SCIENTIFIC ADVISORY BOARD REPORT

Thursday 29th June 2017 | Gavi offices, 2 Chemin des Mines. 1202 Geneva

Attendees:

Scientific Advisory Board panel: Martin Friede (WHO), Patrick Gerland (UN Population Division, Demographic Analysis Branch), Ulla Griffiths (UNICEF), Gagandeep Kang (Christian Medical College, Vellore, India)

Apologies: Kate O'Brien (Johns Hopkins University), Bryan Grenfell (Princeton University)

Vaccine Impact Modelling Consortium members: Tini Garske (Consortium Coordinator, Imperial College), Neil Ferguson (Imperial College), Tim Hallett (Imperial College), Nick Grassly (Imperial College), Azra Ghani (Imperial College), Mark Jit (London School of Hygiene and Tropical Medicine), Olivia Bullock (Gavi), Kim Woodruff (Imperial College), Evgenia Markvardt (Imperial College)

Apologies: Lesong Conteh (Imperial College), David Aanensen (Imperial College), Tove Ryman (Bill & Melinda Gates Foundation)

Additional attendees: Kendall Krause (Bill & Melinda Gates Foundation), Wilson Mok (Gavi), Lara Dearing (Gavi)

Key messages from this report:

- **Quality and reliability of input data** is a critical issue that will directly impact the success and credibility of Consortium generated estimates. Hence, emphasis should be placed on ensuring that the Consortium modellers have access to the best available data sources, whenever possible.
- The Consortium can aid the modellers to gain access to data sets through better **coordination with IHME, various WHO initiatives, and country stakeholders**, as well as provide underlying high-level data sets for input data, where available.
- The Consortium **scope is to remain purely scientific**, while aiming to strategically align with the WHO and other organisations.
- The Consortium **scope is to remain focused** throughout all activities.
- The Consortium **to consider existing guidelines** in the field of health estimates for quality setting, such as the GATHER guidelines.
- **Disease-specific standards** should be considered when developing model quality standards through a process of consultation with disease experts.
- When **engaging with focus countries**, the Consortium should approach countries **through the WHO regional/country offices** to ensure that relationships are built with the appropriate local stakeholders from the start and to secure buy-in.

Meeting objectives:

- Present the Consortium objectives and the proposed activities to the Scientific Advisory Board members;
- Nominate the Scientific Advisory Board Chair;
- Solicit the Board members input on Consortium model quality standards and model review processes;
- Solicit the Board members input on Consortium country engagement strategy and health economics integration into modelling work;
- Solicit the Board members input on other topics pertaining to the Consortium operations.

Session 1- 3: Introduction of the Consortium

Gavi, the Vaccine Alliance

Initially the World Health Organization (WHO) was providing modelled vaccine impact estimates to Gavi. However, as Gavi grew, the types and complexity of their questions changed. As a result, the modelling work was contracted out to different institutions covering a range of relevant diseases and antigens.

With time, Gavi's questions became more strategy and policy-oriented, with a need to better account for uncertainty. Hence, Gavi and the Gates Foundation (the Foundation relies on the same impact data, and the two organisations will be aligning their future targets going forward) decided to outsource the coordination of the modelling work to an external scientifically-led consortium. The RFP (request for proposal) was announced in the summer 2016 and Imperial College London was selected to lead the Consortium for a five-year-long term starting at the end of 2016 / early 2017.

With the establishment of the Consortium, Gavi hopes for 1) better coordination of the modelling work and standardisation of the associated processes; 2) increased scientific rigour and robustness of the estimates, and 3) stronger collaborations across the modelling community with possible positive externalities.

The impact data generated by the Consortium modellers is used at Gavi 1) for performance reporting, tracking progress and assessing impact, 2) for advocacy purposes and demonstrating the value of vaccines to various stakeholders, and 3) for informing strategic and policy decisions, for instance, currently undergoing planning for Gavi 2020-2025 with a focus on sustainability.

Imperial College London

The Consortium will respond to the Gavi and Gates Foundation need to estimate the vaccine impact more accurately striving for the highest level of scientific rigour. The existing model portfolio was absorbed into the Consortium in the first year (10 diseases and ~97 countries). The Consortium will focus on consistency, efficiency, and quality of the estimates over the course of its five-year-term.

The Consortium secretariat consists of the Management Group, and administrative, scientific, and technical teams based at Imperial College London. Multiple modelling groups are sub-contracted and based at various other institutions in the US and the UK. The Consortium will aim to include at least two models per disease for comparison purposes. The secretariat has its own research agenda focusing on methodological developments of the models, and pooling and aggregation of the results across models and diseases.

The Bill & Melinda Gates Foundation

The Gates Foundation aims to ensure that the results of all funded work are accessible widely, such that they are of service in particular to its technical partners and individual countries, in addition to our specific results being used for the Foundation's planning and tracking purposes.

The Vaccine Delivery team at the Foundation has a specific goal: "By 2020, prevent 11 million deaths, 3.8 million disabilities, and 230 million illnesses through high, equitable, sustainable vaccine coverage and supporting polio eradication." To this end, 2011-15 target was to avert 4.2 million deaths, and the actual current estimate is higher, at 4.9 million deaths, based on the WUENIC (WHO/UNICEF Estimates of National Immunization Coverage) estimates. Projecting into the future, if all the variables remain stable, the global community is likely to surpass the goal of 11 million deaths averted by 2020.

From the Foundation's perspective, the ability to better understand uncertainty is key, to make trade-off decisions and prioritise where more data is needed. Moreover, understanding the sub-national estimates is becoming increasingly important for driving policy-decisions and ensuring equity within countries.

Discussion:

Data quality and data sources

Currently Gavi relies on the modellers to advise on the best available data sources for each disease. Data sources that are currently available to the modellers do not always represent the most accurate picture, and conflicting data is often an issue. In such situations, Gavi relies on 'triangulating' of data, a process where several data sources are consulted and compared, and a weighted average is used. In general, demography and mortality, which are important inputs for all the Consortium's models, are heavily modelled in many Gavi countries based on samples of data obtained from such sources as the Demographic and Health Surveys (DHS) and the Multiple Indicator Cluster Surveys (MICS).

The Consortium modellers aim to be transparent about the limitations of the data used and to highlight important gaps in the existing data, which, if filled, could substantially decrease the uncertainty in the current impact estimates. There is potential to collaborate with the Gates Foundation and the Wellcome Trust to fund additional data collection activities or to gain access to existing data sources that are not currently available to the Consortium members.

There are other organisations (for example, Institute for Health Metrics and Evaluations (IHME)) and several initiatives within WHO (for example, WHO/UNICEF joint reporting process for collection of data on country-level and sub-national data) that have access to data sets that would be useful to the Consortium modellers.

Gavi holds country-specific estimates, which are used primarily for advocacy purposes as these are not necessarily endorsed by the countries. Hence, the Consortium will aim to gain access to better data at least for the four focus countries (Pakistan, India, Nigeria, and Ethiopia) as these represent significant investments for both funders. It is suggested to consider data from beyond the government sources. However, it is not always easy to gain access to data as countries themselves might require limited sharing of the data provided to certain groups. Moreover, general coordination is needed as countries are often approached multiple times for the same, or similar, data. One of the aims of the Consortium is to be coordinated with such initiatives within WHO, the Gates Foundation, etc.

It is essential to ensure that the Consortium members are using best available data.

Scope of the Consortium

The Consortium should aim to strategically present itself as a scientific initiative, even if it was established in response to an internal need at Gavi and the Gates Foundation. In this case, the work produced by the Consortium modellers is likely to meet less resistance and to be viewed in apolitical light. However, it is undeniable that the Consortium generated estimates could influence decision making also outside of Gavi/Gates, potentially on questions relating to vaccine coverage, but also vaccine procurement. The Consortium will strive to become a reference point for vaccine impact *estimates* and disease impact *estimates.* There is no ambition to provide final figures to stakeholders outside of the Consortium, but rather serve as an alternative source that could become the *de facto* source, if proven reliable.

A specific area, where the Consortium could add value would be demonstrating the value of improving the routine immunisation programmes in countries versus investing in one-off SIAs. SIAs' planning is rapid and the results are clear and become evident sooner. Instead, adjusting routine immunisation (RI) coverage rates is often perceived as more daunting to plan and challenging to achieve. However, ultimately improving the RI rates could have wider positive impact on the overall health system in the long-term and, hence, prove to be more cost-effective as oppose to administering large-scale SIAs for multiple years in a row.

Session 4: Consortium Challenges and Opportunities

Challenges

The Consortium is a large complex project involving coordination between multiple groups. The scale of our activities will expand and appropriate structures will need to be put in place to ensure success and efficiency. The funding stream is split between two organisations, Gavi and the Gates Foundation, which poses administrative challenges.

The modelling portfolio was inherited from Gavi, and the Consortium needs to develop standards for assessing model quality, while at the same time balancing the funders' desire for consistency and continuity. Moreover, a new transparent process needs to be established for engaging new modellers. Finding new models that capture the endemic burden of disease in a specific way that suits the funders' needs can be difficult.

Another question to address is to what extent are the Consortium generated estimates applicable and reliable on sub-national level. In terms of underlying input data, the biggest difficulty lies in assessing the burden of disease correctly. Furthermore, the vaccines have a long-lasting impact, hence, the demography needs to be projected far into the future which introduces more uncertainty. In general, input data are quite scarce.

Opportunities

Scientific management of the Consortium will likely lead to overall model quality improvements, and technical working groups will capture input from all the participating modelling groups on technical topics of relevance. The Consortium can act as a liaison helping the funders to translate science results into strategic decisions as the credibility and reliability of the estimates improves.

The Consortium will bring together the modellers creating a community, where questions of relevance across the various diseases can be discussed leading to cross-fertilisation of ideas and sharing of data, as appropriate. The scope of the application and usefulness of the estimates will likely continue to expand, and the Consortium's aim is to set-up the structures to support adding further diseases and analyses.

The scientific coordination of the work will add a stronger voice to the modellers as a unified group, for instance, when highlighting the existing data gaps and possibly advocating for data collection in specific antigen areas.

Discussion:

Input data sources

Careful coordination with WHO (EPI and IVIR-AC) will be important to make sure that the data used by the Consortium modellers is defendable in terms of quality standards. However, the Consortium would need to consider other sources of data as well, hence relying on a process of data triangulation to critically evaluate all sources. In addition, CHERG (Child Health Epidemiology Reference Group), now called MCEE (Maternal Child Epidemiology Estimation), might already have data useful to the Consortium and can be approached to request it. Additional level of complexity is added by the fact that for most countries, there is no solid demographic data prior to 1980s. However, earlier period of demographic data is not as problematic for the estimates generation.

Currently, the Consortium modellers use primarily UNWPP data for demography, and WUENIC data for past vaccine coverage, and Gavi's demand forecast for future coverage. Overall, it would be easier for the SAB members to comment on the existing input data source gaps, if the Consortium secretariat presented a list of existing data sources to the SAB members.

Uncertainty analysis

The Consortium is considering working towards producing model ensembles averaging the estimates across models. However, that approach might be too crude. Probabilistic analysis is considered a standard, and providing a range is helpful as it offers a more realistic picture. In the end, two models might be too few to generate model ensembles.

Often model comparison process is viewed as a painful exercise aiming to reconcile the differences between the models, however, it is highly useful and all Consortium models plan to undergo this process. Moreover, it would be highly relevant to emphasize the inputs that drive the uncertainties and the differences between the models, when presenting the estimates to those generating the data to improve their understanding of the modelled estimates.

Continuity and quality

Ultimately as the data improves, the deaths averted figures might change. Similarly, if the model specifications/methodology are changed, the estimates would also shift. The Consortium is developing a software, Montagu, that will implement strict version control and capture the history of impact changes in such cases. With this in place we will follow GATHER (Guidelines for Accurate and Transparent Health Estimates Reporting) guidance on best practices on publishing and analysing health estimates is already available.

It is important to consider the audience to whom the estimates are presented and who uses them. Oftentimes the audience might not be technically versed, and a change (in the methodology or input data) reflected on the estimates might cause misunderstandings. Hence, the ability to trace the changes, and adjust how the data are presented could be helpful (i.e. transparency on what input data is used from country to country, what changed from version to version, while preserving the metadata). Montagu will have functionality enabling this.

The Consortium time span is five years, however, the aim is to set-up the infrastructure (Montagu software to host the models and the data), so that the models could be re-run more efficiently and record any changes that were made transparently. Ultimately, we aim to make the estimates available to more stakeholders beyond Gavi and the Gates Foundation as widely as possible, but will need to bear in mind commercial and communication sensitivities. The access arrangements are yet to be defined in consultation with the funders.

Session 5: Model standards and model review process

Quality standards

With the aim to improve consistency and the reliability of the estimates, the secretariat is considering several minimum standards to evaluate the models. Models should generate the required outputs that respond to the needs of the funders (deaths, cases, DALYs by age over time). Models should have sufficient documentation to allow their replicability, should be fitted to data and capture uncertainty. In addition, as models improve the secretariat would ask them to capture herd immunity effects, where applicable, consider sub-national stratification and disease-specific criteria.

Review process

The secretariat would need to engage in the review process in two scenarios: 1) when additional models are needed in specific antigen areas (with the goal of employing two models per disease) and 2) to ensure the model quality improvement through routine annual

light-touch reviews. The review committees will be comprised of internal Consortium members and external reviewers, where needed. Written feedback will be provided to the groups at the end of each process. While Gavi and the Gates Foundation have their own agenda for the use of the estimates, the Consortium reviews will be driven primarily by its scientific aims considering the output specifications required by the funders.

Discussion:

The secretariat wants to build close relationships with the participating modelling groups, but is cognisant that the amount of funding the Consortium can offer for the modelling work is limited. Therefore, it is important to find the right balance, when requesting groups to undergo the review process.

It is undeniable that some disease-specific standards need to be considered when developing the model quality check-list. This should be done by engaging epidemiologists/disease experts to help set appropriate standards, and possibly involve the disease experts in the model review process as well. The SAB members could suggest disease-specific experts to consult.

It would be unreasonable to expect new model development as part of the Consortium as the funding is limited. When opening a call for new models, it would be more realistic to consider models that would require little adaptation to the types of outputs the Consortium is required to produce. Gavi can advise the Consortium in terms of which modelling results have biggest influence on strategic decisions to help with prioritisation during the model improvement process.

Some modelling groups have established relationships to some country stakeholders and other organisations to gain access to data relevant for their specific disease area and model. Some considerations for open data sharing within the Consortium need to be made to ensure that the groups are coordinated in terms of the existing data sets and the data gaps that need to be addressed.

Session 6: Health Economics

The Consortium will cover 10 diseases, model three outputs (cases, deaths and DALYs) and three scenarios (no vaccination, vaccination without Gavi support, vaccination with Gavi support). Up to now, the DoVE group and Harvard University have performed various economic analyses of these outputs. With the Consortium in place, how can the Consorium best interact with these groups and others to achieve health economics outcomes of greatest impact?

Potential directions include country cost-effectiveness studies, budget impact/affordability, exploring vaccine expansion paths, broader economic benefits, and collaborating with other groups.

Discussion:

DALY disability weights are currently published by IHME, not WHO. This is now based on surveys in many countries, but there are a limited number of categories of infectious diseases with

disability weight information. Also, inputs for DALY calculations such as duration of disability used by the modellers do not always correspond to calculations for costs used by DoVE. The Consortium could help coordinate a wider discussion around the use of DALYs by the Consortium.

The Consortium should focus on exactly what economic analyses are most useful for countries and other stakeholders, and be pro-active in ensuring these analyses are carried out. Budget impact analyses (with or without costs averted by the intervention, depending on the situation) may be the most useful. Analysing treatment costs could be strengthened by in-country work, tying in with work that DoVE has been doing.

Extensive comparison of optimising a basket of interventions including vaccination may be beyond the scope of the Consortium. At the same time, we should avoid working in a 'vaccine silo' and remember that countries have health budgets not vaccine budgets. The Consortium should prioritise giving policy-makers the tools they need to make decisions.

Economies of scale (e.g. due to combined vaccines) are not generally taken into account at present.

Session 7: Country Engagement Strategy

The goal of the country engagement work is two-fold: to improve the quality of the Consortium vaccine impact estimates by gaining access to (sub-national level) data, and also offering the modelling as a tool to answer questions that are most relevant to the four countries (PINE: Pakistan, India, Nigeria, and Ethiopia). The funders proposed the specific countries as these represent major investments and dominate the global disease burden across all Consortium portfolio diseases. Improving the data quality for PINE would have a substantial impact on the overall estimates.

The method of engagement with countries requires thorough thinking before approaching the countries. The countries should be the driving force in the process by setting the questions that the modellers would address. By demonstrating this to the countries, they are likely to provide data that might not be otherwise accessible to the groups. The country work should also be aligned with Gavi and Gates Foundation in terms of the timing of their strategic decision making, when the modelled scenarios would be most useful.

As one of the first steps, the Consortium will perform a landscaping analysis to better understand the individual country context and to gather information on the data that is already available to the modellers. The identified gaps in data will guide the follow-up activities. The modellers from the antigen areas relevant to each of the countries would be engaged early in the process.

Discussion:

When interacting with PINE countries, it is strongly advised to approach the WHO regional and country offices first, which then can connect the Consortium with the appropriate contacts at the local Ministry of Health and NITAGs (National Immunization Technical Advisory Groups) or other relevant sub-committees. The most appropriate contacts at the WHO would be the EPI

(The Extended Programme on Immunization) managers. Other organisations working with the PINE countries are PATH and CHAI.

Coordination with IVIR-AC (Immunization and Vaccine Implementation Research Advisory Committee at the WHO) is also strongly suggested when interacting with the PINE countries. However, IVIR-AC's audience as well as the depth of model evaluation is different from the Consortium's. The Consortium outputs will be used primarily only by Gavi and the Gates Foundation, whereas IVIR-AC provides the official figures to be used by the WHO.

Furthermore, the Consortium needs to closely engage with local stakeholders to ensure buy-in to possibly gain access to better data and achieve fruitful results.

The country engagement work would place pressure on the modelling groups in terms of time commitment, so it is worth evaluating the Consortium capacity. It is strongly advised to control the scope of the Consortium country engagement work as rather narrow and avoid getting involved cold chain and supply chain areas, but rather to focus on sub-national variation in vaccine coverage and disease burden.

Final remarks and discussion

In addition to the discussions relating to each session, the Scientific Advisory Board recommends:

- **To plan the country engagement work thoroughly**. The Consortium should consider a local counterpart that could potentially assist with data collection/coordination. This would possibly require a small dedicated budget. Ethiopia is recommended as the first country. The Consortium should be making a *request* to the countries in a form of an introductory letter disseminated via the WHO regional offices. The modellers could then 'tag on' to a meeting organised by WHO/Gavi/Gates in each country to make the first introduction/connection.
- **To align input data with other organisations and initiatives** (i.e. WHO, CHERG/MCEE, MCC, IHME, etc.).
- **To stay focused** on the Consortium scope.
- **To recruit additional models** in the antigen areas where less than two models are available (i.e. yellow fever and rubella)
- To develop a more detailed **model review timeline.**

Ulla Griffiths was elected as the Chair for the first year of Consortium operations.

The Scientific Advisory Board (SAB) meetings are set to occur once a year during the Consortium annual meetings in February/March. The SAB members will continue to informally advise the secretariat throughout the year, as needed.