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Conference report

Preparing to introduce new maternal immunizations in low- and lower-middle-income countries: A report from the Bill & Melinda Gates Foundation convening "Allies in Maternal and Newborn Care"; May 3–4, 2018

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ABSTRACT

New strategies will be critical to reduce infant mortality and severe morbidity — there are still 5.2 million newborn deaths and stillbirths each year. The decline in newborn mortality has not kept pace with the reduction in under-five deaths and is slowest in low- and lower-middle-income countries (LMICs). Maternal immunization is a promising intervention to protect infants when they are most vulnerable – in utero and their first few months of life, before they can receive their own vaccines. Successfully introducing new vaccines for pregnant women in LMICs will require collaboration between two fields — (1) immunization and (2) maternal, newborn and child health — that use different service delivery approaches, operate under different policy and funding paradigms, and are not always integrated. In May 2018, stakeholders from these distinct communities convened to identify challenges and opportunities associated with delivering new maternal immunizations. Participants agreed that antenatal care is a logical platform. However, in many resource-constrained settings, antenatal care providers are already overburdened, and most women do not receive the recommended number of antenatal visits. Implementing maternal immunization could help increase antenatal care attendance by offering an additional safe and effective intervention that women value. Substantial effort is needed to demonstrate the benefits of maternal immunization to decision-makers and providers, and to ensure that countries and health systems are ready for introduction. To that end, participants identified the following priorities: assure coherence of policies for introducing new vaccines for pregnant women and strengthen maternal health interventions; generate demand for existing, recommended, and new maternal vaccines; conduct socio-behavioral, health systems and implementation research to shape optimal vaccine delivery strategies; and strengthen antenatal and perinatal care quality. To achieve these aims, collaboration across fields will be essential. Given that new maternal vaccines are advancing in clinical development, time is of the essence.

1. Introduction

Over the last three decades, concerted efforts have led to a ~60% reduction in deaths among children under the age of five; however, the decline in newborn and young infant mortality has not kept

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pace – in fact, newborn deaths represent 47% of all deaths among children under the age of five [1]. Maternal immunization – vaccinating women during pregnancy – has emerged as an intervention with the potential to contribute to the reduction of neonatal morbidity and mortality, premature births and stillbirths. Clinical evidence has supported the implementation of maternal immunization programs for influenza, tetanus and pertussis in countries around the world [2]. By transferring immunity to the fetus in-utero and through breastfeeding, maternal immunization can protect newborns from specific infectious diseases in their first weeks of life — when they are most vulnerable [3,4]. Two promising new maternal vaccines against respiratory syncytial virus (RSV) and group B streptococcus (GBS) are in clinical development, with a first-in-class RSV vaccine marking the first time a vaccine is in phase 3 clinical development in pregnant women, and pursuing an indication for use in pregnancy [5,6] https://clinicaltrials.gov/ct2/show/NCT03765073?term=Pfizer+group+b&draw=2&rank=1.

In May 2018, the Bill & Melinda Gates Foundation convened a meeting of global immunization and maternal, newborn and child health (MNCH) stakeholders in Amsterdam to analyze the state of the field and identify challenges and opportunities associated with the delivery of maternal vaccines. The meeting, *Allies in Maternal and Newborn Care: Strengthening Services Through Maternal Immunization*, established broad consensus on the potential value of existing and new maternal immunizations, and on antenatal care services as a logical platform for delivering these vaccines. The need for active collaboration between MNCH and immunization stakeholders was a recurrent topic because of the potential challenges associated with introducing and delivering these vaccines as part of maternal health services. Here we outline perspectives that emerged from the meeting, and recommendations for next steps.

2. Maternal immunization: a high impact opportunity for protecting both mother and child

Every year, approximately 2.5 million neonates die in the first month of life and an additional 2.6 million are stillborn [1,7]. Approximately 99% of newborn deaths occur in low- and lower-middle-income countries (LMICs), where infections are a leading cause of both infant deaths and stillbirths [1,8,9].

A review of evidence suggests that maternal vaccines in development against RSV and GBS could help address infectious disease-related neonatal and infant morbidity and mortality (Fig. 1) [2,10]. An effective vaccine against GBS could also help address pre-term births, stillbirths and, to some extent, maternal morbidity and mortality.

Among the vaccines recommended for pregnant women, tetanus vaccines are the most widely utilized. Between 1999 and 2018, an estimated 154 million women of childbearing age received the recommended two doses of tetanus vaccine as part of the World Health Organization (WHO) Maternal and Neonatal Tetanus Elimination Program. This has contributed to a 96% decrease in neonatal tetanus over three decades [11]. Given this success, efforts are underway to understand the most optimal delivery strategies for tetanus vaccines to pregnant women during antenatal care to strengthen this intervention platform and inform the implementation of other vaccines [12].

In 2012, WHO recommended that countries considering the initiation or expansion of seasonal influenza vaccination programs give the highest priority to pregnant women. Vaccination in pregnancy can help lower influenza-related mortality and morbidity among both pregnant women and newborns [13]. Similarly, in 2015 WHO recommended that countries with a high neonatal pertussis mortality burden consider vaccinating pregnant women with Tdap (tetanus, diphtheria and pertussis) vaccine to protect against neonatal pertussis [14].

Despite specific recommendations, uptake of maternal immunizations has been mixed across high-, middle-, and low-income countries [15]. While there are several existing vaccines recommended during pregnancy, wider acceptance of maternal immunization has been limited by the perception that insufficient safety and efficacy data are available [3]. Uncertainty about the risk of vaccinating women during pregnancy, coupled with perceived safety concerns associated with vaccines in general, plus a low tolerance for risk in any pregnancy intervention, has hindered the implementation of maternal immunization [16]. However, following the 2009–2010 H1N1 influenza pandemic and a resurgence of neonatal pertussis mortality in countries that use acellular pertussis infant immunization, there has been increased interest in maternal immunization, as well as increased support for this strategy based on research [3]. Meeting participants noted that with maternal vaccines in advanced stages of clinical development, there is a need to advance dialogue now and begin preparing for delivery of maternal immunization, given the potential complexity of delivering these vaccines.

3. What is needed to make the case for new maternal immunizations

RSV is a leading cause of acute lower respiratory infection and is responsible for an estimated 1.4 million hospital admissions and 27,300 infant deaths worldwide annually [17]. GBS is a major cause of both sepsis and meningitis in young infants, and a 2015 study found that it was a leading contributor to 90,000 infant deaths and 57,000 stillbirths globally, and potentially associated with up to 3.5 million pre-term births [18]. In addition, GBS is associated with approximately 17,000 cases of severe morbidity in infants, including neurodevelopmental impairment after GBS meningitis and neonatal encephalopathy worldwide. New maternal immunizations in development can potentially help lower mortality as well as morbidity of these two diseases [16,17,19].

If proven effective, new maternal vaccines for RSV and GBS have the potential to reduce infant morbidity and mortality, yet additional work, such as the generation of evidence on disease burden and cost-effectiveness, remains to be done to develop a compelling and comprehensive value proposition for their adoption and to help policymakers evaluate the role of these vaccines alongside other interventions. The need for a strong value proposition for RSV in particular, is pronounced given that the disease is not well understood within the maternal health and larger global health community. Better evidence from LMICs on the disease and economic burden of RSV and GBS will facilitate decisions to introduce these vaccines at the global as well as country-level.

4. Maternal immunization for GBS: Value beyond newborns and infants

While the currently-available approach to addressing maternal GBS – screening during pregnancy and administration of intravenous antibiotics during labor – has led to a significant reduction of GBS early-onset disease in high-income countries, this strategy is often not feasible in low-income settings and does not address late-onset GBS disease. Moreover, selective prenatal maternal GBS culture is not an accurate predictor of early onset GBS disease in neonates, and widespread antibiotic use may contribute to antimicrobial resistance and could potentially affect neonatal microbiome development [20,21]. Given these limitations, new strategies are needed; and maternal immunization holds promise for the prevention of GBS infection among neonates and pregnant

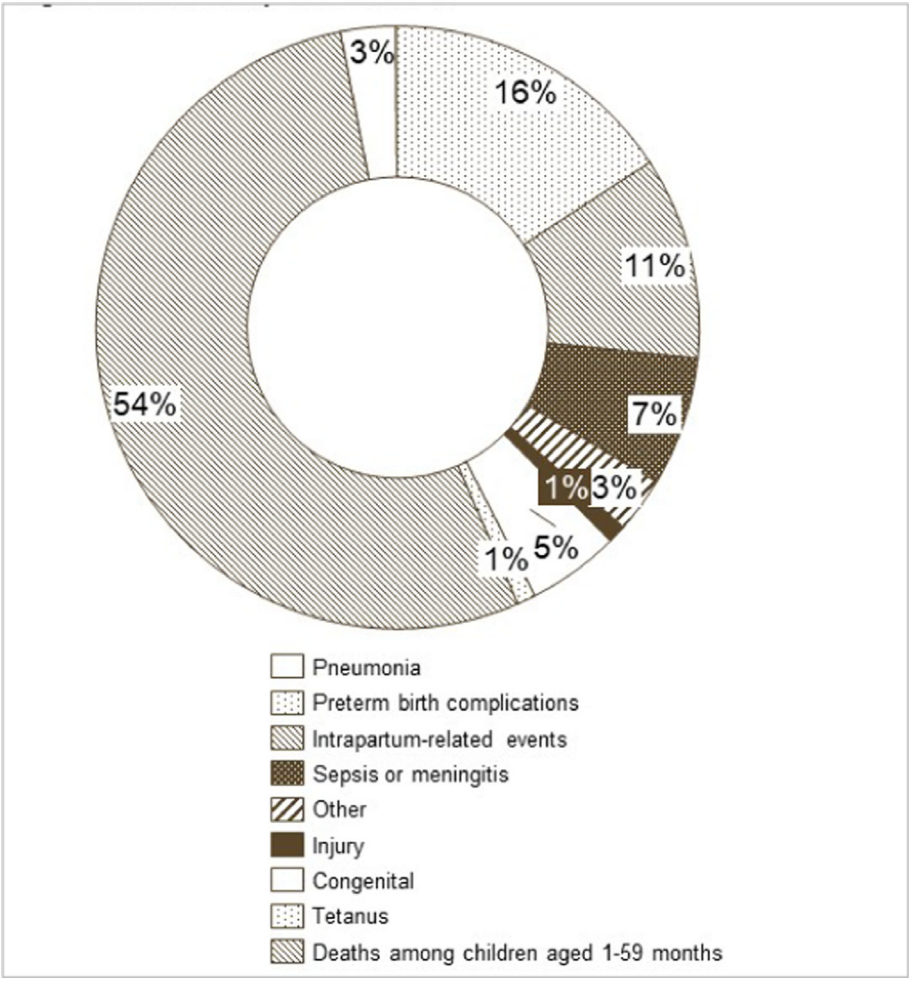

Fig. 1. Global distribution of deaths among children under age 5, neonatal by cause, 2016.

women. Several candidate vaccines are currently in Phase 1 and 2 clinical development [22].

Preliminary cost-effectiveness assessments for GBS indicate that maternal immunization would be a cost-effective intervention in LMICs in Africa, with cost per disability adjusted life year (DALY) ratios similar to other recently introduced childhood vaccines [23]. Since disease incidence and case fatality rates are key drivers of cost-effectiveness figures, reliable, country-specific data on GBS burden are needed to better inform national decision making. During the meeting, presenters emphasized that country-level data on disease burden and cost-effectiveness would help individual countries plan for integration of maternal immunization within the package of MNCH interventions.

While the primary objective of a GBS vaccine would be to reduce GBS-associated neonatal sepsis and stillbirths, maternal immunization for GBS may provide health benefits for women by reducing maternal infection and adverse pregnancy outcomes [24]. An effective GBS vaccine may help avert some of the estimated 33,000 cases of maternal invasive GBS disease worldwide that contribute to maternal morbidity and mortality [18]. It also could help address some of the potential concerns raised about existing prevention options, such as the feasibility or cost-effectiveness of scaling intrapartum antibiotic prophylaxis in low-resource settings, its potential association with antimicrobial resistance, and its inability to guard against late onset GBS disease [21]. The value proposition for GBS vaccines should thus include a nuanced understanding of the vaccine's ability to not only reduce newborn and infant mortality, but also to reduce stillbirths and preterm births, improve delivery outcomes, reduce maternal morbidity and mortality, and improve long-term health outcomes in both mothers and infants.

5. Maternal immunization for RSV: vaccines on the horizon

The current RSV vaccine pipeline includes 18 vaccine candidates in clinical trials; only two trials have evaluated RSV vaccines specifically for use in pregnant women [25]. The most advanced candidate is a RSV Fusion-protein (RSV F) nanoparticle vaccine that has been tested in a phase 3 trial for an indication specifically in pregnant women [26,27]. At least two other candidate vaccines are ready to be evaluated in phase 2 trials in pregnant women.

Preliminary research suggests that a potential RSV vaccine for use in pregnant women could prevent 4.6–6 million RSV cases and 66,000–94,000 deaths in infants per year at a cost of $350–400 per DALY averted. The cost per DALY averted is likely to be lower in countries eligible for Gavi support [28]. Additionally, an RSV vaccine could potentially reduce antibiotic use both for RSV and related, secondary bacterial infections, which in turn could reduce antimicrobial resistance [29]. Because RSV exerts a broader toll on pediatric health and health systems than mortality alone, additional research is needed to illustrate the potential full impact of maternal immunization in this area. Such research would enable the value proposition for RSV vaccines to include, for example, impact on all-cause, pneumonia, and RSV-specific respiratory

Table 1
Potential value proposition of new maternal immunizations for GBS and RSV by population.

POPULATION	POTENTIAL VALUE		
	Primary value proposition		Potential additional value
Newborns and infants (<28 days old; < 1 year old)	**GBS Vaccine**	• Reduce neonatal morbidity and mortality [18]	• Reduce late onset GBS disease
	RSV Vaccine	• Reduce neonatal morbidity and mortality [17]	• Reduce pneumonia and all cause hospitalization and mortality • Reduce antibiotic use
Pregnant women	**GBS Vaccine**	• Reduce maternal GBS infection • Reduce maternal morbidity and mortality related to GBS infection [18]	• Reduce maternal GBS colonization • Increase antenatal care attendance and uptake of services • Improve delivery outcomes
Fetuses	**GBS Vaccine**	• Reduce stillbirths and pre-term births related to GBS infection [18]	• Improve antenatal care delivery and outcomes
Older Children (<5 years old)	**GBS Vaccine**	• Reduce neurodevelopmental impairment related to GBS infection [30]	• Reduce long-term sequelae • Increase child and immunization uptake • Improve childhood growth and development
	RSV Vaccine	• Reduce RSV-associated morbidity and mortality in children under-five • Reduce RSV-associated recurrent wheeze and childhood asthma [31]	• Reduce long-term sequelae • Increase child and immunization uptake • Improve childhood growth and development
Health systems	**RSV and GBS Vaccine**	• Reduce hospitalization among children under-five [16] • Reduce infant hospitalization rates and health care expenditures, which could lead to economic benefits for women and their families [16]	• Improve quality of antenatal care • Improve maternal interventions surveillance systems • Improve vaccine safety surveillance systems • Improve infant and maternal disease outcomes surveillance systems • Improve understanding of burden of disease • Reduce antimicrobial resistance

hospitalization, and potentially also on childhood asthma, and early childhood growth and development.

6. Communicating an expanded value proposition for maternal immunization in LMIC

Given that vaccine candidates for both GBS and RSV for pregnant women have the potential to reach licensure within the next few years, it is increasingly important to plan for their introduction and successful delivery. To do this, we need to better communicate the value proposition of maternal immunization. This means clarifying the impact on fetal and neonatal mortality, and also the potential to reduce stillbirths, avert pre-term births, prevent long term disability and sequelae, reduce antimicrobial resistance, as well as reduce maternal morbidity and mortality. Other benefits may include strengthening existing antenatal care systems, improving the maternal tetanus immunization platform, improving perinatal care and the delivery outcomes, and strengthening and utilizing safety and disease surveillance systems to achieve implementation and specific outcome goals. Presenters and participants identified several elements that should be included in an expanded case for adopting new maternal immunizations (Table 1) [18]:

7. Antenatal care: a challenging but essential platform for introducing maternal immunization in LMICs

Antenatal care is increasingly viewed as a health care platform that provides a range of services beyond basic pregnancy care, which may include malaria services, prevention of mother-to-child transmission of HIV, and education on preventive health, including pediatric vaccines, among other interventions. Antenatal care offers a confluence of factors needed to deliver maternal immunization: multiple opportunities to access the right target population to implement interventions at the right time, and qualified health professionals who can potentially deliver the intervention. As such, participants agreed that antenatal care is the most logical setting to offer maternal immunizations — and to be successful, the maternal health community must play a prominent role in planning for introduction of maternal vaccines. It will be important to address questions and concerns that may arise among global health stakeholders, practitioners and communities about the potential impact of maternal immunization on women and on the provision of antenatal care services.

Delivery of antenatal care services in LMICs often faces its own challenges, including limited human and financial resources, inconsistent quality of care, and context-specific barriers women face in accessing care [32]. Only 64% of women globally are estimated to meet the previously recommended minimum of four antenatal care visits, and the WHO's 2016 guidelines now recommend doubling the number of interactions to eight "contacts." Fortunately, the new guidelines increase opportunities for antenatal visits in the second and third trimester, when maternal vaccination can be administered, but maternal health stakeholders have expressed concerns about the potential for maternal immunization to place an additional burden on overstretched antenatal care systems. Quality, utilization, infrastructure and capacity issues will need to be addressed in parallel with the integration of maternal immunization.

Participants described new approaches to antenatal care that could help increase coverage and improve quality in a way that would facilitate successful introduction of new interventions and address some of the concerns that have been raised. For example, group antenatal care, an approach to antenatal care that places women at the same stage of pregnancy in small group cohorts, is a strategy that is having success in addressing long waits, short visits and poor service quality. The approach, which has been studied in Kenya, Nigeria and Rwanda, aims to empower women through participatory, facilitated learning, peer support and clinical assessment. To date, it has resulted in an increased number of visits and better quality of care — both important to the integration of maternal immunization [33].

New digital technologies also have the potential to improve the way services are connected across a continuum, from pre-pregnancy through childhood, resulting in services that are more coordinated, timely and holistic. For example, new tools and

technologies could help remind pregnant women of antenatal care visits and maternal immunizations and could follow the mother and child offering reminders about child immunizations.

Overall, participants agreed that integrated service delivery has the potential to create a stronger antenatal care platform for the delivery of various interventions including maternal immunizations. The availability of new maternal vaccines could help increase antenatal care attendance by offering an additional safe and effective intervention that women value. Some evidence suggests that integration of other services for malaria, sexually transmitted infections, HIV/AIDS and tuberculosis have led to improvements in uptake of ANC services, particularly in settings where the prevalence of such conditions is high [34]. Efforts to prepare for their introduction could also help bring resources to address existing quality of care and uptake challenges. In addition, decades of experience from WHO's successful Expanded Programme on Immunization could be used to support planning and operationalizing maternal immunization delivery [24].

8. Different worlds: bridging maternal health and immunization paradigms

Collaboration between programs focused on MNCH and immunization at the global, regional and country levels will be essential for introducing new maternal immunizations. At the recent *Allies in Maternal and Newborn Care* meeting, a detailed landscape analysis on the provision of tetanus vaccine to pregnant women identified attributes associated with successful vaccine delivery strategies [12]. Some efforts have been made to strengthen relationships between the immunization and maternal health communities in anticipation of new maternal vaccines, including a series of meetings that brought together key stakeholders to discuss concerns and plot a course forward [24,35,36]. Participants also noted that global adoption of new maternal immunizations and their effective delivery within antenatal care will require harmonization of the different policy processes and ethical paradigms that govern immunizations and maternal health interventions [24].

Presenters reviewed the highly structured nature of vaccine policy decision-making processes at the global and regional levels and shared WHO's early stage initiative to build a similarly structured process for MNCH interventions [37]. Participants discussed the challenges they will face at the country level, where national adoption will require collaboration between often-siloed programs and policy decision-makers. Advisory bodies, such as National Immunization Technical Advisory Groups (NITAGs), can have a major role in advocating for integrated services. They noted that integration of these programs is currently most successful at the service delivery level where, by necessity, a single health care worker often provides both services.

Maternal immunization also bridges differences between the ethical paradigms that govern immunization and reproductive health, and it must account for the interests of both the mother and the infant. The approach to assessing risk for maternal immunization needs to go beyond the traditional approach for vaccines in order to include consideration for vaccines that may benefit only the mother or the infant, acknowledging the importance of a woman's interest in protecting her child. Further, while most vaccines are delivered as part of routine, "opt out" services, reproductive health programming and some maternal health services tend to promote women's agency, engaging women in active decision-making using an "informed choice" model in which they weigh their options, risks and benefits. Maternal immunization will need to straddle these two paradigms. Policy recommendations for new maternal vaccines will need to be based on appropriate benefit-risk assessments across different populations and geographies, and pregnant women will need to be empowered to make informed decisions that are in the best interest of their own health and that of their child. This decision-making will need to be supported with data on disease burden and potential vaccine impact, as well as appropriate safety and effectiveness data to determine and communicate the benefit-risk profile. A truly informed decision-making process will require robust inclusion of women at all levels of policy development and implementation.

9. Preparing for introduction: many questions yet to answer

Questions remain about the most appropriate way to promote acceptance and uptake, deliver vaccination services within antenatal care, and ensure policy-level support. We will need additional data to strengthen the value proposition in such areas as burden of disease, safety and effectiveness, as well as cost effectiveness. We can also learn important lessons from previous service integration efforts in areas such as malaria, HIV and tuberculosis, to guide planning for introduction and delivery of maternal immunization. In addition, implementation research can help define, test and iterate solutions for delivering maternal immunization within antenatal care. Meeting participants identified a wide range of priority needs and actions to support delivery of maternal immunization (Table 2).

In working to address these outstanding gaps and questions, a wide variety of stakeholders should be engaged to identify context-specific research priorities, including the MNCH and immunization communities, in-country implementing agencies, women and policymakers. A more inclusive process helps ensure the relevance of research questions in facilitating eventual uptake

Table 2
Potential research areas to support delivery of new maternal immunizations.

Potential research areas to support delivery of new maternal immunizations	
Policy and planning	• Capture lessons on introducing tetanus toxoid, influenza, and pertussis vaccines for pregnant women • Capture lessons from the integration of other services into antenatal care, such as iron/folate supplementation, HIV testing, or malaria screening and treatment • Determine optimal models for coordination between EPI and MNCH teams within Ministries of Health
Service delivery	• Develop optimal vaccine schedules for all maternal vaccines • Determine optimal delivery models to maximize workflows (e.g., between EPI and maternal health staff) • Understand best practices for reporting and safety monitoring for maternal immunizations
Demand generation	• Develop effective messaging to explain RSV and GBS disease to pregnant women • Understand strategies to build pregnant women's understanding of the importance of maternal immunization and its safety • Understand strategies to build pregnant women's trust with providers • Understand drivers of uptake decisions about vaccines and antenatal care
Capacity and infrastructure	• Understand best approaches to health care provider capacity-building for maternal immunization • Understand best practices in coordination of funding, human resources, supply, training and supervision of immunizations, between maternal health programs and immunization programs
Impact	• Determine the impact of integrating maternal immunization on the quality and utilization of antenatal care

and implementation of approaches identified as promising through the research.

10. Where do we go from here?

The *Allies in Maternal and Newborn Care* meeting clearly demonstrated consensus among participants on the potential value of new maternal immunizations and a shared recognition that delivery through antenatal care offers both challenges and opportunities. However, preparatory efforts are needed around strengthening existing systems and fostering awareness and collaboration among stakeholders to allow for the smooth introduction of a new intervention within the antenatal care platform. Key recommendations from the meeting include:

10.1. Assure coherence of policies for introducing new vaccines for pregnant women and maternal health products

At the global level, efforts are underway to develop policy processes for MNCH interventions that resemble those instituted for vaccines, such as the Strategic Advisory Group of Experts (SAGE) on Immunization. Continued harmonization of policy decision-making at the global, regional, and country levels may enable smoother introduction of interventions that overlap between MNCH and vaccines. Maternal immunization could provide an apt test case for building new, more harmonized approaches to decision-making.

10.2. Increase awareness and generate demand for new maternal vaccines

Although the concept is not new, awareness of the potential benefit offered by maternal immunization is low, particularly in the MNCH community. Efforts should focus on increasing awareness and sharing of relevant data and information as soon as it becomes available (e.g., on the burden of disease, guidelines, vaccine safety and efficacy), including country-specific data to promote country ownership. The introduction of new maternal vaccines requires comprehensive communications strategies to foster dialogue among country and regional stakeholders, providers, communities and women, and the cultivation of champions at multiple levels. Once these new maternal vaccines become available, communications and advocacy frameworks should promote country-level political support to ensure relevant policies are in place for national adoption.

10.3. Conduct socio-behavioral, health systems and implementation research to shape optimal delivery strategies

We have much to learn to prepare for new maternal immunizations. As part of a pre-implementation learning agenda, the field needs a prioritized portfolio of research to identify best practices, address potential challenges and apply lessons from previous efforts, including the introduction of tetanus toxoid, and influenza, and pertussis vaccines for pregnant women in LMIC, and the introduction of other services into antenatal care.

10.4. Strengthen antenatal care quality

Improving the quality of antenatal care services is an important first step in planning for the introduction of new maternal vaccines. New strategies to deliver antenatal care, including group antenatal care, have the potential to strengthen the quality of pregnancy care and prepare a platform that can reach pregnant women with a range of interventions. If proven effective and feasible, we should scale new antenatal care approaches in LMICs that could facilitate the delivery of new maternal immunizations as they become available. Maternal vaccines are one component of high-quality antenatal care services for those women who are most vulnerable. Decades of experience from successful immunization programming can also be applied to help improve the uptake and quality of these antenatal care services.

To achieve these aims and realize the promise of maternal immunization for women and newborns, collaboration across all relevant fields and disciplines will be essential. Given that new maternal vaccines are advancing in clinical development, time is of the essence.

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Declaration of Competing Interest

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References

[1] United Nations Inter-agency Group for Child Mortality Estimation (UN IGME). Levels & Trends in Child Mortality: Report 2018, Estimates developed by the UN IGME. http://www.childmortality.org/files_v22/download/UN%20IGME%20Child%20Mortality%20Report%202018.pdf. Published 2018. Accessed December 19, 2018.
[2] Omer S. Maternal immunization. N Engl J Med 2017;376(13):1256–67. https://doi.org/10.1056/NEJMra1509044.
[3] Vojtek I, Dieussaert I, Doherty TM, et al. Maternal immunization: where are we now and how to move forward?. Ann Med 2018;50(3):193–208. https://doi.org/10.1080/07853890.2017.1421320.
[4] Schlaudecker EP, Steinhoff MC, Omer SB, McNeal MM, Roy E, Arifeen SE, et al. IgA and neutralizing antibodies to influenza A virus in human milk: a randomized trial of antenatal influenza immunization. PLoS ONE 2013;8(8):e70867. https://doi.org/10.1371/journal.pone.0070867.
[5] Bill & Melinda Gates Foundation. Novavax website. novavax.com/page/19/bill-and-melinda-gates-foundation. Accessed December 19, 2018.
[6] Pfizer Begins Phase 1 Clinical Trial to Evaluate Investigational Group B Streptococcus Vaccine. Pfizer website. www.pfizer.com/news/press-release/press-release-detail/pfizer_begins_phase_1_clinical_trial_to_evaluate_investigational_group_b_streptococcus_vaccine. June 19, 2017. Accessed December 19, 2018.
[7] Lawn JE, Blencowe H, Waiswa P, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet 2016;387(10018):587–603. https://doi.org/10.1016/S0140-6736(15)00837-5.
[8] Goldenberg RL, McClure EM, Saleem S, Reddy UM. Infection-related stillbirths. Lancet 2010;375(9724):1482–90. https://doi.org/10.1016/S0140-6736(09)61712-8.
[9] UNICEF. The State of the World's Children 2011. https://www.unicef.org/sowc2011/pdfs/SOWC-2011-Main-Report_EN_02092011.pdf. Published February 2011. Accessed December 19, 2018.
[10] UNICEF. Global distribution of deaths among children under age 5, neonatal by cause, 2016. WHO and Maternal and Child Epidemiology Estimation Group (MCEE) provisional estimates 2017. https://data.unicef.org/wp-content/uploads/infograms/10141/index.html.
[11] Maternal Neonatal Tetanus Elimination (MNTE). World Health Organization website. http://www.who.int/immunization/diseases/MNTE_initiative/en/. Updated March 2019. Accessed April 9, 2019.
[12] Maternal Immunization and Antenatal Care Situation Analysis (MIACSA). https://www.who.int/maternal_child_adolescent/epidemiology/miacsa-maternal-immunization/en/. Accessed April 9, 2019.
[13] WHO, Weekly Epidemiological Record (WER), 23 November 2012 vol. 87, no. 47 (pp. 461-476) [EN/FR] http://www.who.int/wer/2012/wer8747.pdf?ua=1. Accessed November 14, 2018.

[14] WHO, Weekly Epidemiological Record (WER), 28 August 2015 vol. 90, no. 35 (pp. 433-460) [EN/FR http://www.who.int/wer/2015/wer9035.pdf?ua=1. Accessed November 14, 2018.
[15] MacDougall DM, Halperin SA. Improving rates of maternal immunization: challenges and opportunities. Hum Vaccin Immunother 2015;12(4):857–65. https://doi.org/10.1080/21645515.2015.1101524.
[16] Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: a review of the evidence of selected inactivated and live attenuated vaccines. Vaccine 2014;32(52):7057–64. https://doi.org/10.1016/j.vaccine.2014.09.052.
[17] Shi T, McAllister DA, O'Brien KL, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modeling study. Lancet 2017;390(10098):946–58. https://doi.org/10.1016/S0140-6736(17)30938-8.
[18] Seale AC, Bianchi-Jassir F, Russell NJ, et al. Estimates of the Burden of Group B streptococcal disease worldwide for pregnant women, stillbirths, and children. Clin Infect Dis 2017;65(Suppl 2):S200–19. https://doi.org/10.1093/cid/cix664.
[19] Scheltema NM, Gentile A, Lucion F, et al. Global respiratory syncytial virus-associated mortality in young children (RSV GOLD): a retrospective case series. Lancet Glob Health 2017;5:e984–91. https://doi.org/10.1016/S2214-109X(17)30344-3.
[20] Le Doare K, O'Driscoll M, Turner K, et al. Intrapartum antibiotic chemoprophylaxis policies for the prevention of group B streptococcal disease worldwide: systematic review. Clin Infect Dis 2017;65(Suppl_2):S143–51. https://doi.org/10.1093/cid/cix654.
[21] Seedat F, Geppert J, Stinton C, Patterson J, Freeman K, Brown S, et al. Universal antenatal screening for group B streptococcus may cause more harm than good. Br Med J 2019;364:I463. https://doi.org/10.1136/bmj.l463.
[22] Song JY, Lim JH, Lim S, Yong Z, Seo HS. Progress toward a group B streptococcal vaccine. Hum Vaccin Immunother 2018. https://doi.org/10.1080/21645515.2018.1493326.
[23] Russell Louise B, Kim Sun-Young, Cosgriff Ben, Pentakota Sri Ram, Schrag Stephanie J, Sobanjo-ter Meulen Ajoke, Verani Jennifer R, Sinha Anushua. Cost-effectiveness of maternal GBS immunization in low-income sub-Saharan Africa. Vaccine 2017;35(49):6905–14. https://doi.org/10.1016/j.vaccine.2017.07.108.
[24] Swamy GK, Beigi RH. Maternal benefits of immunization during pregnancy. Vaccine 2015;33(47):6436–40. https://doi.org/10.1016/j.vaccine.2015.08.035.
[25] WHO. WHO Vaccine Trial Tracker. https://docs.google.com/spreadsheets/d/19otvINcayJURCMg76xWO4KvuyedYbMZDcXqbyJGdcZM/pubhtml#. Accessed April 18, 2019.
[26] Mazur NI, Higgins D, Nunes MC, et al. The respiratory syncytial virus vaccine landscape: lessons from the graveyard and promising candidates. Lancet Infect Dis 2018;18(10):e295–311. https://doi.org/10.1016/S1473-3099(18)30292-5.
[27] PATH. Advancing RSV Maternal Immunization: A Gap Analysis Report. https://www.path.org/resources/advancing-rsv-maternal-immunization-gap-analysis-report/. Published July 2018. Accessed December 19, 2018.
[28] Pecenca C. RSV maternal impact and cost-effectiveness in LMICs. Oral presentation at: Allies in Maternal and Newborn Care; May 2018; Amsterdam, Netherlands.
[29] Lipsitch Marc, Siber George R. How can vaccines contribute to solving the antimicrobial resistance problem?. mBio 2016;7(3). https://doi.org/10.1128/mBio.00428-16.
[30] Kohli-Lynch M, Russell NJ, Seale AC, et al. Neurodevelopmental impairment in children after group B streptococcal disease worldwide: systematic review and meta-analyses. Clin Infect Dis 2017;65(suppl_2):S190–9. https://doi.org/10.1093/cid/cix663.
[31] Bacharier LB, Cohen R, Schweiger T, et al. Determinants of asthma after severe respiratory syncytial virus bronchiolitis. J Allergy Clin Immunol 2012;130(1):91–100.e3. https://doi.org/10.1016/j.jaci.2012.02.010.
[32] Ritchie LMP, Khan S, Moore JE, et al. Low-and middle-income countries face many common barriers to implementation of maternal health evidence products. J Clin Epidemiol 2016;76:229–37. https://doi.org/10.1016/j.jclinepi.2016.02.017.
[33] Onguti, B, Suhowatsky S, Wambua J, Kabue M, Grenier L. Group Antenatal Care; A transformational service delivery model to improve quality and service utilization through radical re-organization of care in low and middle income countries. Poster presented at: Fifth Global Symposium on Health Systems Research. October 8–12, 2018; Liverpool, UK.
[34] de Jongh TE, Gurol-Urganci I, Allen E, Zhu NJ, Atun R. Integration of antenatal care services with health programmes in low- and middle-income countries: systematic review. J Glob Health 2016;6(1):. https://doi.org/10.7189/jogh.06.010403010403.
[35] Ortiz JR, Neuzil KM, Ahonkhai VI, et al. Translating vaccine policy into action: a report from the Bill & Melinda Gates Foundation Consultation on the prevention of maternal and early infant influenza in resource-limited settings. Vaccine 2012;30(50):7134–40. https://doi.org/10.1016/j.vaccine.2012.09.034.
[36] Sobanjo-Ter Meulen A, Abramson J, Mason E, 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;33(47):6388–95. https://doi.org/10.1016/j.vaccine.2015.08.047.
[37] Hombach J. Vaccine policy decision-making at global level. Oral presentation at: Allies in Maternal and Newborn Care; May 2018; Amsterdam, Netherlands.