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

Advisory Committee Meeting
Geneva, 4-6 October 2011
The Department of Immunization, Vaccines and Biologicals thanks the donors whose unspecified financial support has made the production of this document possible.

This document was published by the

_Initiative for Vaccine Research (IVR)_

of the Department of Immunization, Vaccines and Biologicals

**Ordering code: WHO/IVB/12.03**

**Printed: February 2012**

This publication is available on the Internet at:

www.who.int/vaccines-documents/

Copies of this document as well as additional materials on immunization, vaccines and biologicals may be requested from:

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Printed by the WHO Document Production Services, Geneva, Switzerland
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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 estimates. 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
3. WHO/UNICEF estimates of national immunization coverage (WUENIC)

Overview (M. Gacic-Dobo)

The WHO/UNICEF coverage estimation process began in 1999. Methods were reviewed, approved, and first released in 2001, and have been updated annually since 2001. Estimates of routine coverage for ten antigens have been made for all WHO and UNICEF member states each year for the period 1980 - 2010. The major criticism from previous reviews of the estimates was the lack of replicability, consistency and transparency between estimation methods.

The WHO and UNICEF working group developed a formal knowledge reasoning and representation (KRR) system called WUENIC (WHO and UNICEF estimates of national immunization coverage). This uses computational logic to represent the estimates, data, decisions, and rules which the working group uses to derive the estimates. In 2009, QUIVER reviewed the revised method and ongoing activities to improve transparency and estimation methods. QUIVER found this approach appropriate and recommended exploring the use of survey confidence intervals to establish “support” thresholds, as well as validation of the estimates and encouraged using serosurveys. However, QUIVER was unable to make recommendations regarding uncertainty in the estimates and recommended further research. Analysis of survey microdata, comparison with biomarkers, and cross-calibration with epidemiological modelling were suggested.

The purpose of this session was to update QUIVER on progress made since 2009 review.

Update (T. Burton)

WHO and UNICEF rules have been formalized and implemented in a computer-based language to automatically produce the 2009 and 2010 revisions.

WHO and UNICEF remain concerned regarding the possible magnitude of the systematic (or non-sampling error) associated with survey results, and are reviewing them for evidence of recall bias. The current rules use surveys to validate estimates reported by national authorities and, in the event of disagreement, to establish an alternative estimate. The operational definition of a disagreement is a difference above 10% of the reported estimate. QUIVER recommended that confidence intervals of survey results be considered as threshold. WHO and UNICEF have commissioned the re-analysis of surveys to produce confidence intervals for appropriate cohorts.
The use of serosurveys was encouraged to validate coverage estimates. WHO and UNICEF propose to conduct a literature search for existing results. However, cost and difficulty in interpretation make it problematic to conduct serosurveys for the sole purpose of validating coverage. Biomarkers for new vaccines (such as pneumococcal, Hib and rotavirus vaccines), as well as their interpretation, remain an unexplored issue.

Generalization of validation results to other settings is problematic due to variation between and within countries. The robustness of the WHO/UNICEF estimates vary between countries and, within countries, over time. Hence a linguistic grading of each estimate based on the scope, quality and source of information is proposed. This would have three categories: fairly confident (well supported, high precision, multiple sources, consistent data), somewhat confident (lower precision, conflicting information / lack of confirmatory data / single consistent estimate) and not confident (inconsistent data, low precision, multiple inconsistent sources or single inconsistent source).

Discussion

The formal logit approach of describing the estimates was regarded as reasonable and should be continued. The linguistic grading of the estimates was also thought to be acceptable, and less misleading than numerical uncertainty intervals.

Validation of estimates with mortality and morbidity data and disease models is helpful. However, heterogeneity of risk factors and subnational differences in access to health services will make validation using disease data complex. Subnational differences may be important since they can lead to localised outbreaks even when the majority of the population are vaccinated. While validation using serosurveys would be desirable, such surveys can be expensive, difficult to implement and require large sample sizes. Interpretation of the results is not straight forward due to the difficulty in distinguishing between natural and vaccine-induced protection. Hence serosurveys may not be a large scale solution.

Other methods to validate coverage were recommended, such as the Lessler method (Lessler J et al. PloS Med 2011, Measuring the Performance of Vaccination Programs Using Cross-Sectional Surveys: A Likelihood Framework and Retrospective Analysis.) Also, new technology to improve the quality of recording and reporting immunizations could be explored.

Summary points and recommendations

- QUIVER is satisfied with the overall approach to estimating vaccine coverage, including the use of a qualitative assessment of the robustness of estimates rather than quantitative uncertainty intervals.
- QUIVER recommends validation of estimates, ideally using multiple external data sources such as serosurveys, mortality and morbidity data. QUIVER, however, recognizes that heterogeneity of risk factors and sub national differences in access to health services will make validation using data complex.
- QUIVER recommends exploring application of new technology to improve the quality of recording and reporting immunizations.
4. Global burden of pertussis

Introduction (E. Simons/ P Strebel)

Estimates of the global burden of pertussis rely on natural history models which are poorly parameterised due to the lack of data collection on pertussis. A model was presented at the 2010 QUIVER meeting which elicited expert opinions about key parameters (risk of transmission, disease and death) for pertussis modelling. QUIVER 2010 endorsed the approach and the use of expert elicitation given the shortcomings in the data, but suggested that the approach should be validated, and encouraged funding of studies to collect primary data.

Model presentation (R. Tebbens)

Results from the pertussis expert elicitation exercise were presented. A panel of eight experts were interviewed remotely (using telephone or internet), using the Cooke method which weighs values from each expert based on their performance on calibration questions. Seven experts provided complete responses, but only three of these were used in the final model after weighing for performance. The inclusion of values from all seven experts with equal weights for each increased the uncertainty in results.

The experts reported that the elicitation process was useful to identify data gaps and motivate studies. However, the questionnaire was challenging due to lack of data, questionnaire fatigue and dependence between inputs that may be dynamically related. Experts also suggested that more consensus could be achieved through a Delphi-like approach.

Review and group discussion

QUIVER members were not satisfied with the use of weighing for the results. In particular, one expert contributed to a large part of the weighted results and four experts received zero weight using Cooke's method of combining elicitation results. The calibration questions asked were perceived to be difficult even for experts in the field to answer. Hence the use of unweighted responses was recommended. QUIVER also suggested consideration of different ways to combine results from each expert besides the current method of adding the uncertainty distributions from each expert, given that additive methods would lead to wider uncertainty bounds than multiplicative approaches.
The uncertainty in the model results also highlights the importance of conducting more field studies in low and middle income countries, both for informing the parameters in a more robust way, as well as for external validation of the expert values. There are existing data from a study in Senegal; however, these data are likely to be well-known by the experts so may not be appropriate for external validation. In high income countries, there are few cases or deaths due to pertussis, so data collection for validation may have to take place on a regional level (eg. all of Europe) rather than country level.

Sensitivity analysis on the model may reveal which parameters are most important for further studies. However, there were concerns that the simplified structure of the model (which does not incorporate infection transmission dynamics or the influence of natural immunity on infection risk) may reduce its usefulness for guiding further research on the most influential parameters to consider.

The estimates for the global burden of pertussis were comparable (within large ranges of uncertainty) to previous estimates from a model by Crowcroft and colleagues. However, they are much higher than estimates from the Institute for Health Metrics and Evaluation (IHME) based on proportionate mortality studies by verbal autopsy.

**Summary points and recommendations**

- QUIVER is satisfied with the overall approach but remains concerned about the lack of primary data.
- QUIVER recommends the use of unweighted results from all seven experts.
- QUIVER recommends alternative ways of combining results and comparing the method used to several alternatives.
- QUIVER suggests validating the parameter estimates against data from Senegal and Europe as a first step, although primary data from developing countries that is currently not publicly available would provide a more compelling comparator for validation.
- QUIVER continues to encourage the funding of more primary studies to collect data directly, using the model to understand what the most influential parameters are.
5. Global Good Polio Model

**Introduction (R. Sutter)**

Endemic polio transmission is still ongoing in 4 countries (Nigeria, India, Pakistan and Afghanistan). However, wild type 2 poliovirus has not been seen since 1999. Guidance is required on several issues around polio vaccination, such as the feasibility of switching from trivalent to bivalent oral polio vaccine and associated risk of type 2 circulating vaccine-derived poliovirus (cVDPV2) emergence, as well as the role of inactivated polio vaccine in risk mitigation. The KidRisk model has been reviewed by QUIVER and has been used to inform WHO guidance on these issues. However, more sophisticated models are required to address emerging questions as well as to cross-validate the KidRisk model.

**Model presentation (K. Nigmatulina)**

Intellectual Ventures is a for-profit company that finances the Global Good Fund to bring solutions such as epidemiological modelling and data analysis to developing countries. The aim is to develop a tool that can be distributed freely and used broadly. The epidemiological model is modular, so it incorporates polio, malaria, HIV and TB-specific code in a general framework.

The polio model is an agent-based SEIR model, which incorporates immunological response, viral evolution, contact structure and spatial distribution. The model address questions such as the risk of cVDPV emergence, implications of wild type-2 virus cessation as well as the effectiveness of different vaccination strategies. The general framework for the polio model is in place, and parameterisation (based on literature review) is close to completion. Further data from Tajikistan, Nigeria, Pakistan and other countries will be used to validate the model. An alpha release of the polio model has been sent to subject matter experts, modelling concepts experts and QUIVER members for review.

**Review (B. Grenfell)**

The ability to switch between a simple and complex model is useful. However, it is important to ensure that users do not make the model too complicated and get misleading results, especially since it is aimed at policy makers.
Review (J. Koopman)

The incorporation of realistic aspects of polio natural history such as immunity informed by Nigerian data is welcome, since vaccine waning can have a large effect on the success of eradication efforts. A simple model constructed by James Koopman illustrated this.

The model should be used to determine the parameter ranges where cVDPV is a threat, using data on the early effects of vaccination and genetic sequencing to estimate parameters. However, to get a stable estimate for viral evolution parameters from Nigerian data, the number of free parameters needs to be reduced.

Review (G. Gomes)

The modular structure of the model is useful to guide users, because it may be difficult to keep track of the accuracy of individual parameters. $R_0$ is not an input parameter in the model, but a conglomeration of many aspects of disease transmission.

Review (K. O’Reilly)

The model may need more transparency around the sources of information used to inform parameters, as well as investigation of uncertainty around their values. Also, it is important to see analytically how $R_0$ was derived in the model since it is the measure used to compare models and disease scenarios. Studies from Nick Grassly (Imperial College) have found that there is strong evidence for asymptomatic transmission in individuals in contact with polio cases, if they have fewer than three doses of vaccine.

General discussion

It may be useful to incorporate an inference component to the model so that the parameters can be fitted based on an observed epidemic curve.

The immunity components of the model rely on serological markers of susceptibility and hence may not reflect true susceptibility. Also, the serosurveys are using outdated technology. It is now possible to look at the whole spectrum of avidity, in order to distinguish between vaccine and wild-type antibodies.

It is important to make polio data available to Intellectual Ventures as well as other modellers working in the field.

The model is a good approach to guiding policy and identifying knowledge gaps, but QUIVER advised against making it widely available to policy makers without sufficient guidance about interpreting results.
Summary points and recommendations

- QUIVER believes that the EMOD model polio eradication is a potentially promising approach. Comparisons with epidemic data and publication of the model are essential steps to guiding policy and identifying evidence gaps.

- More primary data on polio should be made available for all models. QUIVER recommends that polio related data should be made available for multiple modeling groups to encourage comparison of results using different approaches.

- QUIVER recommends the development of an inference module within the model so that parameters be estimated using epidemic data.

- QUIVER recommends that creating a clearer user interface for turning on/off higher level modules would be beneficial and would give a better overview of the model components.

- QUIVER believes that the model may need some transparency about the source of parameter values, measures of uncertainty around them, and the way key quantities such as R0 are calculated. QUIVER understands that a publication is in process.

- QUIVER recommends multi-variable sensitivity analysis.

- Given the complexity of the model it is important to educate and caution users on the capabilities and limitations of the software. QUIVER encourages ensuring potential users understand how to use the model and interpret its results.
6. Malaria vaccine modelling

Overview (V. Moorthy)

A malaria vaccine candidate called RTS,S has been developed by GlaxoSmithKline (GSK) in partnership with the PATH Malaria Vaccine Initiative, and is currently undergoing phase III trials in children aged 6 weeks - 17 months old. Full trial data will become available in 2014, and if they are favourable SAGE and the Malaria Policy Advisory Committee (MPAC) may advise that a WHO recommendation for use will be justified.

Report from the joint QUIVER/JTEG subgroup (P Milligan)

Guidance from models is needed to inform policy recommendations about vaccine introduction, such as the cost-effectiveness of adding vaccination to existing preventive measures, the optimal age group for catch-up vaccination and the relationship between age of immunisation and impact of vaccination on malaria transmission. In 2010, QUIVER suggested that comparative modelling of malaria was premature until there was a fuller assessment of the status of the field of malaria vaccine modelling. A joint QUIVER/JTEG subgroup met in March 2011, and compiled a spreadsheet summarising the structure, key assumptions, outcomes and data for available malaria models.

Four models were evaluated, developed by the Swiss Tropical and Public Health Institute (Swiss TPH), Imperial College, Intellectual Ventures and GSK respectively. An end user interface developed by PATH/MVI for the Swiss TPH model was also evaluated.

Both the Swiss TPH and Imperial model suggest that infant and child vaccination will have minimal impact on transmission unless catch-up is extended to older children and adults. The greatest impact and best cost-effectiveness is seen in medium transmission settings. In high transmission settings, it has been suggested that reduction of malaria transmission may actually be counterproductive due to the “Snow effect” (first described in Snow RW et al. Lancet 1997; 349:1650). Snow and colleagues suggested that measures to reduce transmission in high endemicity areas may also reduce the development of protective immunity during childhood, and hence shift the burden of malaria to older age groups where severe disease is more likely to occur. However, these conclusions are highly dependent on limited data from field studies to inform the relationship between transmission and age-dependent incidence of clinical malaria, severe disease and malaria-related mortality. Data on underlying vaccine efficacy, mode of action, duration of protection, heterogeneity of risk and gametocyte carriage is also very limited. It is still unclear whether severity of disease is linked to age alone, or to prior exposure to infection. Hence the validity of these assumptions needs to be investigated before using model conclusions to inform deployment of vaccination.
Review (M. Postma)

Good models are crucial to inform vaccination policy given the complexity of malaria natural history and epidemiology. It is vital to design studies to analyse the potential adverse effects of vaccination such as the “Snow effect” and changes to parasite genetic diversity. The vaccine trial data, especially from the placebo arm, may help to inform this and hence should be placed in the public domain. The results of models should also be used for the design of phase IV trials.

Review (J. Koopman)

The potential for malaria vaccines to produce adverse effects (the “Snow effect”) must be investigated as a vaccination programme with harmful effects would have a detrimental effect on vaccine uptake. However, such an investigation is difficult due to the complexities of malaria antigen structure and immunity. The feedback mechanisms that malaria has evolved in response to immunity need to be incorporated realistically. Unfortunately, there is no escaping the need for complex models that require good data to parameterise. Population-level data from phase IV trials is especially crucial. Also, the joint effects with other interventions such as bed nets need to be investigated as these may help to ameliorate potential adverse effects (the Snow effect).

Review (R. Steketee)

Several models suggest that vaccination can reduce transmission in low and medium transmission settings if delivered to individuals at a wide age range. This merits further exploration. In particular, modellers need to inform data collection from field studies so they can determine the precise age range and coverage needed to achieve such an effect.

Discussion

The Imperial group is working with GSK to look at vaccine trial data, in order to investigate vaccine impact across a range of endemicity settings. It is also important to note that there are relatively few settings with such high transmission rates that a potential “Snow effect” may occur, so this issue should not dominate vaccine introduction discussions, particularly as the issue is not new, and is not specific to vaccines. Furthermore country experience to date has not indicated that reductions in transmission have led to increases in morbidity. The view from malaria control programmes is that decreases in malaria transmission are highly desirable and must be sustained. In fact major reductions in disease burden have been achieved in multiple settings through reduction of malaria transmission and associated reductions in cases and deaths.

The impact of changing parasite diversity in low transmission settings still needs to be investigated. This includes the persistent circulation of distinct strains in a population, as well as the effect on transmission of circulating strains. Again, this could be informed by data from phase IV trials.
A further issue is that there are very few data on the burden of malaria in low transmission settings such as India. It is important to understand severe disease in adults since the introduction of intervention such as bed nets will create more low transmission settings.

The publication of phase III trial results as well as further data from programmatic settings may encourage other modelling groups to become involved in malaria.

Progress is being made in the field of malaria vaccine modelling, although it may still be premature to conduct comparative modelling. However, the models may be sophisticated enough for modellers to make suggestions about key data needs, particularly about indirect population-level effects of vaccination. There is interest in continuing the QUIVER/JTEG collaboration.

**Summary points and recommendations**

- QUIVER is encouraged by the progress being made in malaria modelling.
- QUIVER recommends further exploration of model uncertainties including key gaps in model fitting and epidemiological data, and their relative importance in model predictions.
- QUIVER would like to see consideration of how indirect effects of vaccination (such as effects on transmission / herd immunity, waning natural immunity and possible increases in severe cases due to age shifts in infection) can be measured in vaccine trials.
- There should be institutional arrangements to make data available more broadly.
- QUIVER is interested in continuing its collaboration with JTEG and other groups on malaria vaccine models, and encourages additional modellers to enter the field.
7. Impact and cost-effectiveness tools

Overview (R. Hutubessy)

Several impact and cost-effectiveness tools are available to support country-level decision making and priority setting. These include: (i) PAHO’s TriVac tool to strengthen the infrastructure and processes for decision making in the WHO PAHO region (now being transferred to other regions with the establishment of the ProVac International Working Group), (ii) the LiST tool being used in ministries of health and international partner agencies. Both were discussed during an internal IVB lunchtime seminar in October 2010.

TriVac presentation (A. Clark, B. Jauregui)

The TriVac model was developed in response to requests for technical support for economic evaluation by PAHO countries. It allows economic evaluation of vaccination against Haemophilus influenzae type B (funded by the GAVI Alliance), Streptococcus pneumonia and rotavirus (funded by PAHO’s ProVac Initiative). An HPV model is in development that uses outputs from the Harvard microsimulation model for parameterisation.

The tool consists of a simple static cohort model, although up to 20 stacked cohorts can be combined. Parameters are not calibrated at the country level; instead preloaded data on the burden of disease for all WHO member states are used. One-way sensitivity analyses are possible; probabilistic sensitivity analyses are being developed using triangular distributions around uncorrelated parameters.

The TriVac model is delivered as part of package of capacity building so that country-level teams can learn concepts of cost-effectiveness analysis. PAHO sets up a country team that feeds into the national immunisation technical advisory group.

Review (E. Sinanovic)

The comparator for the vaccine intervention is do nothing, which may make vaccination look more cost-effective than if it was being compared with current practice in each country. For example, there are other ways of treating rotavirus diarrhoea such as zinc supplementation.
Some methodological concerns around the economic assumptions include the way productivity losses are estimated (using the human capital or friction approach), how double counting for the value of lost time is handled, and how high unemployment is taken into account.

Direct and indirect outcomes should be reported separately, and both costs and benefits should be reported separately as totals for each alternative. This will allow easier comparability with non-vaccine interventions.

**Review (N. Chaiyakunapruk)**

The model structure appears to have face validity, but there has not been any model validation using post-introduction data. However, the GAVI Alliance currently have a request for proposals to perform this kind of validation. Also, although the interface is well documented, there is little description about the data sources.

It is important that the tool is not a stand-alone product, but is embedded within a system for capacity building and technical support. The process of collaboration needs to involve different stakeholders within the country, including those from civil society.

**Review (M. Brisson)**

The interface is well-designed and clear, but the model description lacks details about the way long-term sequelae and survival are modelled after the 5 years time horizon, and how parameter values are sourced.

If all three vaccines are examined at the same time, there may be the issue of competing risks which is not captured. However, a microsimulation model for Bangladesh and Peru which looked at the issue of competing risks among several pathogens suggested that it was not an important effect, so this was dropped as a priority.

The model interface and documentation needs to state the limitations of the model clearly. Simple models can easily lead to biased estimates. Uncertainty analyses can often provide small credibility intervals providing false sense of robustness.

**General discussion**

One feature of the model is that under the current thresholds (of GDP per capita and three times GDP per capita), all vaccines evaluated are cost-effective in all the countries evaluated. Contextualisation by comparing vaccination with other interventions was suggested, as well as head-to-head comparisons between vaccines with different antigens. Head-to-head comparisons between vaccines from different manufacturers would also be useful, although such fine distinctions may be unreliable in a static model. The feature to allow break even vaccine prices to be estimated was removed because the break even price for cost-effectiveness was consistently higher than the manufacturers’ offered prices.
The issue of dynamic effects was raised by several reviewers and the overall group. Although there was a static adjustment for herd immunity for vaccinated cohorts and serotype replacement, more complicated effects such as indirect protection across cohorts and shifts in the age of infection are not considered. For example, indirect protection to adults is a key benefit of pneumococcal vaccination. Introduction of a dynamic component to the model would also help to build capacity by stimulating training of local people to develop and interpret dynamic models.

There is a need for an independent group of experts to champion the development of a dynamic component to the model, since decision makers often prefer very simple and quick models. However, the component can be developed very quickly since the model already allows multiple cohorts. There is a danger that the static model will give misleading results even though it allow rapid evaluation. This is particularly the case when comparing between interventions. Also, there are several other aspects (such as the HPV model) that are already implemented as black boxes that decision makers may not understand.

QUIVER members were appreciative of the model, and willing to collaborate on incorporating dynamic modelling. However, there were concerns about the comparability with non-vaccine interventions.

**Summary points and recommendations**

- QUIVER is appreciative of the TriVac model, and particularly of the way in which it is being used to build capacity for evidence-based decision making.
- QUIVER recommends the transparent incorporation of a dynamic component into the model, and several members are willing to work with the TriVac team to enable this.

**Lives Saved Tool (LiST) presentation (N. Walker)**

The Lives Saved Tool (LiST) is a proportionate mortality model that estimates the impact of scale up of a single or multiple interventions on outcomes. It is intended for use in programme planning on the national and sub-national level to decide on interventions to reduce child and maternal mortality, as well as estimating the impact of old, new and emerging interventions. The work was supported by the Bill and Melinda Gates Foundation and the Child Health Epidemiology Reference Group (CHERG), and has resulted in about 50 review papers on the effectiveness of different interventions.

Around 80 interventions can be examined, including pneumococcal, rotavirus, DTP, measles and meningitis vaccination. Polio and BCG vaccination can also be added but their impact is minimal. Herd immunity is incorporated as a static adjustment, but is only used by default for measles interventions. The model is unable to handle end game analyses or estimate serotype replacement. Ongoing work includes comparing outputs with measured changes, improving linkages between family planning and maternal/child mortality, including new vaccines, estimating impact beyond 0-5 year olds and updating with new clinical trial information.
Review (J. Edmunds)

The tool is easy to use, well documented, allows multiple interventions and competing risks, has a sophisticated demographic engine and is well supported by extensive systematic reviews. However, only the interventions included can cause mortality to decline; hence mortality will not decline if they are not scaled up. This may overestimate their impact since mortality may decline due to general public health improvement. Key areas to improve are the need for testing predictions against emerging data (both from primary studies and other models e.g. for measles (Chen et al. 2011)) and for incorporating uncertainty in results. Also, the model assumes that uptake of interventions is uniform across the population rather than being clustered among easier to reach groups. The incremental costs of scaled up interventions are assumed to be linear which is unknown for many immunisation programmes. It is also important to flag up the static nature of the model which makes it inadequate for some kinds of epidemic infectious disease modelling such as measles.

Review (F. De La Hoz Restrepo)

The strength of the tool is that it is able to approximate the impact of multiple interventions on the same cause of mortality, and the impact of different risk factors on the same health problem. Also, the tool is easy to use, transparent and comes with pre-loaded data although new interventions can also be added. However, it assumes that every intervention has an independent effect (even though some interventions may potentiate each other). The impact of vaccination is conservative, based on comparison of model output with rotavirus vaccine impact in Columbia and measles vaccine impact using the WHO/IVB model. However, it is a useful tool to validate data from countries with poor surveillance, and to make quick estimates of the potential impact of different measures.

Review (M. Brisson)

It is difficult to understand the precise mechanics of the model, and particularly how competing risks for the same causes of mortality are estimated. The methodology used to estimate the impact of vaccination also needs to be more transparent. Limiting the age range for impact to under five year olds means that shifts in age of death or life years gained outcomes are not fully captured. Also, the static adjustment for herd immunity needs to be compared to dynamic models and real life results.

Review (N. Chaiyakunapruk)

A key issue is model contextualisation. The model has been compared against data in some settings, but may not be valid in other settings. It may also be useful to compare it against the TriVac tool. Also, it is parameterised mainly using international studies, when local data may often be more relevant. Further weaknesses are the lack of uncertainty analysis, limited time horizon (5 years), limited incorporation of herd immunity and lack of description of how the model could be used as part of a collaborative process.
Discussion

Uncertainty analysis has yet to be incorporated into LiST because it is not seen as a priority by some people promoting the use of it. The documentation is not always up to date with software because the process is resource intensive. Some analyses of the impact of clustering of uptake of interventions has been performed using DHS data, which suggests that it may not have a large effect. However, it may be an issue for the population outside DHS surveys.

LiST may not be suitable for dedicated vaccine planning, because it does not incorporate many aspects of vaccines such as waning protection and type replacement. It is more useful for general maternal and child health planning that includes vaccination. It also cannot reflect the potential for outbreaks if vaccine coverage is scaled down; hence the interface gives a warning to users if this is attempted. Disease-specific models may be more appropriate to examine interventions within a single disease area. The strength of LiST is that it allows results for different kinds of interventions to be compared.

Collaboration with country partners would be useful, but there is currently no funding for this, so collaboration is conducted with organisations that have links within countries.

The GAVI Alliance has used both TriVac and LiST for multiple purposes. When results from TriVac and LiST are compared, there are differences at the country-level mainly due to assumptions about cause-specific mortality. TriVac uses 2006 estimates from the Global Burden of Disease survey, while LiST uses estimates for 2008. It may be useful to continue model comparisons with antigen-specific models for vaccines such as rotavirus, pneumococcus and HPV.

QUIVER concluded that LiST offers many possibilities but does not seem well suited as presently configured for measles and perhaps other epidemic diseases. There are more specific tools that should be used for that purpose. Members encouraged comparisons with TriVac, other models and primary data.

Summary points and recommendations

- QUIVER believes that the LiST tool offers many opportunities, but at present it does not seem well configured for estimating the impact of epidemic diseases such as measles in part because of the lack of being able to capture indirect effects.
- Neither LiST nor TRIVAC adequately capture temporal dynamics of infectious diseases.
- QUIVER would encourage the use of more specialised tools for such situations.
- QUIVER recommends regular comparisons of results with emerging data.

SESSIONS FOR DISCUSSION
8. Generalised cost-effectiveness analysis of EPI and new vaccines

Overview (J. Lauer, M. Johri)

A model for Generalised cost-effectiveness analysis of EPI and new vaccines was developed as part of a WHO-CHOICE/IVB collaboration. This assess the population costs, effects and cost-effectiveness of selected commonly used, underused and newly available vaccines in all 17 WHO subregions that have low and middle income countries. Vaccination is compared either to current coverage or to no use of vaccination (the null scenario). The null scenario allows the benefit of current vaccination coverage to be seen. Diseases are modelled with a susceptible-infected-recovered (SIR) model structure, but with no infection transmission.

Discussion

QUIVER is appreciative of the WHO Generalized CEA framework for EPI and new and under utilised vaccines. The null scenario was constructed by using the Human Development Index to stratify regions, conducting a literature review to explore disease burden prior to vaccination, and consultation with IVB experts. However, it is less robust than the current coverage scenario.

A dynamic component may be possible to include by including incorporating a time-varying force of infection into the existing ISR model structure.

QUIVER members felt that comparisons between CHOICE, LiST and TriVac may be interesting.
9. ProVac initiative

Presentation (B. Jauregui)

ProVac is a PAHO initiative, funded by the Gates Foundation, that aims to strengthen national capacity for evidence-based decision making on new vaccine introduction. Its activities include strengthening the decision making infrastructure, developing tools like TriVac for cost-effectiveness analysis, training national teams, collecting evidence, advocating for evidence-based decisions, planning effective introduction when supported by evidence and measuring impact. The initiative currently encompasses rotavirus, pneumococcal, HPV and influenza vaccines, with plans to extend to dengue and malaria vaccines. A vaccination programme costing and budget analysis tool is also being developed. The long-term vision of ProVac is to harmonise different tools to form a single decision-making package, and to allow comparisons with other health interventions.

ProVac has been awarded a grant (together with WHO, CDC, PATH, the Sabin Vaccine Institute and the SIVAC Initiative) to roll out to other regions as part of the ProVac International Working Group. This will begin with regional workshops (in EMRO, EURO and AFRO regions), pilot pneumococcal and rotavirus cost-effectiveness analyses as well as HPV costing studies using the WHO costing tool.

Discussion

QUIVER is appreciative of the ProVac Initiative that encourages a comprehensive decision-making approach which incorporates good evidence and economic modelling. It would be useful to compare results using TriVac with those from other models. The process of seeing different results can help decision makers, and prevent over-reliance on a single model. There are currently moves to compare results with dynamic models. Also, the pneumococcal component of the model was compared with other pneumococcal vaccination models in a WHO comparison exercise.

The ProVac process is useful in developing an approach to vaccine decision-making which incorporates evidence, good studies and economic modelling regardless of the tools deployed.
10. Measles investment case

Introduction (A. Dabbagh)

Progress has been made in reducing measles mortality and morbidity, with the goal of 90% mortality reduction achieved by 2008 by five out of six WHO regions. SAGE and the World Health Assembly have endorsed the goal of eradication, as well as of 95% mortality reduction in 2015 compared to 2000. However, measles resurgences have been seen in the last few years in some regions for various reasons such as funding shortfalls and weak country-level commitment. Hence WHO has identified the need for an investment case for eradication, that would consider the supporting evidence base but also look at the benefits, risks and costs of eradication compared to status quo. A request for proposals to put the case together was developed with input from the QUIVER subgroup on measles. The contract was awarded to Kimberley Thompson (Kid Risk Inc.) collaborating with Ann Levin (independent consultant).

Discussion

Overview of work plan (K. Thompson)

An overview of the main questions that need to be addressed in order to construct a case of measles eradication, as well as the plan for addressing them, was presented. The initial plan is to engage stakeholders in discussions about questions, evaluate prior measles models and develop an integrated dynamic economic model for measles, develop global rubella model components, integrate the two models, perform analyses and explore timing of eradication efforts as they relate to the measles eradication initiative.

Discussion

QUIVER members were encouraged by the investment in modelling eradication well before the measles end game had been reached. However, they emphasised the need to consider heterogeneity in vaccine uptake, which is a key driver during the eradication phase. This requires models that do not simply aggregate entire populations, as well as exploration of the behaviour of vaccine refusers and hard-to-reach groups within individual countries. There also needs to be an exploration of pragmatic factors such as political will and preparedness. The UK may present a good case study to explore many of these issues. Hence the present work may be a means of highlighting key research priorities for the next decade rather than an end in itself.
11. Dengue burden of disease

Introduction (J. Schmitz)

Dengue vaccine development has advanced to phase III clinical evaluation and a first dengue vaccine may become available in a few years. Reliable disease burden estimates are important to inform decision-making on vaccine introduction at the country level. There is a need for methodologies to better describe the dengue disease burden, including studies of disease incidence, health outcomes and cost of illness.

Presentation (O. Wichmann)

Studies to estimate dengue disease incidence at country level have recently been conducted by the Pediatric Dengue Vaccine Initiative (PDVI) in Thailand and Cambodia (Wichmann et al., 2011; Vong et al., 2011). These studies were based on multi-year, community- or school-based prospective cohort studies involving active fever surveillance and laboratory confirmation of dengue cases. By comparing disease incidence observed in the cohorts to cases reported by national surveillance systems for the respective province, age-group and year, multiplication factors were derived, which are thought to reflect the level of under-recognition by national surveillance. These regional multiplication factors were then applied to nationally reported cases to obtain more accurate estimates of hospitalized and non-hospitalized case numbers at country level.

The results of the studies suggest that reliance on reported case numbers from national surveillance systems can lead to considerable underestimation of dengue incidence. This is particularly true for outpatient dengue cases, which contribute significantly to the overall disease burden.

Discussion

Regional multiplication factors were used for national case estimates, rather than directly extrapolating the incidence observed in cohort studies to the country level. The underlying rationale is that multiplication factors reflect the level of under-recognition by the national surveillance system, which is expected to show less regional variation than disease incidence.

The variation of results obtained in different years implies that studies should be conducted for several years. The study period included an outbreak year with very high incidence in Cambodia. The pattern of higher and lower incidence years observed in Thailand during the study period seemed quite typical when compared to surveillance data from an available long-term time series. Co-circulation of dengue virus serotypes and predominance of particular strains was also seen in both countries.
The quality of the presented studies was commended. QUIVER believes that this type of study is needed, and that similar studies should be repeated in other countries. However, concerns were raised about the significant resource requirements for conducting these cohort studies. Further discussion is needed on methodological approaches adapted to resource-limited settings. For example, non-vaccinated control groups of dengue vaccine efficacy trials could be used as data sources for disease incidence and outcomes in different endemic countries, if available.
12. Broader economic impact of vaccination

Overview (A. Somanathan)

An ad hoc WHO consultation was held in Toronto, Canada on July 13-14, 2011 following the International Health Economics Association (iHEA) meeting, to discuss ways of capturing the full economic impact of vaccination beyond what is evaluated in traditional cost-effectiveness methods. Preliminary results from an ongoing systematic literature review and a survey of decision makers organised by the WHO were presented. A number of other academic groups also presented results of primary studies as well as secondary analyses. The meeting concluded with the presentation of a draft conceptual framework and dashboard of outcome measures that could be presented.

Discussion

Members of QUIVER felt that this was a useful approach, especially to enable policy makers to compare health care investments to those in other sectors. However, issues around the time horizon for effects, the use of rate of return vs. net present value methods of accounting, robustness of evidence and comparisons with other child health measures were important to consider. The development of guidelines would be helpful to avoid “advocacy economics”, as would further studies to ensure that the links between immunisation and outcomes are evidence-based.
13. Yellow fever disease burden

Overview (W. Perea-Caro)

WHO estimates that approximately 200,000 cases and 30,000 deaths occur annually due to yellow fever each year. Since cases are substantially under-reported, this figure is based on a static model by Lara Wolfson. The model uses data from a single serological study (Monath and Nasidi, 1993) based in Nigeria in the 1950s to 1970s. Based on these results, yellow fever vaccination was rolled out to the 12 highest risk countries. However, there are a further 21 endemic countries, and the case for vaccination in those countries needs to be examined.

Discussion

QUIVER members felt that it would be useful to divert a small part of the resources invested in vaccination to conducting serosurveys in the remaining endemic countries. These could be based on existing serum banks or surveys for other antibodies to save time and money. It may also be worth investing in a more sophisticated model, although the main limitation is data rather than model complexity. The establishment of a working group consisting of QUIVER members, independent modelling experts and YF disease experts was suggested to develop a work plan on YF burden estimation.
14. Monitoring the expanded EPI estimates of disease burden

Overview (T. Burton)

Since 1974 immunisation programmes at all levels have been informed by data on cases and deaths of vaccine-preventable diseases, number of children vaccinated, and cases and deaths prevented by vaccination. Models are used when burden and coverage data are missing or inaccurate, as well as to estimate the impact of vaccination since this cannot be measured using empirical data alone.

Measles burden model (E. Simons)

Estimates of measles mortality have been made annually since 1998, informed by three progressively more refined models (Stein 2003, Wolfson 2007, Ferrari 2011). The 2011 model addresses QUIVER’s recommendations to incorporate surveillance data, transmission dynamics and herd immunity, use objective definition for countries with reliable surveillance data, explore variation in the reporting fraction over time, account for background mortality and explore evidence of a secular trend in measles case fatality ratios. The advantage of the model is that it utilises surveillance data and is responsive to trends in data. Data inputs are mostly country-specific and have been reviewed by immunisation programme managers. Uncertainty intervals around estimates reflect variability in input data rather than ad hoc assumptions.

Estimating child causes of death (C. Mathers)

The Child Health Epidemiology Reference Group (CHERP) has been working with WHO to estimate causes of child death since the early 2000s. The work is funded by the Gates Foundation. Up to now, this has produced annual cross-sectional estimates, with the most recent estimate for 2008 published in the Lancet 2010 and World Health Statistics 2010. However, CHERG has recently expanded this work to a multi-year trend analysis.

One issue with the CHERG model is that mortality due to each cause needs to sum to a total mortality envelope (based on DHS data). Hence when temporal spikes occur in one cause of death, this causes estimates of mortality due to all other causes (except for measles and HIV) to be adjusted downwards to fit into the envelope.
The Institute for Health Metrics and Evaluation (IHME) is leading the Global Burden of Disease 2010 study (also funded by Gates Foundation) which is also estimating child mortality. The analysis will be completed by November 2011 and published in summary by early 2012. A WHO expert consultation will be held to advise on the use of GBD 2010 results by WHO. This will involve chairs or their nominees from major WHO expert groups. The results are not based on natural history models because it is difficult to get estimates of case fatality ratios from studies. Instead they rely on death registration data, verbal autopsy studies and other epidemiological studies.

**Discussion**

The effect of measles epidemics may not be well captured in the model. A temporal spike in measles mortality may cause an increase in mortality due to other causes, followed by a decline in the following year due to increased population-level immunity as well as the harvesting effect. However, these effects are not captured in WHO estimates. The all-cause mortality envelope is the constraining factor, since data on all-cause child mortality are more robust than for cause-specific mortality. However, DHS data are sparse and not suited to look at subnational estimates during an epidemic year. Measles incidence may vary geographically, so it may be necessary to map outbreaks against DHS clusters. It may be better to use a disease-specific model for the measles component.

QUIVER members suggested that all groups producing mortality estimates to work together, and noted that the Bill and Melinda Gates Foundation is funding such activities from both CHERG and IHME. So far the debates have occurred in the scientific literature rather than in face-to-face meetings.

WHO will conduct an expert consultation to decide on the use of Global Burden of Disease 2010 estimates within WHO. There are difficulties with using them since the input data are not always available. However, some regional WHO officers may want to use them. WHO was encouraged to work on a communication strategy to responding to the estimates when they are published. If these data are going to be used as a baseline for the Decade of Vaccines, there may be utility in having different estimates, and comparing the changes over the decade by each method.

QUIVER suggested that mortality estimates based on natural history models were preferable to a proportionate mortality approach, since the latter cannot account for deaths with multiple contributory causes.
Summary points and recommendations

- 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. However, natural history and surveillance-based methods are preferable to proportionate mortality methods for monitoring mortality in epidemic-prone diseases like measles.

- Burden of disease models should attempt to incorporate contributing causes of death

- QUIVER encourages all groups to make their data readily available to facilitate comparisons between models.
A. Hinman

QUIVER’s achievements since it began include the publication of a WHO guide on standardisation of economic evaluation of immunization programmes (Walker et al 2008), evaluation of several modelling efforts (such as the measles burden of disease model, measles eradication models and polio eradication models), collaboration with SAGE, CHERG and other advisory committees, comparison of cost-effectiveness tools for pneumococcal, rotavirus and human papillomavirus vaccination, as well as setting up working groups on child mortality estimation methods (with CHERG), pertussis, dengue, malaria and the measles end game.

In the future, it was proposed that QUIVER be expanded to advise IVR more broadly on implementation research (operational research on vaccine delivery, assessment of surveillance and monitoring). The proposed name for the new group would be the Immunization and Vaccine Implementation Research (IVIR) advisory committee. This would require an expanded committee with more frequent meetings.

QUIVER members highlighted the risk of dropping focus on quantitative issues following the expansion. Suggested solutions included forming a subcommittee with quantitative expertise, as well as having the quantitative and non-quantitative aspects of the committee meet at alternative times.
Annex A: Meeting Agenda

Chair: A. Hinman
Overall Meeting Rapporteur: M. Jit

TUESDAY, 4 OCTOBER 2011

08:30-09:00 – Registration
09:00-09:15 • Introduction and Charge to the Committee
  • Adoption of the agenda
  • WHO/UNICEF estimates for national immunization coverage (WUENIC) session
  Rapporteur: M. Gacic-Dobo
  9.15-10.15
  • Introduction (5’)
  • Update on WUENIC methods (15’)
  • QUIVER review (10’)
  • Discussion (30’)
  Rapporteur: M. Gacic-Dobo

10.15-10.45 Coffee break

Burden of pertussis disease model session
10.45-12.00
  • Introduction (5’)
  • Pertussis expert elicitation – methods and procedures (10’)
  • Pertussis BoD results (10’)
  • QUIVER review (10’)
  • Discussion (45’)
  Rapporteur: E. Simons

12.00-13.00 Lunch break

Vaccine Impact modeling session
13.00-15.00
  • Global Good Polio Model
  • Introduction (5’)
  • Model presentation (20’)
  • QUIVER review (35’)
    – QUIVER members
    – External reviewer
  • Discussion (60’)
  Rapporteur: R. Sutter/V. Moorthy

15.00-15.30 Coffee break

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<th>Time</th>
<th>Session Description</th>
<th>Speaker(s)</th>
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<td>15.30-17.30</td>
<td>• Introduction (5’)</td>
<td>V. Moorthy</td>
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<td>• Malaria vaccine modeling (20’)</td>
<td>P. Milligan</td>
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<td>• QUIVER review (30’)</td>
<td>M. Postma/ J. Koopman</td>
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<td>– QUIVER members</td>
<td>R. Steketee*</td>
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<td>– External reviewers</td>
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<td>• Discussion (35’)</td>
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<td>17.45</td>
<td>Adjourn / Cocktail</td>
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### WEDNESDAY, 5 OCTOBER 2011

**Impact and Cost-Effectiveness model session**

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<td>08.30-10.30</td>
<td>• Introduction (5’)</td>
<td>R. Hutubessy</td>
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<td>• PAHO TriVac model (20’)</td>
<td>A. Clark</td>
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<td>• QUIVER review (30’)</td>
<td>R. Laxminarayan* / E. Sinanovic*</td>
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<td>– QUIVER members</td>
<td>M. Brisson / N. Chaiyakunapruk</td>
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<td>10.30-11.00</td>
<td>Coffee break</td>
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<td>11.00-13.00</td>
<td>• Lives Saved Tool (LiST) (20’)</td>
<td>N. Walker</td>
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<td>• QUIVER review (30’)</td>
<td>J. Edmunds / F. De La Hoz Restrepo</td>
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<td>– QUIVER members</td>
<td>M. Brisson / N. Chaiyakunapruk</td>
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<td>13:00-14.00</td>
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**For discussion session**

**Rapporteur:** M. Jit

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<td>14.00-14.30</td>
<td>Generalized Cost-effectiveness Analysis of EPI and new vaccines (10’)</td>
<td>J. Lauer/M. Johri</td>
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<td>14.30-15.00</td>
<td>PAHO’s ProVac Initiative update and expansion to other WHO Regions (10’)</td>
<td>B. Jauregui</td>
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<td>15.00-15.30</td>
<td>Measles investment case: a description of approach and methodology</td>
<td>A. Dabbagh/K. Thompson*</td>
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<td>15.30-16.00</td>
<td>Coffee break</td>
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**For discussion session (cont’d...)**

**Rapporteur:** M. Jit

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<td>16.00-16.30</td>
<td>Studies and methods for estimating dengue BoD (10’)</td>
<td>O. Wichmann</td>
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<td>16.30-17.00</td>
<td>WHO Broader economic impact of vaccines study (10’)</td>
<td>A. Somanathan</td>
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<td>17.00-17.30</td>
<td>Yellow Fever Disease Burden: What can we do to move from Myth to Reality (10’)</td>
<td>W. Perea</td>
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**THURSDAY, 6 OCTOBER 2011**

For discussion session (cont’d…)

**CHERG/QUIVER session**

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<td>9.00 - 10.30</td>
<td>Introduction (5’)</td>
<td>T. Burton</td>
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<td>Example of measles (10’)</td>
<td>E. Simons</td>
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<td>WHO/IER role (10’)</td>
<td>C. Mathers</td>
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<td>Discussion</td>
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10.30 – 11.00 Coffee break

11.00 – 12.00 Summary and recommendations

12.00 – 13.00 Future directions QUIVER

13:00 Closure
Annex B: List of Participants

Advisory Committee Members

Dr Fulgentius Baryarama, Centres for Disease Control and Prevention (CDC)-Uganda, Uganda Virus Research Institute, (UVRI), P.O. Box 49, Entebbe, Uganda*

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The World Health Organization has provided technical support to its Member States in the field of vaccine-preventable diseases since 1975. The office carrying out this function at WHO headquarters is the Department of Immunization, Vaccines and Biologicals (IVB).

IVB's mission is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. The Department covers a range of activities including research and development, standard-setting, vaccine regulation and quality, vaccine supply and immunization financing, and immunization system strengthening.

These activities are carried out by three technical units: the Initiative for Vaccine Research; the Quality, Safety and Standards team; and the Expanded Programme on Immunization.

The Initiative for Vaccine Research guides, facilitates and provides a vision for worldwide vaccine and immunization technology research and development efforts. It focuses on current and emerging diseases of global public health importance, including pandemic influenza. Its main activities cover: i) research and development of key candidate vaccines; ii) implementation research to promote evidence-based decision-making on the early introduction of new vaccines; and iii) promotion of the development, evaluation and future availability of HIV, tuberculosis and malaria vaccines.

The Quality, Safety and Standards team focuses on supporting the use of vaccines, other biological products and immunization-related equipment that meet current international norms and standards of quality and safety. Activities cover: i) setting norms and standards and establishing reference preparation materials; ii) ensuring the use of quality vaccines and immunization equipment through prequalification activities and strengthening national regulatory authorities; and iii) monitoring, assessing and responding to immunization safety issues of global concern.

The Expanded Programme on Immunization focuses on maximizing access to high quality immunization services, accelerating disease control and linking to other health interventions that can be delivered during immunization contacts. Activities cover: i) immunization systems strengthening, including expansion of immunization services beyond the infant age group; ii) accelerated control of measles and maternal and neonatal tetanus; iii) introduction of new and underutilized vaccines; iv) vaccine supply and immunization financing; and v) disease surveillance and immunization coverage monitoring for tracking global progress.

The Director's Office directs the work of these units through oversight of immunization programme policy, planning, coordination and management. It also mobilizes resources and carries out communication, advocacy and media-related work.