Vaccine xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Discussion

Path to impact: A report from the Bill and Melinda Gates Foundation convening on maternal immunization in resource-limited settings; Berlin – January 29–30, 2015

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ARTICLE INFO

Article history:
Available online xxx

Keywords:
Maternal immunization
Vaccines
Pregnancy
Neonates
Infants
Global health

ABSTRACT

Global initiatives such as the Millennium Development Goals have led to major improvements in the health of women and children, and significant reductions in childhood mortality. Worldwide, maternal mortality has decreased by 45% and under-five mortality has fallen by over 50% over the past two decades [1]. However, improvements have not been achieved evenly across all ages; since 1990, under-five mortality has declined by ~5% annually, but the average decrease in neonatal mortality is only ~3% per year.

Against this background, the Bill and Melinda Gates Foundation (BMGF) convened a meeting in Berlin on January 29–30, 2015 of global health stakeholders, representing funders, academia, regulatory agencies, non-governmental organizations, vaccine manufacturers, and Ministries of Health from Africa and Asia. The topic of discussion was the potential of maternal immunization (MI) to achieve further improvements in under-five morbidity and mortality rates in children, and particularly neonates and young infants, through targeting infectious diseases that are not preventable by other interventions in these age groups. The meeting focused on effective and appropriately priced MI vaccines against influenza, pertussis, and tetanus, as well as against respiratory syncytial virus, and the group B *Streptococcus*, for which no licensed vaccines currently exist.

The primary goals of the BMGF 2015 convening were to bring together the global stakeholders in vaccine development, policy and delivery together with the Maternal, Newborn and Child Health (MNCH) community, to get recognition that MI is a strategy shared between these groups and so encourage increased collaboration, and obtain alignment on the next steps toward achieving a significant health impact through implementation of a MI program.

1. Introduction

Millennium Development Goal 4 targeted a decrease in under-five mortality by 2/3 between 1990 and 2015 [1]. Latest figures show the rate has been halved from 1990 to 2012, representing an annual decline of ~5% per year (Fig. 1). However, the annual decline in neonatal mortality has only been ~3% per year; neonatal mortality now accounts for 44% of under-five mortality, and this may increase to ~55% by 2035 [2]. This makes neonates a major target for future initiatives to achieve the Sustainable Development Goals for 2030 currently under discussion.

Globally, more than half of the 2.76 million neonatal deaths annually are associated with infections (22%) or pre-term births (35%), and 10–50% of stillbirths are estimated to be a consequence of maternal infections [3]. Much of the improvement in child health has been achieved through targeted vaccinations in Extended Program on Immunization (EPI). However, such programs cannot protect the substantial vulnerable population of newborns and young infants who are too young to receive their own routine immunizations, e.g., pertussis vaccination from 6 to 8 weeks of age fails to protect against the significant disease burden in the first month of life [4]. Maternal immunization (MI) offers an innovative

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http://dx.doi.org/10.1016/j.vaccine.2015.08.047

Please cite this article in press as: Sobanjo-ter Meulen A, et al. Path to impact: A report from the Bill and Melinda Gates Foundation convening on maternal immunization in resource-limited settings; Berlin – January 29–30, 2015. Vaccine (2015), http://dx.doi.org/10.1016/j.vaccine.2015.08.047

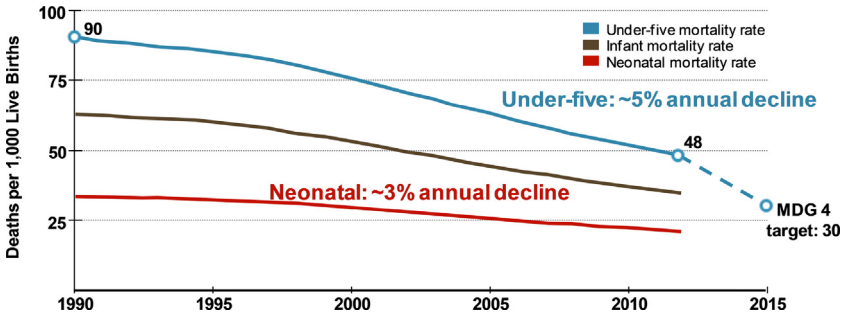

Fig. 1. Global under-five (U5), infant and neonatal mortality rates (1990–2012).

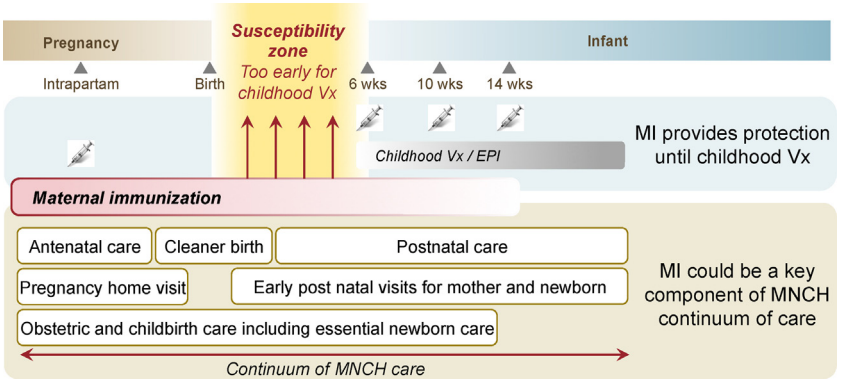

Fig. 2. How MI could complement the MNCH continuum of care.

approach to improve the health of mother, fetus and infant and may significantly impact neonatal mortality. As MI targets pregnant women for immunization, such an initiative can be integrated in the continuum of care of Maternal, Newborn and Child Health (MNCH) programs to build upon their established interactions between pregnant women and antenatal health care providers (Fig. 2).

MI could potentially have substantial impact on both maternal and infant mortality for some diseases for which there already are, or soon will be vaccines (e.g., influenza, tetanus, malaria, hepatitis E). Focus of the Bill and Melinda Gates Foundation (BMGF) 2015 convening was on the potential impact of MI on five pathogens – influenza, group B *Streptococcus* (GBS), pertussis, respiratory syncytial virus (RSV) and tetanus – that are serious causes of neonatal morbidity and mortality. The three main objectives of the meeting were (i) to identify the key challenges (and potential solutions) that would prevent MI having a major impact on preventable neonatal mortality due to these infectious diseases in low income (LIC) and low-middle income (LMIC) countries, (ii) the strategic priorities for successful implementation of MI, and (iii) how to ensure increased collaboration between the global stakeholders in the vaccine and MNCH communities to align on a path forward, with the goal of creating a sustainable MI platform to address the current unmet needs in maternal, neonatal and infant health.

Presentations and subsequent discussions in five categories covered the issues surrounding maternal immunization – the investment case, the current evidence base, regulatory and policy issues, market dynamics and funding, and implementation.

2. Investment case

To kick-off the meeting the BMGF presented high-level cost-effectiveness modeling analyses of four of the five MI targeted vaccines as these will be required to inform investments in MI. Tetanus was excluded from the analyses as it is already being implemented as a well-established maternal vaccination program with favorable cost-effectiveness in many of the LIC/LMIC countries. The main outcome from the current modeling analyses was to illustrate the paucity of data necessary for an MI investment case for influenza, RSV, GBS, and pertussis, which could be seen as a call to arms for the research that needs to be done at regional and global levels. Better understanding of the diseases and the potential impact of maternal vaccination on health outcomes in the mother and the fetus, such as stillbirths and pre-term deliveries, as well as longer term sequelae in newborns, are essential if any modeling effort is to produce coherent results to guide future investment in MI.

3. Evidence base

The current state of knowledge and the requirements for further research to enhance the evidence base and establish some of the key parameters for each pathogen, were discussed in detail in this session.

3.1. Tetanus

The current status of the established Maternal and Neonatal Tetanus Elimination (MNTE) program was presented as an example of lessons learned, to define the needs for better surveillance and studies to assess impact for each of the other pathogens. In addition to vaccinating pregnant women the four components of the MNTE program include vaccination of women of reproductive age in high-risk areas, clean delivery and cord care at birth by trained personnel, and measures to improve surveillance to assess the improvements in prevention and treatment of neonatal tetanus. Over 15 years, the MNTE has resulted in elimination (to 1 in 1000 live births) of neonatal tetanus in 35 of the 59 involved countries, and in many regions of other countries, with a decrease in neonatal tetanus deaths from 200,000 in 2000 to 49,000 in 2013 [5].

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