

# **GAVI Alliance Value of Vaccines Meeting**

14-15 January 2013 Le Palace de Menthon, Menton-Saint-Bernard, France

## 1. Executive Summary

- 1.1 The GAVI Alliance convened 25 technical experts in health and development, economics, cognitive development, epidemiology, disease burden and economic modelling, and vaccines to:
  - 1. achieve consensus on ways to explore the broader developmental, social and economic impact of vaccines;
  - 2. identify existing studies, data sources or work to be leveraged to evaluate the broader impact of vaccines; and
  - 3. provide recommendations on the short, medium and long term work plan, including methodological issues to address.

(See Annex I: Agenda, Annex II: List of Participants)

- 1.2 The group agreed that GAVI's continued commitment to accelerating access to interventions to allow children to live to their greatest potential will be even more important going forward in the future. Improved understanding of the contribution of vaccines to child development and equity is critical to achieve the GAVI mission.
- 1.3 The group reviewed the existing evidence for the impact of vaccines on health outcomes, healthcare costs, productivity, and the broader economic and social effects. Although some evidence exists, gaps and methodological challenges remain as important limitations. Opportunities are frequently missed in planned research activities to evaluate the broader impacts of immunization in vaccine efficacy and effectiveness studies. A clear understanding of information needs for key stakeholders will assist in prioritization of research to fill identified evidence gaps.
- 1.4 Participants identified opportunistic and aspirational activities and prioritized these by short-, medium-, and long-term time frames for completion.



### Short-term activities included:

- Call for data sources and catalogue of existing and new studies to see opportunities for analyses and add-ons.
- Scope and conceptually develop an overarching model which can fit each piece of framework together (with preliminary VOI analysis).
- Develop a research agenda for impact evaluation alongside new vaccine introductions.

#### Medium-term activities included:

- Primary data collection on VSL, willingness to pay, and disease burden in low resource environments.
- Collaboration with the INDEPTH network to explore scope for new studies/study designs/analyses.

### Long-term activities included:

- Prospective data collection alongside new phase III and IV vaccine trials (e.g. pneumo, rota, malaria).
- Explore intermediate biomarkers to outcomes of disease and vaccination.
- 1.5 In addition to a prioritized set of activities, participants indicated an interest in maintaining a network to facilitate the linking of research opportunities.

## 2. Opening and purpose of the meeting

- 2.1 The meeting was opened by Seth Berkley, CEO of the GAVI Alliance. He began by welcoming all participants and providing an overview of the objectives of the meeting and the significance of the challenge at hand.
- 2.2 The desired outcomes were defined as follows:
  - Determine how best to obtain benefit-cost calculations for vaccination more broadly, but also by specific antigens/vaccine, and possible analysis by country;
  - Obtain a better understanding of the timing of the benefits;
  - Explore new methods to measure benefits realisation, which could include randomized controlled trials and other approaches;
  - Identify short-term, mid-term and long-term research priorities for the value of vaccines.
- 2.3 The findings from this Value of Vaccines meeting will inform a broader set of global activities including:
  - Commission on Investing In Health
  - Measurement of outcomes of health and development in the post-2015 time period
  - Child Survival Summit Goal of reducing preventable child deaths by 2030

# 3. Shaping the evidence base on the broader value of vaccination

- 3.1 David Bloom, Professor at Harvard University, provided an introduction for the need to measure the impact of health interventions. Health has traditionally been seen as an outcome of development and over the last decade there is an appreciation that more evidence is needed to demonstrate the links between health and economic development. Dr. Bloom provided an overview as to how health can lead to development:
  - Healthier workforce is a more productive workforce.
  - Health can affect income through education as children have better attention, longer attendance and improved cognitive function.
  - Effects on population health through demographic transitions (e.g. reduced fertility and increased female participation in the labour force).
- 3.2 Raymond Hutubessy, Health Economist at WHO, provided an overview of the WHO Value of Vaccines framework (Annex III), which outlines the current understanding of the different benefits accrued through immunisation and the evidence available to support the link. The framework has been used to drive consensus amongst academics on: 1) methods to quantify benefits, 2) research areas to prioritise and 3) findings to inform the development of tools used by decision makers. The framework will be applied to individual vaccines and more work will be required to further elucidate causal pathways and evaluate the strength of the evidence in coming months through expert solicitation.
- 3.3 Seth Berkley presented an overview of the history of vaccine development, emphasizing the new developments and the future pipeline. Most of the existing evidence on value of vaccines is for traditional EPI vaccines. With the accelerated development of a large number of other vaccines, there will be a large amount of new information that could be generated to contribute to the evidence base. Dr. Berkley indicated we should also aim to understand the benefits of a "fully immunized child" (Annex IV).

### Discussion

- We can learn a lot from other areas of health and other literature such as malaria (e.g. malaria 1968 Barlow paper).
- In addition to understanding the broader benefits of specific antigens, we should also improve the evidence base on the impacts by sequence and combination of vaccines as well as non-specific effect outcomes.
- Need to look at the benefits of vaccines in the context of other health interventions, other outcomes (e.g. linking of income growth to poverty, impact of dengue on tourism), and the distribution of benefits across different constituencies.



- Need to look at vaccine and health impacts within the context of timing of the outcome (e.g. economics/demographic dividends should be explicit about time horizons).
- Need to better understand the challenges with vaccine delivery as this is a critical part of the pathway in understanding and estimating potential benefits of vaccination in addition to the vaccine antigen-specific benefits.
- Randomized controlled trials (RCTs) provide an opportunity to measure the broader impacts of vaccination. It can take a long time to measure benefits prospectively but this can also be done retrospectively in places where adequate data collection is in place for these measures.
- Vaccine effectiveness data may be more useful in understanding the benefits of vaccination than efficacy data.

### The next steps identified were:

- Strong suggestion to obtain empirical data collection for studies. Important to strike a balance between theoretical modelling (which is needed) with practical experience and empirical data collection.
- Ensure that a "value of vaccine" agenda takes into consideration the evidence needs for the intended audience, which can include officials from the Ministry of Health, Ministry of Finance and donors.

### 4. Measuring the broader value of interventions

- 4.1 Hope Johnson, Head of Programme Outcomes & Impact at GAVI Alliance, provided an overview of examples from other sectors where broader impacts of interventions had to be measured and communicated, focussing primarily on examples from climate change and infrastructure development. The session further examined whether these methods could be applied to immunisation. Several similarities from these sectors and vaccine studies and lessons learned for vaccine research include:
  - Modelling methods for impacts are not immediate and may accrue over longer term, including modelling the entire biologic-outcome systems;
  - Acknowledging uncertainties in modelling and substitute with empirical data as possible;
  - Using threshold analysis rather than incremental analysis, for e.g. measuring cost to achieve a certain societal benefit;
  - Using databases with socio-economic information in addition to healthrelated data;
  - Consider using broader databases and proxy measures where data is unavailable or incomplete, which could then be connected back to vaccines.
- 4.2 Baudouin Standaert, Head of Health Economics at GlaxoSmithKline Biologicals, presented the value of vaccines from the vaccine industry-perspective. The presentation showed that the role of vaccines and

importance of health has shifted over time. Because of this shifting role, there is a need for new economic assessment methods to show impact especially for low- and middle- income countries. Analysis indicated that the focus in low income countries tends to be more about health in economy, whereas in high income countries, the focus is more on the economy of health.

### Discussion

- Participants highlighted communicating the results to the population at large is a challenge. In the absence of sufficient data it is important to build models, as it allows one to assess the depth and breadth of data needed (e.g. through sensitivity analysis). It can also help the research community to decide what critical areas are in need of more data. However, a model still requires good empirical data to improve statistical validity and assumptions.
- Participants also suggested that there were lessons that could be learned from the education sector including the linkage to human capital.
- Since development issues are multifaceted, the group was cautioned against employing arguments that state vaccines or education alone can lead to economic development, as developed societies have economic growth without vaccines, and institutions can play a large role in development.
- The group suggested that there needs to be a consensus on the type of output (lives, survival, economic growth, equity, etc.) we wish to demonstrate through these methodologies. This would allow a better understanding of the data and methods required.
- Given the importance of standard methods across priority setting areas, the economics of vaccines research methods should align with accepted or evolving health economics methods.
- Other considerations would also include strategies to optimise output, e.g. administering 3 vaccines at once or including other interventions.
- The time horizon over which the benefits are measured will also impact the value of the intervention.

# 5. Measuring the broader value of vaccines

- 5.1 Sachiko Ozawa, Assistant Scientist at Johns Hopkins University, highlighted the current gap in evidence and presented the results from the Decade of Vaccines Economics Project (DOVE). In light of limited primary data, Dr. Ozawa outlined the work of her team in using alternative methods for measuring benefits, such as the value of statistical life (VSL). The method derives estimates from individual judgments of trade-offs between financial rewards and increased mortality risk and thereby estimates the "value" of an intervention, independent of an analysis of costs averted through reduced mortality and morbidity. It has been used in other areas of health including TB, HPV, HIV/AIDS and is useful because it:
  - · captures value of a small decrease in mortality risk;
  - captures full consequences of premature mortality into one value; and



is in line with the Copenhagen Consensus
 (http://www.copenhagenconsensus.com/CCC%20Home%20Page.aspx)

#### Discussion

- VSL values vary across countries and there are no VSL studies based in Africa, highlighting a strong need.
- Herd protection beyond target age group needs to be factored into VSL calculations (as VSL values are individual rather than community valuations).
- An additional consideration is how to capture/determine opportunity cost of capital when using the VSL model.
- Extensive sensitivity analyses add more dimensions to the VSL study. It helps
  determine if the number is robust and identifies the important factors and
  directs future data collection.
- Even with the sensitivity analysis conducted, the availability of empirical data
  is a major limitation. Further work of the group includes analysis with life
  expectancies, but this makes it difficult to incorporate benefits. Dr. Ozawa et
  al are working to determine ways to link health models and economics models
  to address this.
- 5.2 Till Barnighausen, Associate Professor at University of KwaZulu-Natal, presented the impact of measles vaccines on educational attainment in South Africa in a setting with sub-optimal levels of coverage. They found a significant association of measles vaccine coverage with level of school grade attainment in sibling-pairs after controlling for intrinsic factors, including birth order, education levels of parents, household wealth. No sex-specific differences were detected. The results indicate that, for every six children vaccinated with measles "buys" one year school grade attainment.

### Discussion

- There was a suggestion to incrementally construct a cost benefit analysis, adding in a new benefit sequentially leading to a more expanded cost benefit analysis framework. Data limitations were highlighted as a challenge for this proposed analysis.
- There was a suggestion that this type of study could be replicated in other settings where similar information is available (e.g. DHSS sites).
- 5.3 Dean Jamison, Professor at University of Washington, presented on methods and preliminary findings of the financial protection provided to community through the use of low-cost interventions including immunisation. This research is a form of an extended cost-effectiveness analysis which evaluates the financial protection trade-offs provided by different health interventions. Early findings from a study in India indicate better financial protection with rotavirus vaccine compared with treatment alone, and greater projection in the poor vs. wealthy.



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#### Discussion

- The group agreed that financial protection is another important measure for understanding the broader impacts of vaccines.
- 5.4 David Bishai, Professor at Johns Hopkins University, presented methods and results of a study measuring the impact of measles vaccination on equity of health outcomes. This study found that the ratio of under-five mortality between the highest to lowest socioeconomic quintile was better in the vaccinated compared with the unvaccinated population, but findings may be limited due to selection bias from the increased likelihood that the healthiest families are more likely to accept measles vaccination.

### Discussion

- The group suggested that it would be useful to assess changes in under-five mortality rates by equity strata with measles vaccine use and this could be carried out using available DHS datasets.
- 5.5 Julia Driessen, Assistant Professor at University of Pittsburgh, presented methods and results of a study measuring the impact of maternal tetanus vaccination on child educational attainment using three sources of data in Bangladesh (immunization data from a cholera vaccine trial, DSS data for equity measures, and educational attainment data). This study found an average gain of 0.25 years of schooling for children from low socioeconomic backgrounds due to maternal tetanus vaccination and authors postulate that it is possible that greater educational attainment may be possible if compared to a control group of no vaccine rather than cholera vaccine as used in this analysis. The next steps for study are to collect earnings data to evaluate productivity gains.

### Discussion

The group highlighted the importance of publishing negative findings as these
improve our understanding of the causal pathways for broader impacts of
vaccination. It was highlighted that negative findings may be due to either lack
of power to detect differences (e.g. was there sufficient tetanus vaccination to
observe an impact) or due to true lack of association.

## 6. Identifying critical outcomes to measure the value of vaccines

6.1 In this session, the group identified key stakeholders and prioritized information needs by stakeholder. The results of this discussion were mapped and provided in Annex V. The results indicate that evidence on health effects and health care costs are a high priority across most stakeholders. In addition, the information on the impact to productivity and the broader economic measures is of less importance. This last finding may be due to the traditional lack of availability of these types of data to inform stakeholder decisions.



### 7. Opening of Day 2: Priority Setting

- 7.1 Seth Berkley opened the second day of the meeting reflecting on some of the key points from the previous day. He indicated that prioritization of the research questions and studies would be the primary focus of Day 2.
- 7.2 Prabhat Jha, Professor at University of Toronto, provided an overview of the Indian Million Deaths Study (MDS) as an example of how low cost solutions can be used to provide reasonable measures of health inequities to inform prioritization of low cost improvements to improve child health.
- 7.3 Karlee Silver, Program Officer at Grand Challenges Canada (GCC), provided an overview of their "Saving Brains" initiative. The program focuses on a biological perspective to further elucidate pathways from brain development, to school attainment and physical development. Dr. Silver noted that some evidence is available on the link between infections and cognitive development, but noted that few studies evaluate the entire causal pathway or the specific impact of vaccines as part of this process. The role of vaccines administered at the time of peak brain development, prevention of infection and the downstream impacts should be evaluated. The GCC is funding some research focused on improved understanding of the causal pathways in the first 1000 days of life including pseudo-longitudinal studies, randomized controlled trials and new economics grants. It was noted that vaccines could also be evaluated.

## 8. Identifying evidence gaps and methodological challenges

8.1 The participants divided into two breakout groups to review the existing evidence, and identify gaps and methodological challenges in measuring the broader impacts of vaccines. For ease of reference, the table below illustrates their findings by domain/area.

Domain/area	Comments	Gaps
		•
Health effects	Most of evidence available on value of vaccines is in this	<ul> <li>Need for empirical data on burden (morbidity and mortality) of vaccine-preventable diseases, particularly for older vaccines.</li> </ul>
	area	Data gaps on:  impact of vaccines on mortality;  indirect benefits and potentially synergistic effects of multiple vaccines;  impacts of vaccines on equitable health outcomes;  impact of older vaccines or reduction/withdrawal of vaccines;
		<ul> <li>vaccine impact on other diseases (e.g. occurrence of other respiratory diseases for PCV, antibiotic resistance, long-term impact on occurrence of NCDs.</li> </ul>
Healthcare costs	Reasonable amount of evidence on healthcare costs averted	Empirical data linking treatment costs averted to impact on household finances, to help improve modelled estimates.



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Domain/area	Comments	Gaps
Productivity gains	Few studies identified directly linking vaccination to productivity gains - important for death and long-term illness outcomes	<ul> <li>Links to productivity gains and vaccines could be measured through vaccine clinical trials.</li> <li>Gaps related to methodological challenges- how to value productivity through the informal economic sector.</li> </ul>
Broader economic benefits	Limited empirical evidence – important for VSL and willingness to pay models	<ul> <li>No explicit gaps mentioned, but noted limitations for VSL and willingness to pay models:</li> <li>Studies often require micro-studies of behaviours and decision-making at the household level.</li> <li>The limited evidence base is often not generalizable to other settings.</li> <li>VSL data is often limited from developing countries and particularly for child health.</li> <li>Willingness to pay studies are less frequently conducted for child health.</li> <li>The effect of vaccines on GDP is likely to be small and full income approaches are needed</li> </ul>
Social effects	Some evidence exists, but limited to measurement of level of educational attainment not cognitive improvements.	<ul> <li>Demographic dividend consequences (i.e. lower child mortality = lower fertility) which could be assessed using DSS data. Results likely to produce smaller effect sizes compared with previous years as current rates of child mortality are much lower.</li> <li>Additional equity consequences including status of women (e.g. discrimination, violence against women, access to education) are not included in the WHO framework.</li> <li>Social effects ideally should be evaluated in experimental studies but due to long time to event burden studies (e.g. case-control) are often used.</li> <li>Evaluation of improved equitable access to vaccines for women through additional outreach and health systems strengthening.</li> </ul>

8.2 In summary, the group indicated that there are often missed opportunities to measure these broader impacts of vaccines as they are often removed from studies during budget negotiations/reviews or are often added as after-thoughts/add-on studies. Long-term studies, preferably randomized trials, are needed as it takes many years to observe some of the vaccine-preventable outcomes. We should also conduct research on measurement of the broader impacts in both the vaccinated and those who benefit from population vaccination through herd effects.

## 9. Identifying potential opportunities and solutions

9.1 The participants divided into four breakout groups to generate ideas on opportunistic and "blue sky" or aspirational research ideas to be prioritized in the short-, mid-, and long-term time horizon to strengthen the evidence base for the broader impacts of vaccination.

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### 9.2 Opportunistic research included:

- A call for open-resource data sets that could be leveraged;
  - Catalogue current and past vaccine trials and linked follow-up studies to identify potential opportunities to measure the broader impacts of vaccination;
- Leverage previous Phase 3 trial community randomised trials or longterm cohort studies to:
  - Estimate direct and indirect effects of vaccination;
  - Retrospectively find survivors/descendants and obtain information on earnings and educational attainment/cognitive development;
  - Assess gender disparities in outcomes;
  - Could evaluate either routine vs. new vaccines or fully immunized vs. not fully immunized child for comparison.
- Studies conducted in DSS settings (e.g. INDEPTH) or as follow-up to trials should be prioritized. Potentially add on relevant research questions to studies currently underway.
- Evidence on effects of withdrawal and suspension of service interruptions should be evaluated (pentavalent suspension Sri Lanka, Ukraine, Western Europe measles, Pakistan, US).
- Compare existing evidence (e.g. RCT, cohort or DSS data) on vaccine impact across countries in "natural experiments" using: a) different vaccine sequencing for introduction of new vaccines; b) those with phased versus national roll-out of vaccines; and c) those with varying levels of immunization coverage.
- Literature review of effects of immunization on school participation (e.g. review in five states in India).
- Attempt to reassess existing VSL studies dividing the morbidity consequences into cost of illness, disaggregating long-term consequences and disutility of illness.

### 9.3 Aspirational research ideas included:

- Commission a new RCT or long-term prospective study building in active follow-up for assessments of broader impacts of vaccines including cognition and child development
  - Study sites:
    - DSS to allow for improved follow-up and measurement of broader impacts including equitable outcomes;
    - Nordic countries where there are complete registries;
    - Island countries with low degree of migration.
  - Research questions:
    - Should include process questions based on current developmental pathways;
    - Assess expressed value of vaccines for families and other key stakeholders including MOH through focus groups and conjoint analyses;

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- Measure impact of the fully immunized child, optimal dosing schedules and vaccine regimens/sequencing for new vaccine;
- Incremental impact of vaccines and other child health interventions (e.g. vaccines, treatment, vitamin supplementation);
- Use latest technology and biomarkers to standardize outcome assessments (e.g. brain scans for cognition outcomes).
- Impact of improved service delivery and increased immunization coverage
  - Costing and impact of universal coverage and benefits of the fully immunized child;
  - Use of sample surveys that feed into HMIS rather than one-off surveys.
- Use of regret theory to improve our understanding of public trust and negative perceptions of vaccines.
- Impact of evidence generation on decision-making (public, politicians, etc.,).

### 9.4 Additional recommendations:

- Measure the value of health using vaccines as the entry point.
- Use the accepted framework of broader impacts of vaccines and generate evidence to further elucidate pathways.
- Encourage vaccine manufacturers to conduct trials in settings amenable to active follow-up to measure broader impacts of vaccines.
- Use conjoint analyses to prioritize research for key stakeholders.
- Consider use of contingent willingness to pay methods to overcome methodological challenges of cost-benefit analyses (e.g. EPA in USA).
- Establish a Value of Vaccines Reference Group similar to the CHERGtype consortium to develop and assess methods and synthesize the evidence.

## 10. Prioritizing the evidence

- 10.1 The participants divided into two breakout groups to prioritize research ideas for the short-, medium-, and long-term time horizons to strengthen the evidence base for the broader impacts of vaccination.
- 10.2 Short-term activities included (bold indicates highest priorities):
  - Call for data sources and catalogue of existing and new studies to see opportunities for analyses and add-ons.
  - Scope and conceptually develop an overarching model which can fit each piece of framework together (with preliminary VOI analysis).
    - Make the WHO BEIVIP framework and relationships live and populate the model with existing data and new evidence to be added as it becomes available.
  - Develop a research agenda for impact evaluation alongside new vaccine introductions.

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- Understand what percentage of the birth cohort fully received EPI vaccines (step towards "fully immunised child").
- Supplement existing literature reviews with grey literature, quantitative synthesis.
- Start discussions with vaccine manufacturers on including add-ons and additional outcomes to their trials.
- 10.3 Medium-term activities included (bold indicates highest priorities):
  - Primary data collection on VSL, willingness to pay, and disease burden in low resource environments.
  - Collaboration with the INDEPTH network to explore scope for new studies/study designs/analyses.
  - Full quantitative modelling of overall BEIVIP framework (utilising both vaccine and non-vaccine pathways).
  - Conduct stakeholder surveys to better understand their information needs.
  - Additional analyses, add-ons and follow ups of existing studies (e.g. linking back to social benefits).
  - Write a book on The methods and evidence of the total, overall & diseasespecific effects of vaccines and economics of immunisation programmes (exposition of technically accurate methods to use).
- 10.4 Long-term activities included (bold indicates highest priorities):
  - Prospective data collection alongside new phase III and IV vaccine trials (e.g. pneumo, rota, malaria).
  - Explore intermediate biomarkers to outcomes of disease and vaccination.
  - Build evidence base with sufficient number of studies from different settings to make general statements (not just based on single study).
  - Studies on redesigning/optimising vaccine schedules.
  - Studies on impact of health systems strengthening.
  - Economics on alternative GAVI strategies (countries, antigens).

#### Discussion

- The research should generate additional understanding of methodologies and impacts of vaccines with a focus on issues relevant for the GAVI business plan including access to new vaccines, increased coverage, and factors considered for decision making.
- The GAVI focus should be on the impacts (in total and by antigen) of the fully immunized child including improved service delivery and protection afforded and broader impacts.
- Studies should be prioritised that: 1) include multiple outcomes of interest
  (e.g. social cognitive outcomes; school attendance, retention, educational
  attainment); 2) evaluate the broader and long-term impacts; and 3) address
  challenges in measuring expanded outcomes (e.g. changes in cognition,
  improvements in educational outcomes; family spill over effects and
  psychological effects associated with this).

 The importance of vaccine and delivery cost variation should be the focus of near-term discussions, including incremental cost-effectiveness of expanding coverage and addition of new vaccines for GAVI and countries.

### 11. Closing session

11.1 In the final session, each participant was given the opportunity to provide some final reflections and remarks. Participants commended GAVI for convening and creating the beginning of a community, where for the first time, it gathered a unique group comprised of epidemiologists, modellers, economists and people who understand the field.

#### General comments:

- There is still a role for cost-effectiveness in understanding the value of vaccines in addition to cost-savings and cost-benefits.
- Vaccines don't deliver themselves therefore we need to pay attention to the delivery system. Need to have improved costing of delivery, expanding coverage, the financial system and alternative structures for aid (e.g. across different levels of government and inter-government relations).
- Further elucidate the interaction between vaccines and early childhood development.
- Continue to measure mortality impact as this will also reduce morbidity but should also strengthen the evidence for prevention of morbidity, particularly long-term effects and child development.
- Focus of discussion for this meeting has been on vaccines but most of the causal pathways are through improved health leading to ambiguity in terms of attribution of vaccine benefits. Need to advocate for investment in health and the type of evidence needed to support this.
- Need to be very clear on target group(s) for the evidence, and gaps relevant to those stakeholders.
- Imperative to be mindful of the time-horizon of different key stakeholders and to measure benefits for similar time frames (e.g. average health minister is in position for 14 months therefore benefits should be estimated for a 1-2 year time horizon).

### Suggested areas for **follow-up** included:

- Interest in having a reoccurring half/full day symposium on Value of Vaccines annually possibly added on to existing relevant meetings (e.g. IHEA) rather than the occasional panel discussion within larger meetings.
- The existing WHO BEIVIP framework would be slightly refined with additional feedback through this meeting.
- Suggestion for GAVI to commission some research (4-5 studies) then
  reconvene the participants in a 12-18 months to review findings and
  attempt to publish a journal supplement on the Value of Vaccines. This
  could include tracking the children from prior PCV trials to assess their
  cognitive abilities and educational attainment. MenAfriVac trial is a
  good opportunity to do this type of research.



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- It was noted that GAVI is not a research organization but has an important role as a convenor in the field of vaccines and some limited research opportunities. This meeting would stimulate research and it was acknowledged that funding is a critical issue to be able to strengthen the evidence base on the broader impacts of vaccines. GAVI should be proactive and discuss the importance of prioritization of research on the value of vaccines. Donors and GAVI could contribute funds and partner with other organizations to support research in this area.
- A published meeting report would be distributed to help bring discussions to a wider audience and help identify key messages/outcomes.
- 11.1 Seth Berkley closed the Summit by thanking all participants for their contributions and summarized the importance of the ongoing work in this field and suggested the following next steps to be taken.

### **Next steps:**

- Commission some short-term activities and discuss the importance and potential opportunities for additional and longer-term activities in this field with other donor and partner agencies to move this research agenda forward as it will be even more critical in GAVI 4.0 (i.e. 2016-2020 business cycle).
- In an effort to communicate more widely, the group will draft a 600 word commentary for publication. This meeting report will also be made publicly available.
- Foster development of networks across researchers from a range of disciplines to generate new opportunities for collaboration to conduct critical research in this field. GAVI hopes to garner this momentum and seeks participant input into how to keep the community engaged going forward (e.g. create a virtual community for information sharing, annual meeting, CHERG-type group for Value of Vaccines, etc.)

### **Annexes**

- 1. Meeting Agenda
- 2. List of Participants
- 3. WHO Value of Vaccines framework
- 4. Representation of the Fully Immunized Child
- 5. Key stakeholders and prioritized information needs

### Annex 1. Meeting Agenda

VALUE OF VACCINES MEETING
Hosted by GAVI Alliance
14-15 January, 2013
Le Palace de Menthon
Menthon-Saint-Bernard, France

**Objectives:** The GAVI Alliance is convening a meeting of technical experts in health and development economics, cognitive development, epidemiology, disease burden and economic modelling, and vaccines to:

- 1. achieve consensus on ways to explore the broader developmental, social and economic impact of vaccines;
- 2. identify existing studies, data sources or work to be leveraged to evaluate the broader impact of vaccines; and
- 3. provide recommendations on the short, medium and long term work plan, including methodological issues to address.

**Strategic Questions:** There are five strategic questions participants will address to assist in achieving the meeting objectives.

- 1. Which types and amount of evidence are needed to <u>continue</u> investments in vaccines? To <u>increase</u> investments in vaccines?
- 2. Are there impacts of immunisation that we have yet to identify? If so, what are they and how can we best address them?
- 3. Are there examples from other sectors of work to measure the broader impacts of interventions (i.e. outcomes, methods, data sources)? Are these applicable to immunization?
- 4. Are there existing data sources that could be leveraged to evaluate the value of vaccines?
- 5. Are there advancements in statistical or research methods that can be employed to overcome previous challenges of measurement (e.g. attribution of outcomes to vaccines in a context of use of multiple health interventions)?



### **AGENDA**

DAY 1: REVIEWING THE EVIDENCE				
08:30 - 08:45	Opening remarks	Seth Berkley		
08:45 – 09:00	Introductions	Seth Berkley		
09:00 – 09:15	Review of strategic questions, meeting objectives and agenda  Background Documents:  • Meeting cover letter, meeting agenda	Seth Berkley		
	aping the evidence base on the broader value of va IR: Zulfiqar Bhutta	ccination		
09:15 – 09:35	Overview of the evidence needs and evolution of the generation of evidence on the broader impacts of immunization	David Bloom		
09:35 – 09:50	Framing the current evidence Objective: To outline the identified broader impacts of immunization and summarize the strengths and limitations of the current evidence base.  Background Documents:  • Deogaonkar R et al. Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries. BMC Public Health 2012, 12:878  • Ozawa S, et al. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: A systematic review. Vaccine (2012),http://dx.doi.org/10.1016/j.vaccine.2012.10.103  • Value of Vaccines evidence mapping (draft)	Raymond Hutubessy		
09:50 – 10:00	Vaccine Pipeline: Implications for future evidence needs Objective: To review the pipeline of vaccines and implications for types of evidence needed to support future investments in vaccines.	Seth Berkley		
10:00 – 10:30	Discussion Strategic questions:	Zulfiqar Bhutta		



	<ol> <li>Which types and amount of evidence are needed to <u>continue</u> investments in vaccines?         To <u>increase</u> investments in vaccines?     </li> <li>Are there impacts of immunisation that we have yet to identify? If so, what are they and how can we best address them?</li> </ol>			
10:30 – 11:00	Photo session and coffee break			
	asuring the broader value of interventions			
11:00 – 11:10	Learning from other sectors Objective: To illustrate the approach used to measure the broader impacts of non-health-related interventions.	Hope Johnson		
11:10 – 11:30	Learning from other stakeholders: Valuing vaccines in industry Objective: To illustrate the industry approach to value vaccines within a portfolio of vaccine and other health interventions.	Baudouin Standaert		
11:30 – 12:15	Discussion	Seth Berkley		
PM	Strategic questions:			
	3. Are there examples from other sectors of work to measure the broader impacts of interventions (i.e. outcomes, methods, data sources)? Are these applicable to immunization?			
	<ul><li>Other reflections on Strategic Questions 1- 3?</li></ul>			
	Background Documents:     Other Sector Examples summary document			
12:15 – 13:30	Lunch			
SESSION 3: Measuring the broader value of vaccines SESSION 3 CHAIR: David Bloom				
13:30 – 15:30	Case studies: Value of Vaccines Objective: To use case studies to demonstrate the range of methods and data sources used, and lessons learned in measuring the broader value of vaccines.			
13:30 – 13:50	Health and Productivity: DOVE	Sachi Ozawa		



13:50 – 14:10  2. Outcome-related productivity Gains: Measles in South Africa  14:10 – 14:30  3. Macroeconomics and Financial Protection: Can low cost interventions like rotavirus immunization provide protection against financial risk?  14:30 – 14:50  4. Equity: Measles vaccination and equity of health outcomes in Bangladesh Background Documents:  • Bishai D, Koenig M, Khan, AM (2003). Measles vaccination improves the equity of health outcomes: evidence from Bangladesh. Health Economics, 12(5):415-9. (please see supplemental reading list)  14:50 – 15:10  5. Social gains: Tetanus and school attainment in Bangladesh Background Documents:  • Canning D, Razzaque A, Driessen J, Walker D G, Streatfield P K, Yunus M (2011). The effect of maternal tetanus immunization on children's schooling attainment in Matlab, Bangladesh: follow-up of a randomized trial. Social Science & Medicine, 72: 1429-1436.  15:10 – 15:30  Discussion  What are the lessons learned and implications for future efforts to measure the broader impacts of vaccines?  15:30 – 16:00  Coffee break		<ul> <li>Ozawa S, Stack ML, Bishai DM, Mirelman A, Friberg IK, Niessen L, Walker DG, Levine OS. During the 'Decade of Vaccines' the lives of 6.4 million children valued at \$231 billion could be saved. Health Aff 2011, 30:1010–1020.</li> <li>Stack ML, Ozawa S, Bishai DM, Mirelman A, Tam Y, Niessen L, Walker DG, Levine OS. Estimated economic benefits during the 'Decade of Vaccines' include treatment</li> </ul>	
14:10 – 14:30  3. Macroeconomics and Financial Protection: Can low cost interventions like rotavirus immunization provide protection against financial risk?  14:30 – 14:50  4. Equity: Measles vaccination and equity of health outcomes in Bangladesh Background Documents:  • Bishai D, Koenig M, Khan, AM (2003).  Measles vaccination improves the equity of health outcomes: evidence from Bangladesh.  Health Economics, 12(5):415-9. (please see supplemental reading list)  14:50 – 15:10  5. Social gains: Tetanus and school attainment in Bangladesh Background Documents:  • Canning D, Razzaque A, Driessen J, Walker D G, Streatfield P K, Yunus M (2011). The effect of maternal tetanus immunization on children's schooling attainment in Matlab, Bangladesh: follow-up of a randomized trial. Social Science & Medicine, 72: 1429-1436.  15:10 – 15:30  Discussion  What are the lessons learned and implications for future efforts to measure the broader impacts of vaccines?	13:50 – 14:10	Aff 2011, 30:1021–1028.  2. Outcome-related productivity Gains: Measles in	
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What are the lessons learned and implications for future efforts to measure the broader impacts of vaccines?	14:50 – 15:10	Bangladesh Background Documents:  Canning D, Razzaque A, Driessen J, Walker D G, Streatfield P K, Yunus M (2011). The effect of maternal tetanus immunization on children's schooling attainment in Matlab, Bangladesh: follow-up of a randomized trial. Social Science &	Julia Driessen
15:30 – 16:00 Coffee break	15:10 – 15:30	Discussion  What are the lessons learned and implications for future efforts to measure the broader impacts	David Bloom
	15:30 – 16:00	Coffee break	

SESSION 4: Identifying critical outcomes to measure the value of vaccines SESSION 4 CHAIR: Anne Mills



16:00 – 16:15	Instructions for Break out groups	Anne Mills
16:15 – 16:45	Break out group Session 1: Identifying critical evidence Objective: To identify critical evidence needed to measure the value of vaccines in the future by domain and stakeholder.	Group Facilitators: Zulfiqar Bhutta (Health effects), David Evans (Health care costs), David Bloom (productivity), Dean Jamison (Economics), Sharmila Mhatre (Social effects)
16:45 – 17:15	Reconvene: Breakout groups present to the larger group Objective: To discuss the critical evidence by domain and stakeholder.	Chair/ Group Facilitators
17:15 – 17:30	Day 1 Summary	Seth Berkley
DAY 2: PRIORIT	Y SETTING	
09:00 – 09:15	Announcements and Overview of Day 2	Seth Berkley
SESSION 5: Ide SESSION 5 CHA	ntifying evidence gaps and methodologic challeng	es
09:15 – 09:45	Break out group Session 2: Review of the quality of the existing evidence, identification of evidence gaps and methodologic challenges Objective: To evaluate the quality of existing evidence, identify critical evidence gaps and methodological challenges in measuring the value of vaccines.  Background Documents:	Group Facilitators: John Edmunds Ramanan Laxminarayan
	Deogaonkar R et al. Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries. BMC Public Health 2012, 12:878	
	Ozawa S, et al. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: A systematic review. Vaccine (2012), <a href="http://dx.doi.org/10.1016/j.vaccine.201">http://dx.doi.org/10.1016/j.vaccine.201</a>	



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	<u>2.10.103</u>			
	<ul> <li>Value of Vaccines research mapping (draft)</li> </ul>			
09:45 – 10:15	Reconvene: Breakout groups present to the larger group Objective: To discuss the quality, gaps and methodologic limitations of the current evidence	Chair/ Group Facilitators		
10:15 – 10:45	Coffee Break			
10:45 – 11:15	Breakout group Session 3: Identifying the potential opportunities and solutions Objective: To generate ideas for: 1) opportunistic use of existing data or field sites that could be leveraged to measure critical outcomes where there are currently gaps or key limitations; and 2) blue sky options for designing the <i>ideal</i> research study to evaluate the value of vaccines.	Group Facilitators: David Bishai Bruce Lee Sharmila Mhatre Lisa Prosser		
11:15 – 12:00	Reconvene: Breakout groups present to the larger group Objective: To discuss the potential opportunities and solutions. Strategic questions:	Moderator/ Group Facilitators		
	4. Are there existing data sources that could be leveraged to evaluate the value of vaccines?			
	5. Are there advancements in statistical or research methods that can be employed to overcome previous challenges of measurement (e.g. attribution of outcomes to vaccines in a context of use of multiple health interventions)?			
12:00 – 13:00	Lunch			
SESSION 6: Prioritizing the evidence SESSION 6 CHAIR: Dean Jamison				
13:00 – 13:45	Break out group Session 4: Priority setting Objective: To establish short-, mid-, and long-term priorities.	Group Facilitators: Mark Jit, Dagna Constenla		
13:45 – 14:30	Reconvene: Breakout groups present to the larger group Objective: To discuss the priority research activities	Chair/ Group Facilitators		



	by timeframe.	
14:30 – 15:00	Coffee Break	
15:00 – 15:45	Finalizing short-, mid-, and long-term research priorities for measuring the value of vaccines Objective: To establish research priorities for measuring the value of vaccines by timeframe.	Dean Jamison
15:45 – 16:00	Day 2 Summary	Seth Berkley
16:00-16:30	Closing Remarks	Seth Berkley

### Annex 2. List of Participants

### 1. Professor (Mr) Dean T Jamison

Adjunct Professor University of Washington

### 2. Dr (Mr) Raymond Hutubessy

Health Economist Initiative for Vaccine Research (IVR) Implementation Research (IMR) WHO

### 3. Professor (Ms) Anne Mills

Vice Director & Professor of Health Economics and Policy London School of Hygiene and Tropical Medicine (LSHTM)

### 4. Dr (Mr) David Evans (regrets)

Director Health Financing and Social Protection WHO

### 5. Professor (Mr) Prabhat Jha

Canada Research Chair in Health and Development University of Toronto

### 6. Dr (Ms) Karlee Silver

Program Officer Grand Challenges Canada

### 7. Professor (Mr) David M. Bishai

Director Interdepartmental Health Economics Program Johns Hopkins University

### 8. Professor (Mr) John Edmunds

Head of IDE

London School of Hygiene and Tropical Medicine (LSHTM)

### 9. Professor (Mr) Bruce Lee

Associate Professor of Medicine, Epidemiology, and Biomedical Informatics Director, Public Health Computational and Operations Research (PHICOR) Group University of Pittsburgh

### 10. Ms Julia Driessen

Assistant Professor University of Pittsburgh

### 11. Professor (Mr) Ramanan Laxminarayan

Vice President, Research and Policy PHFI India

### 12. Dr (Mr) Mark Jit

Mathematical modeller/health economist HPA

### 13. Professor (Ms) Lisa Prosser

Associate Professor

### **GAVI Alliance Value of Vaccines Meeting**

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Department of Paediatrics' and Communicable Diseases /Associate Professor (secondary),

Department of Health Management and Policy - University of Michigan

### 14. Dr (Ms) Dagna Constenla

Associate Scientist, Director, Economics and Finance, IVAC Johns Hopkins University

#### 15. Ms Farah Naz Hashmani

Child Health Consultant
Sada Welfare Foundation at National Institute of Child Health

### 16. Dr (Ms)Ulla Griffiths

Lecturer in Health Economics LSHTM

### 17. Dr (Ms) Sachiko Ozawa

Assistant Scientist Johns Hopkins University

### 18. Professor (Mr) Till Bärnighausen

Associate Professor at Africa Centre for Health and Population Studies University of KwaZulu-Natal, South Africa

### 19. Professor (Mr) David Bloom

Professor of Economics and Demography Harvard University

### 20. Dr (Mr) Anders Nordstrom

Ambassador for Global Health Swedish Ministry for Foreign Affairs

### 21. Dr (Mr) Zulfigar Bhutta

Head Division of Maternal and Child Health Aga Khan University

### 22. Dr (Ms) Sharmila Mhatre

Program Leader IDRC 3

### 23. Professor (Ms) Maureen Black

Co-Principal Investigator University of Maryland

### 24. Dr (Mr) Baudouin Standaert

Head of Health Economics GlaxSmithKline Biologicals

#### 25. Dr (Ms) Christine Stabell Benn

Medical doctor Bandim Health Project at Statens Serum Institut

### **GAVI Secretariat:**

Seth Berkley, CEO Helen Evans, Deputy CEO



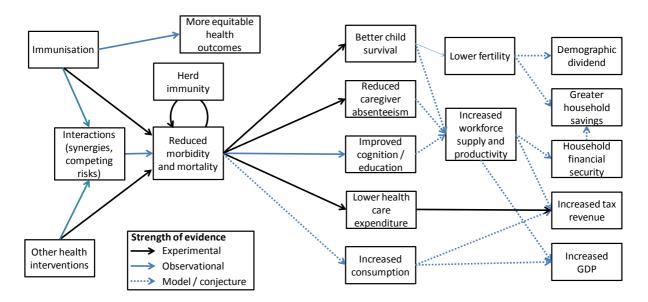
Geoff Adlide, Director, Advocacy & Public Policy Peter Hansen, Director, Monitoring & Evaluation Lori Sloate, Deputy Director, Advocacy & Public Policy Hope Johnson, Head Programme Outcomes & Impact



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Annex 3. WHO Value of Vaccines Framework



Annex 4. Representation of the Fully Immunized Child





# Annex 5. Key stakeholders and prioritized information needs.

	Domain				
Stakeholder	Health effects	Healthcare costs	Productivity	Broader Economics	Social effects
МОН	Н	M	L	L	L
MOF	M	Н	Н	Н	M
MOED	L	L	L	L	Н
MOP/Planning Commission	L	н	н	н	Н
Local health authorities	Н	М	L	L	L
Vaccine Industry	Н	Н	Н	Н	Н
Donors	Н	Н	M	M	Н
WHO	Н	L	L	L	M
UNICEF	Н	Н	L	L	M
World Bank	M	Н	Н	Н	M
Parliamentarians	Н	L	L	L	Н
NITAGs	Н	M	L	L	L
Health NGO	Н	М	M	L	M
Health Service Providers	Н	Н	L	Ĺ	L
Employers	М	Н	Н	L	L
Families	Н	Н	Н	Ĺ	Н
Media	Н	L	L	L	M