2020 WHO Product Development for Vaccines Advisory Committee (PDVAC)
Virtual Consultation 2: Update from the Burden of Enteric Diseases working group
11 May 2020
CHAIR: David Kaslow

Context

Investment in vaccine product development and policy decisions for introduction are informed by the impact that the vaccine is expected to have on disease burden. However, there is often a lack of epidemiological data to inform vaccine impact assessments and cost-effectiveness studies, and decisions are based on burden models that extrapolate disease data. Policy decisions are mostly informed by protection against mortality, and do not fully consider the effect the vaccine may have on the morbidity burden, or broader population-based effects.

A number of enteric vaccine candidates are in clinical product development, including those to address the burdens of *Shigella*, enterotoxigenic *E.coli*, norovirus and non-typhoidal *Salmonella*. As part of its mission to advance vaccine development that addresses significant unmet public health need globally, WHO is embarking on efforts to better evaluate and communicate the full value of vaccines, while candidates are in the early stages of product development. The Full Vaccine of Vaccines Assessment (FVVA) is a concept that describes the global value of a vaccine and aims to articulate the full direct and indirect effects of a vaccine. The intent of FVVA is to support decision-making across the continuum of vaccine development and uptake, with a line-of-sight to sustainable socio-economic and public health impact.

Two main modelling groups provide mortality estimates by pathogen: the Institute for Health Metrics and Evaluation (IHME) at the University of Washington and the Maternal Child Epidemiology Estimation (MCEE) group, led by Johns Hopkins Bloomberg School of Public Health. In 2018, PDVAC reviewed the global diarrhoea mortality estimates for under five-year-olds from these two groups. While estimates from a decade or ago were closely aligned, more recent estimates for 2016 have diverged, particularly with respect to numbers of deaths attributable to different enteric pathogens. This has impacted prioritization and investment decisions for vaccines in the development pipeline. For this reason, PDVAC recommended the formation of an independent working group of subject matter experts to explore the differences between the IHME and MCEE estimates, and to assess the respective strengths and limitations of the estimation approaches adopted, including a review of the data on which the estimates are based. This working group was established in 2018 and is called the Burden of Enteric Disease Working Group (BoED WG).

While infections with enteric pathogens result in substantial mortality, the morbidity impact due to malnutrition, stunting and cognitive impairment can last long after the initial infection took place. To comprehensively assess the full vaccine value and inform vaccine prioritization and use, both mortality and morbidity need to be explicitly quantified. However, there is a lack of alignment on how to measure, analyse and present morbidity associated with enteric infections, and as such the value of enteric vaccines is under-estimated.

This PDVAC session will review the outputs of the BoED WG group since the 2018 PDVAC recommendation and consider the potential scope expansion of this group to evaluate current data and methodology to assess morbidity for these pathogens.

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Objectives of the meeting

The objectives for the virtual PDVAC meeting on 11 May 2020 are to:

1. Review the status of workstreams related to improving quantification of the under 5 mortality, caused by individual enteric pathogens;
2. Discuss the impact of findings and their potential implications to future under 5 mortality estimates;
3. Provide an overview of the proposed expansion of the working group scope to evaluate the data and methodology to quantify the morbidity burden of enteric pathogens.

Background reading:

- Meeting Report: WHO Workshop on modelling global mortality and aetiology estimates of enteric pathogens in children under five. Cape Town, 28-29th November 2018, Prudden et al, 2020.
- Troeger C, Colombara D V., Rao PC, Khalil IA, Brown A, Brewer TG, et al. Global disability-adjusted life-year estimates of long-term health burden and undernutrition attributable to diarrhoeal diseases in children younger than 5 years. Lancet Glob Heal. 2018;
- Anderson JD, Bagamian KH, Muhib F, Amaya MP, Laytner LA, Wierzba T, et al. Burden of enterotoxigenic Escherichia coli and shigella non-fatal diarrhoeal infections in 79 low-income and lower middle-income countries: a modelling analysis. Lancet Glob Heal. 2019;

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Start times:

06:00 Seattle; 8:00 Lima; 9:00 Washington DC; 14:00 London; 15:00 Johannesburg; 15:00 Geneva; 18:30 New Delhi, 21:00 Beijing; 22:00 Seoul

Time (Geneva CEST)	Topic	Duration	Detail	Moderators, speakers
15.00 – 15.10	Welcome and introductions			David Kaslow (PATH) and Martin Friede (WHO)
15.10 – 15.15	Introduction: session overview & objectives	5’	Summary the purpose of the session and highlight of PDVAC’s 2018 recommendations related to this work	Birgitte Giersing (WHO)
15.15 – 15.20	Summary of workstreams related to mortality of enteric pathogens	5’	High-level description of all workstreams that investigated the differences in the burden of U5 mortality for enteric pathogens.	Mateusz Hasso-Agopsowicz (WHO)
15.20 – 15.35	Results of the study grading analysis	10’ + 5’	Findings of the quality assessment of studies that were used to calculate mortality estimates	Mateusz Hasso-Agopsowicz (WHO)
15.35 – 15.50	Analysis of the systematic review of odds ratios	10’+5’	Results of the analysis of the systematic review of odds ratios of developing diarrhoea when a pathogen is detected in stool.	Benjamin Lopman (Emory)
15.50 – 16.05	Analysis of the systematic review of case fatality rates	10’+5’	Results of the analysis of the systematic review of pathogen specific case fatality rates.	Virginia Pitzer (Yale)

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16.05 – 16.20	Results from the meta-analysis of input studies	10'+5'	Results from the meta-analysis of studies used to calculate mortality estimates, and the impact of IHMEs model adjustments on mortality estimates.	James Platts-Mills (U. Virginia)
16.20 – 16.25	Perspectives on scope and outcomes from PDVAC members of the BoED WG	5'	Brief reflections from PDVAC members who are also members of the BoED working group	Cherry Kang (THSTI) Peter Smith (LSHTM) Claudio Lanata (IIN)
16.25 – 16.35	Perspectives on findings from the mortality modelling groups	10'	Potential implications from the systematic reviews and meta-analysis on future mortality estimates	Hmwe Kyu (IHME) Bob Black (MCEE)
16.35 – 16.55	Discussion	20'	**For discussion and endorsement:** • Have the outcomes of the BoED WG led to improved understanding of the data inputs and data processing that inform the mortality estimates? • (How) could the outcomes of this work improve robustness and credibility of mortality estimates? • Does PDVAC have any recommendations as to how this work can be incorporated into future mortality estimates and to inform research agenda around enteric pathogens?	Rob Breiman (Emory) – BoED WG chair
16.55 – 17.00	Anticipated outcomes, timelines, next steps	5'	To inform on proposed outcome, their timelines, and next steps	Mateusz Hasso (WHO)
17.00– 17.20	Expansion of scope to morbidity	10'+10'	**For discussion and endorsement:** To inform, discuss and agree on the proposed scope of work to measure the impact of enteric infections on morbidity	Ibrahim Khalil (WHO)
17.20 – 17.45	Closed session	25'		PDVAC committee only