO estimates on the global yellow fever burden are currently dependent on results by a single study. There is an urgent need for investment into serological surveys in endemic countries to inform decision making about vaccine deployment.
- Estimates of measles mortality have been made annually since 1998, informed by progressively more refined models.
- There are several approaches to estimating the global burden of disease. There is value in each of these approaches, and QUIVER would recommend the use of all of them to continue to monitor progress in the Decade of Vaccines.
- QUIVER believes that there is a role for both epidemiologic (natural history) and proportionate mortality approaches in estimating the burden of disease. Proportionate mortality modellers should consider incorporating surveillance data as well as vital registration and verbal autopsy data.
- Both WHO and the Institute for Health Metrics and Evaluation are producing estimates of childhood mortality by cause. QUIVER would encourage both groups producing mortality estimates to work together, and notes that the Bill and Melinda Gates Foundation is funding both efforts.

2. Introduction and charge to the committee

J. Hombach

The fifth meeting of the QUIVER advisory committee was introduced. Briefly, QUIVER was set up as a technical committee advising the Strategic Advisory Group of Experts (SAGE) due to increasing demand for the use of quantitative methods in evaluating vaccines. A recently conducted review of the activities of the Initiative for Vaccine Research (IVR) suggested that IVR should take a strong role in shaping the overall agenda for the introduction of new vaccines and immunisation systems. Hence IVR is looking to enlarge the scope of QUIVER to give advice on the formulation of priorities for implementation research.

The chair, members and rapporteur of QUIVER were thanked for their contributions, along with the WHO secretariat and the Bill and Melinda Gates Foundation for financial support.

SESSIONS FOR RECOMMENDATION