VANISH-HBV: VACCINATION OF NEWBORNS – INNOVATIVE STRATEGIES TO HASTEN ELIMINATION OF HEPATITIS B VIRUS IN KINSHASA PROVINCE, THE DEMOCRATIC REPUBLIC OF THE CONGO

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ABSTRACT

Alix Judith Nicole Boisson: VaNISH-HBV: Vaccination of Newborns - Innovative Strategies to Hasten elimination of Hepatitis B Virus in Kinshasa Province, the Democratic Republic of the Congo
(Under the direction of Bruce Fried and Peyton Thompson)

Across the globe, and specifically in sub-Saharan Africa (SSA), viral hepatitis is one of the leading global infectious killers despite the availability of an effective preventative vaccine. The Democratic Republic of the Congo (DRC) introduced the three-dose HBV vaccine (HepB3) in 2007, and yet HBV prevalence remains high, especially among children under age five. HBV exposure at a young age is associated with more severe liver disease; if infected at birth via mother-to-child transmission (MTCT), an infant has a 70-90% chance of developing chronic HBV infection and a 25% chance of mortality. Vaccination, particularly administration of the birth-dose (BD) vaccine against HBV (HepB-BD) within 24 hours of delivery, is one of the most effective tools to interrupt MTCT. Because few SSA countries currently distribute HepB-BD, little knowledge or guidance exists for effective implementation of timely HepB-BD vaccines, streamlined alongside ongoing BD vaccines (oral polio—OPV0—and tuberculosis—BCG).

This study assesses determinants of ongoing BD vaccines' (OPV0 and BCG) uptake at the community (i.e., vaccine stigma, mother's socio-demographic characteristics, and care-seeking patterns) and facility (i.e., clinic's capacity) levels. Guided by community input, the study develops an implementation strategy to overcome barriers and streamline vaccine delivery services by combining HepB-BD with other routine BD vaccines (OPV0 and BCG). Aim 1 evaluates immunization trends using existing survey data from an continuous quality improvement study in 105 maternity clinics uptake in the Kinshasa Province in order to understand barriers to uptake of timely infant vaccines. Aim 2 explores

reported determinants at the community and facility levels and identifies solutions for effective BD delivery by conducting focus groups with key informants and expectant mothers. Aim 3 develops a proposed implementation strategy (streamlining administration of OPV0, BCG, and HepB-BD with an educational initiative) that addresses identified barriers to uptake of birth-dose vaccines. The proposed implementation strategy aims to reduce the prevalence of HBV and other vaccine-preventable illnesses among children in the DRC by developing an effective, streamlined implementation strategy for timely BD vaccine distribution.

This dissertation is dedicated to my grandfather, Dr. James E. Veney, for believing in me.

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LIST OF ABBREVIATIONS

AIC	Akaike information criterion
ANC	Antenatal care
BCG	Bacille Calmette-Guérin vaccine
BD	Birth-dose
BHM	Andersen Behavioral Health Model
CBPR	Community-based participatory research
CDC	Center for Disease Control
CFIR	Consolidated Framework for Implementation Research
CHW	Community health worker
CQI	Continuous Quality Improvement
DRC	Democratic Republic of the Congo
DTP	Diphtheria Tetanus Toxoid and Pertussis
EPI	Epidemiology
Gavi	The Vaccine Alliance
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HepB3	Three-dose hepatitis B vaccine
HepB-BD	Hepatitis B birthdose vaccine
HIV	Human immunodeficiency virus
IM	Intervention mapping
IQR	Interquartile range
LMIC	Low and middle income country
LTFU	Loss-to-follow-up
MCH	Maternal and Child Health

MTCT	Mother-to-child-transmission
NFP	Non-profit organization
OOC	Out-of-cold-chain
OPV0	Oral polio vaccine at birth
PEV	Programme Élargi de Vaccination (National Immunization Program)
PRECEDE	Predisposing, Reinforcing, and Enabling Constructs in Educational/environmental Diagnosis and Evaluation
RCT	Randomized Control Trial
SARA	Service Availability and Readiness Assessment
SCT	Social Cognitive Theory
SD	Standard Deviation
SSA	Sub-Saharan Africa
UNC	University of North Carolina
UNICEF	United National Children's Fund
USD	United States dollar
WHO	World Health Organization

CHAPTER 1 : INTRODUCTION

1.1 Background

Viral hepatitis claims over one million lives annually and now surpasses HIV, tuberculosis, and malaria as one of the leading global infectious killers.[1] The World Health Organization (WHO) estimates that over 60 million individuals in sub-Saharan Africa (SSA) are infected with chronic hepatitis B virus (HBV),[2] and that the majority are unaware that they are carriers.[3,4] An effective vaccine against HBV has been in existence since 2000 in most SSA countries. Despite the availability of the vaccine, HBV causes 200,000 deaths[1] and 350,000 infant cases via mother-to-child transmission (MTCT) annually in SSA.[5] The Democratic Republic of the Congo (DRC) introduced a three-dose HBV (HepB3) vaccine in 2007, yet HBV prevalence remains high among children under age five (2.2%).[6] HBV exposure at a young age is associated with more severe liver disease. If infected at birth, via MTCT, an infant has a 70-90% chance of developing chronic HBV infection and 25% chance of mortality thereafter.[7] Provision of the HBV vaccine series is the most effective (>95%) prevention measure against MTCT, if the first dose is administered within 24 hours of birth (HepB-BD).[8–10] Currently, infants do not receive the first dose of HepB vaccine until 6 weeks in most of SSA, thus leaving them vulnerable to infection via MTCT.

As part of the WHO's Global Strategy to eliminate hepatitis by 2030, many high burden countries in SSA, including the DRC, have committed to providing HepB-BD in the near future, but the vaccine is not yet available in the DRC nor in most of SSA. Health system readiness to administer a timely vaccine, particularly in very resource-limited settings, therefore remains in question. Gavi, the global vaccine alliance, is sponsoring the distribution costs for the HepB-BD vaccine across SSA; the DRC plans to apply for sponsorship on the next round of global distributions. In preparation for the future roll-out of HepB-BD in the DRC, this study will assess the readiness for the uptake of timely HepB-BD in Kinshasa,

the capital of the DRC. In a preliminary study conducted by UNC, in which HepB-BD vaccine was provided free of charge, uptake was only 68.2%, with only 76.7% receiving it on time, i.e., within 24 hours after birth.[11] These rates were comparable to the uptake of other routine birth-dose (BD) vaccines–oral polio (OPV0) and tuberculosis (BCG)–(69.1% for both, unpublished data), suggesting a vaccine delivery problem within the health system.

This study built upon this preliminary work and leveraged the existing research infrastructure in Kinshasa to assess barriers to uptake of ongoing BD vaccines (OPV0 and BCG) at the community (i.e., vaccine stigma, mother's socio-demographic characteristics, and care-seeking patterns) and facility (i.e., clinic's capacity) levels. Because HepB-BD is not yet available in DRC, BCG was used as a proxy for HepB-BD for the purposes of the analyses. Like HBV, tuberculosis is a serious infectious diseases that leads to severe childhood illness and infant mortality.[12,13] BCG is administered at birth to prevent serious illness, and can therefore be used as a proxy for the eventual HepB-BD, which follow a similar pattern. After identifying the barriers, in partnership with local stakeholders, I incorporated newfound knowledge into an implementation strategy, guided by the Implementation Mapping Framework,[14,15] to streamline vaccine delivery services by co-administering the HepB-BD with OPV0 and BCG.

1.2 Significance

1.2.1 Hepatitis B virus (HBV): Inadequate immunization

Across sub-Saharan Africa (SSA), hepatitis B virus (HBV) prevalence is higher than anticipated, despite the widespread vaccination. The primary form of prevention is currently the three-dose HBV vaccine (HepB3), available globally since 1982,[16] but only available in the DRC since 2007. Vertical, or mother-to-child, transmission (MTCT) is a significant contributor to the ongoing HBV epidemic; thus, prevention of MTCT is the cornerstone of any strategy in the fight against HBV. Administration of a birth-dose of HBV vaccine (HepB-BD) within 24 hours of delivery interrupts perinatal transmission in >95% of cases,[8,9] and should be followed with an additional two or three routine doses of HBV vaccine.

Despite its proven effectiveness, only 14 of 54 countries in SSA have introduced HepB-BD within their routine immunization schedules. The DRC has yet to introduce HepB-BD. In recent

years, Gavi, the global vaccine alliance, began sponsoring distribution costs for the HepB-BD across countries in SSA. The DRC is applying to Gavi for inclusion in the next round of global distributions of Hep B-BD by Gavi. In January 2020, a delegation including representatives from UNC, the CDC, WHO, and the Programme Élargi de Vaccination (PEV)—the national vaccine implementation program in the DRC—met with the Deputy Minister of Health to promote universal HepB-BD vaccination in the DRC. These discussions among key stakeholders will continue as the Ministry prepares to apply for Gavi funding. Data from this proposed study will inform childhood vaccination policy by providing a framework for implementing the HepB-BD once it becomes available in the DRC. Because few SSA countries currently distribute HepB-BD, little guidance exists for effective implementation of timely vaccine at the facility level. During a March 2021 stakeholder's meeting hosted by the Global Coalition for the Elimination of Hepatitis, the consensus among global HBV policymakers was that HepB-BD is fundamental for the elimination of HBV in SSA, but that the major challenge of distribution must be overcome in order to successfully implement HepB-BD.[17] This research was significant for developing context-specific guidelines for effective, timely, and streamlined vaccine administration in the DRC, which can be disseminated across other SSA countries alongside HepB-BD distribution.

1.2.2 Delivery in maternal and child health clinics : Vaccine implementation challenges

A pilot study in maternal and child health (MCH) clinics in Kinshasa found that only 68.2% of infants received timely HepB-BD despite its provision free-of-charge,[11] and only 69.1% of infants received birth-doses (BD) of both OPV0 and BCG.[11] Further, another study in Kinshasa found that only 84.7% of infants were fully vaccinated with OPV0 and BCG by 24 weeks of age.[18] Despite OPV0 and BCG being authorized and provided at birth in the DRC, vaccine coverage is still low. Few studies exist to better understand the reasons for low uptake, but studies on ***effective*** HepB-BD implementation approaches in SSA are even more sparse.[19–21] Although prior studies have clearly shown the effectiveness of HepB-BD in preventing MTCT,[22–26] it was only introduced to SSA countries over the last decade, and research evaluating best implementation practices is lacking. Many countries that have included HepB-BD to their national immunization schedules report the vaccine's low or mixed uptake status of the

vaccine. A study assessing timely HepB-BD in countries where HepB-BD was already available found that only 9% of infants who received HepB-BD in the Gambia and 13% in Nigeria were vaccinated within 24 hours of delivery.[19] As noted, this is due to the lack of guidance and importance placed on timely uptake of the vaccine.[2,17]A streamlined strategy to administer timely HepB-BD alongside current BD vaccines, OPV0 and BCG, addresses the low uptake of all three vaccines. Prior interventions had neither incorporated an intervention mapping framework and implementation strategy alongside distribution nor streamlined BD vaccines (HepB-BD, OPV0, and BCG).

This study was important because it used an intervention mapping approach to guide the development of a packaged BD vaccine strategy, beginning with the initial context considerations ***before*** introducing the evidence-based practice to the host setting. This research addressed recurring barriers to timely vaccine delivery by proactively incorporating implementation methods at the study's onset. Further, site-specific knowledge regarding the organizational climate, barriers, and intervention guidance were ascertained through semi-structured interviews with facility-level stakeholders. I explored vaccine hesitancy, knowledge, and care-seeking trends through interviews with expectant mothers. I also sought stakeholders' perspectives from various facility types—private, public, catholic, protestant, not-for-profit, urban, and rural— to consider unique facility-level challenges in developing a relevant, applicable, and sustainable implementation strategy.

1.2.3 Barriers and effective strategies for vaccine implementation

It is well established that childhood immunizations against diseases such as hepatitis B, tuberculosis, and polio avert 1.2 million deaths each year.[27] As such, childhood immunization remains one of the most cost-effective public health measures globally. However, SSA consistently faces high under-five mortality rates. This is mainly attributed to diseases that are vaccine-preventable.[28] Notably, the DRC is one of ten countries that, combined, account for 60% of unvaccinated children worldwide.[29] A systematic review on the barriers to childhood immunization in SSA found three primary barrier levels: parental/caretakers barriers, health system barriers, and providers barriers—with the majority of their findings falling within the former two categories.[30] The two major barriers among parents and caretakers

are: parents not being knowledgeable about immunization[31,32] and lack of trust in vaccines.[32,33] At the health system level, factors impeding the delivery process of vaccines include shortages at the health facilities[31,32,34] and transportation of vaccines.[31,34] Finally, lack of knowledge among facility staff[31,34] and policies restricting the use of multi-dose vaccine vials with a short shelf-life for fewer children than are available doses[34,35] were reported as barriers at the provider level.

Previous vaccine uptake studies used conceptual models such as Andersen's Behavioral Health Model (BHM) and the Consolidated Framework for Implementation Research (CFIR) to examine the factors associated with the utilization of immunization services.[36,37] Therefore, I used both to identify challenges within this specific study's context. By conducting a needs assessment to identify the determinants to timely birth-dose vaccines that exist in Kinshasa, I utilized an intervention mapping approach to targeted challenges in order to develop an approach for successful streamlining of timely birth-dose vaccines. The needs assessment consisted of a literature review of experiences introducing HepB-BD in other contexts (Chapter 2), a quantitative study (Chapter 3 and aim 1), and a qualitative study (Chapter 4 and aim 2) that guided the development of an intervention mapping approach (Chapter 5 and aim 3).

1.2.4 Kinshasa Province: Uniquely receptive environment

Kinshasa's MCH clinical care system offers a uniquely receptive and collaborative environment in which to introduce this study. A continuous quality improvement (CQI) initiative at 105 maternity centers throughout Kinshasa Province, DRC (NIH R01 HD08799306, PI Yotebieng)[38,39] laid the groundwork for more rigorous implementation initiatives. The studies fostered a receptive environment within the healthcare delivery system. In order to develop a context-specific strategy for BD vaccinations, this study leveraged existing partnerships, enabled collaboration within the clinical healthcare network, and built upon the organizational infrastructure.

In conclusion, the context-specific implementation strategy was significant by providing evidence to improve timely BD vaccine delivery in Kinshasa, DRC, which can be adapted to other low-resource settings.

1.3 Research aims

Aim 1. To determine the relationship between mother-infant pair characteristics and quality facility immunization care on timely uptake of existing BD vaccines (OPV0, BCG) in the DRC. This was a secondary analysis of data from an NIH-funded study with 2,500 mother-infant pairs enrolled across 105 health facilities (three from each of the 35 health zones) in Kinshasa who were followed for at least one year postpartum. All participating facility administrators were also surveyed for facility service availability and readiness.

Aim 2. To gain an in-depth understanding of key contextual factors explaining barriers to effective BD vaccine uptake through semi-structured interviews with expectant mothers and informants. Leveraging existing research infrastructure, I designed and conducted semi-structured interviews with facility-level key informants and expectant mothers, to explore barriers and facilitators to timely BD vaccine uptake. I also solicited stakeholders' perspectives for ideal implementation solutions for streamlining BD vaccines.

Aim 3. To develop an implementation strategy (streamlining birth-dose vaccine administration of OPV0, BCG, and HepB-BD alongside an educational initiative) for the uptake and timely administration of birth-dose vaccines using an intervention mapping approach. I used identified determinants to infant BD vaccines and the six intervention mapping steps to develop of an implementation strategy guiding effective, complete, and timely BD vaccine uptake.

The long-term goal of this study is to reduce the incidence of HBV and other vaccine-preventable illnesses among children in the DRC by developing an effective, streamlined implementation strategy for timely BD vaccine distribution in facilities. This study provided a foundation for the future roll-out of a universal HepB-BD vaccine. This seminal research provided guidance for SSA countries to effectively introduce HepB-BD, streamline BDs, and decrease the national prevalence of HBV infection among infants.

1.4 Innovation

This study was innovative in several ways: First, it established an empirically driven and context-specific implementation strategy for HepB-BD uptake ***before*** its introduction and scale-up in the DRC. Historically, interventions fall short in low-resource settings because implementers often overlook the preliminary groundwork for learning the intervention's environment.[40] This study was grounded in implementation science provided by the theoretical frameworks of the Andersen Behavior Health Model (Aim 1), CFIR (Aim 2 & 3), and the Intervention Mapping Framework (Aim 3), which guided the systematic uptake of evidence-based practice into routine practice. Second, the study incorporated input from expectant mothers and key stakeholders to develop implementation strategies. While SSA-based qualitative studies have explored determinants for supporting infant vaccine implementation efforts,[41,42] to my knowledge, no such studies explored determinants to implementing HepB-BD and other BD vaccines in MCH clinics. Data on determinants of vaccine delivery ascertained through semi-structured interviews incorporated essential stakeholders' perspectives. Integrating perspectives of both expectant mothers and key informants ensured a sustainable and scalable intervention and contributed greatly to implementation research in SSA.

CHAPTER 2 : IMPLEMENTATION APPROACHES FOR INTRODUCING AND OVERCOMING BARRIERS TO HEPATITIS B BIRTH-DOSE VACCINE IN SUB-SAHARAN AFRICA

2.1 Introduction

Six years after the World Health Organization (WHO) African Regional Committee convened to develop a hepatitis elimination strategy, hepatitis B virus (HBV)-related mortality remains high at 200,000 deaths per year in sub-Saharan Africa (SSA).[1,43] The committee identified the prevention of HBV in children as a priority, aspiring to lower seroprevalence of hepatitis B surface antigen-positivity among children aged younger than 5 years to less than 2% by 2020 and less than 0.1% by 2030.[44]

Mother-to-child transmission (MTCT) is a significant driver of the ongoing HBV epidemic. HBV exposure at a young age is associated with more severe liver disease; if infected at birth, an infant has a 70%–90% chance of developing chronic HBV.[2,7] The WHO estimates that chronic HBV affects more than 100 million individuals in the African region.[2] With an estimated risk of MTCT of 38.3% among women who have HBV, over 350,000 infants are infected annually via MTCT in the African region.[5] Thus, preventing MTCT of HBV is a cornerstone of effective strategies against the HBV epidemic in SSA. The birth-dose of HBV vaccine (HepB-BD) is the most effective (>95%) prevention measure against MTCT if administered within 24 hours of birth[8,9] and followed by completion of two or three routine immunizations.[10] Despite the availability of the HBV vaccine since 1982, few SSA countries administer the birth- dose vaccination due to implementation challenges and a lack of HBV burden awareness.[16]

The global health community understands the importance of the HepB-BD vaccine, which has led to Gavi, the Vaccine Alliance, sponsoring distribution costs for the HepB-BD vaccine across SSA.[45,46] Though these efforts are ongoing, as of April 2021, only 13 of 48 countries (27%) in SSA have

introduced HepB-BD,[47] falling short of the WHO Africa Regional Committee goal of at least 25 countries by the end of 2020 (**Figure 2.1**).[47,48] Vaccination schedules for pentavalent, which includes the HBV vaccine, vary between countries. Some SSA countries still use a standard vaccine schedules (three doses of hepatitis B vaccine), typically given at six, 10, and 14 weeks of life. Although this schedule is practical, immunizing infants beginning at 6 weeks does not prevent vertical transmission from HBV-infected mothers to their infants.

Barriers to HepB-BD implementation in SSA exist across the supply chain and care continuum. Key barriers include lack of evidence of HBV seroprevalence and rates of MTCT, financial costs of vaccine distribution, insufficient cold-chain storage, lack of trained community health workers (CHWs), and a high proportion of at-home births.[2] Given these challenges, HepB-BD implementation practices must be in place alongside vaccine distribution to ensure effective vaccine delivery, especially in rural and under-resourced settings. We discuss existing determinants of HepB-BD uptake in SSA countries at the policy, facility, and community levels and propose solutions for stakeholders to introduce HepB-BD in low- and middle-income countries (LMICs). While the literature often discusses solutions at the policy and facility levels, we argue that researchers and stakeholders should place more emphasis on community-level interventions, especially in highly rural contexts.

2.2 Materials and methods

Iterative scoping reviews were performed using PubMed to identify articles published between January 2010 and August 2020 that discussed methods for country-level implementation of HepB-BD. We used the following key terms in the search: “hepatitis B birthdose vaccination,” “HepB-BD,” “hepatitis B birth-dose vaccination,” “hep b birthdose,” and “HBV birth-dose vaccination.” Because immunization system implementation science is relevant to HepB-BD implementation efforts in LMIC settings, we also reference this broader swath of the scientific literature. Literature was drawn only from articles published after 2010 to maintain relevance, as evidence-based immunization implementation science is a fast-developing field. In addition to articles identified through PubMed, we also extracted

findings from gray literature, case studies, and research performed in SSA, but we expanded the search to Southeast Asia (SEA), in part due to the successful introduction of HepB-BD in SEA.

2.3 Results

In all, 598 reports were identified, and 39 were relevant and reviewed for this publication (Table 2.1). To be included, articles had to describe research introducing the HepB-BD within a low-resource country or data-backed guidance for the inclusion of HepB-BD. Of articles included, 13 reports focused solely on SSA. We categorize vaccine uptake determinants in three domains with immediate relevance to HepB-BD implementation: policy-, facility-, and community-level barriers and solutions. Major themes, barriers, and solutions are outlined in **Table 2.1**.[20,49–65]

2.3.1 Policy level

The first step toward HepB-BD implementation requires the development of clear policy recommendations and changing national vaccine schedules to include HepB-BD. Advocates and other stakeholders must first synthesize setting-specific evidence of HBV prevalence and solutions. Next, policymakers and other relevant players must be engaged to convey the need for HepB-BD and relevant policy change. These efforts must address two persistent barriers to national policy change: a lack of of political will and insufficient evidence.

Lack of political willingness: Advocacy

Countries often lack the political will to enact policies that mandate HepB-BD within 24 hours of birth, ensure vaccine availability at every facility, and ensure an adequate supply chain of HepB-BD.[66] A lack of awareness of the vaccine's effectiveness and insufficient advocacy for HepB-BD often contribute to the policy-level determinants. Vaccine supporters can foster political will by engaging relevant stakeholders, decision-makers, and effective in-country advocacy groups across all health care systems and socioecological levels.

Engaging a united interdisciplinary group of stakeholders is more effective for supporting multilevel HepB-BD implementation efforts to address existing barriers. Primary stakeholders may include ministries of health and finance, donor agencies, external academic and nongovernmental or

multilateral organizations involved in the programming, and drug manufacturers. Relevant literature also stresses the importance of other groups in achieving political commitment for in-country HepB-BD uptake, such as professional societies, medical associations, and community and religious leaders.[67]

São Tomé and Príncipe and Nigeria demonstrated success by calling on the private health sector, physicians and nurses, and hepatology associations in advocacy efforts to steer the government towards introducing HepB-BD.[3,68] Although stakeholder buy-in is crucial in any setting, country-specific groups and associations differ by context, and setting-specific partners should be identified and supported. This collaborative approach is required to develop an effective and sustainable intervention with HepB-BD champions at every socioecological level. To achieve uptake, stakeholders should understand the importance of advocating alongside partners in different but related sectors such as cancer prevention disease-specific[2,3] or safe motherhood care advocacy group. Strengthening the case for universal HepB-BD by engaging diverse stakeholders will press decision-makers to pledge political commitment.

Finally, advocacy among decision-makers for national policies to mandate the timely delivery of the vaccine within the 24-hour requirement and the pre-positioning of vaccines in the maternity wards are both critical to ensuring high uptake of HepB-BD. A study in Nigeria provided recommendations for improving HepB-BD uptake among infants.[66] During the time of the study, national-level policymakers in Nigeria had not introduced a policy mandate. While the National Primary Health Care Development Agency in Nigeria recommends that all infants receive HepB-BD, the immunization window ranges from the birth of the newborn to two weeks of age. Compared to a similar study in the Philippines that had introduced a policy mandating infant immunization within the 24-hour window, the uptake of HepB-BD in Nigerian hospitals (26.2%) was much lower than in the Philippines hospitals (87%).[66] Therefore, a study's primary takeaway was to mandate a policy for HepB-BD immunization of newborns within 24 hours of delivery.

Lack of political willingness: Affordability

In addition to advocacy, affordability and cost-effectiveness are key determinants of political willingness. Deceleration of vaccine uptake occurs due to financial uncertainty or concern over the

availability of resources.[3] Quantitative impact estimates are recommended for policymakers, as they solidify plans for start-up, maintenance, and opportunity costs. Cost-effectiveness and scalability analyses can be achieved using models derived from country-specific pilot studies or similar studies from neighboring countries.

Experience from other SSA countries can be used to demonstrate a favorable return on investment. Preliminary research confirms the affordability of HepB-BD, which costs only US$0.20 per 10-dose vial, making it one of the least expensive vaccines available.[45,67–69] Various studies analyze the affordability of HepB-BD both in SSA and in SEA.[10,21] A notable study comparing three strategies of universal HepB-BD, targeted HepB-BD, and the pentavalent vaccine alone indicated that the addition of a universal HepB-BD prevented the largest number of additional MTCT cases and was the preferred strategy at a willingness-to-pay threshold of US$150 per infection prevented.[70] Success stories from other SSA countries are also useful in achieving political commitment because they demonstrate clear return-on-investment through sustained improvements in coverage rates following policy change. Empirical successes include the introduction of HepB-BD into the Gambia in the 1990s, Botswana in the 1990s, Namibia in 2014–2015, and São Tomé and Príncipe in 2019.[19,21]

The vaccine's scalability improves returns[10,21] but also introduces challenges in building adequate vaccine reserves and meeting costs of large-scale distribution. A solution is to apply for sponsorship from Gavi,[45,46] support that is especially important when a government lacks budgetary flexibility. During the coronavirus disease (COVID-19) pandemic, donors' financial commitments have shifted from noncommunicable to infectious diseases, especially in LMICs. Countries around the world may turn to LMICs to guide how best to tackle infectious diseases. While global stakeholders are recognizing the risk of communicable diseases, maintaining regular vaccinations is now more critical than ever to avoid the emergence of twin epidemics.

Need for effective recommendations

Consensus recommendations for HepB-BD implementation are lacking but necessary to translate political will into effective action. We suggest developing site-specific recommendations that draw upon research and literature, international guidelines,[71] and feedback from diverse stakeholders, including people living with HBV.[72] We propose two ingredients for building a strong recommendation: a well-constructed strategy based on local experience and the application of knowledge gleaned from implementation theory perspectives. It is crucial to develop a comprehensive implementation strategy from the outset that is grounded in theory and uses the latest innovations to overcome any barriers to HepB-BD uptake.[40] Public health policies and practices disseminated by WHO are a logical starting point and are guided by the most comprehensive health research knowledge to improve global health worldwide.[73,74] Additionally, research from neighboring and comparable settings should be used to develop recommendations.[71] Finally, implementers should continuously revisit and evaluate HepB-BD recommendations to incorporate recent innovations and improve any implementation implementation determinants.[75]

2.3.2 Facility level and logistics

The primary delivery site for HepB-BD is health facilities, which include public hospitals, clinics, health centers, and private health facilities. Given the diversity of settings where HepB-BD might be administered, attention should be given to setting-specific challenges such as lack of community health workers' (CHW) knowledge/training on HBV and prevention through vaccination, logistical challenges in administering the vaccine within 24-hours of birth, difficulty in tracking newborn vaccine status, vaccine stockouts, systemic vaccine stigma, local opportunity costs, and the negative impact of user fees for immunizations.

Knowledge and training of health workers

Provider-level HepB-BD knowledge in health facilities is an essential driver of vaccine uptake. Knowledge may be lacking at two levels: recognizing the benefits of HepB-BD and general training for

timely administration of the vaccine.[19,76] Lack of awareness of vaccine benefits, stigma, and gaps in knowledge among CHWs, as well as variable vial size and concern for wastage, may hinder HepB-BD uptake.[19,76]

One solution to address the lack of awareness and overcome stigma about HepB-BD is educating staff on the vaccine's benefits and shortcomings. Sharing success stories demonstrating HepB-BD's effectiveness can educate and motivate facility staff and cultivate HepB-BD champions.[76] Data should be shared on the only reported negative consequence of HepB-BD—an anaphylactic reaction caused by previous HBV exposure—which rarely occurs after about one in one million doses of the vaccine.[19] Alleviating any fear or bias against vaccinating newborns and ensuring provider buy-in is critical for introducing HepB-BD in their communities and ensuring its sustainability.

While HepB-BD's narrow time window may reduce provider willingness to adopt the vaccine, providing straightforward written guidelines, conducting initial and refresher training, and providing supportive supervision can ease the burden of the vaccine's specific logistical challenges.[19] Training should occur in all facilities within a community—whether publicly or privately operated. The complete multidisciplinary workforce should be involved to ensure vaccine coverage for all involved in the training/vaccination process in anticipation of wide-scale distribution.[19,67] Training objectives may include assigning vaccine-related duties to a specific role. A study in China determined the success of a strategy incorporating the vaccine-administration role to the obstetrician, clearing up potential confusion in terms of vaccination responsibilities.[19,67] A Nigerian study found that vaccine oversights were vastly avoided when staff completed a vaccine-related checklist before discharging mother-infant pairs.[19] Finally, staff may be trained to streamline the HepB-BD vaccine with the vaccines for TB and polio to improve timely vaccination. To date, four SSA-based studies have assessed the effect of all three vaccines outside of the 24-hour window, and five studies have measured the rate of individual vaccine uptake within 24 hours of delivery, but no study has evaluated the effect of streamlining the three vaccines at birth.[77] The WHO confirms that the three vaccines do not interfere with one another's immune

responses.[74] Since the facility already offers one or both vaccines, health staff may leverage existing training experience for administering HepB- BD.[74]

Another challenge to administering the vaccine in the 24-hour window is the various vial sizes (single-, two-, six-, 10-, or 20-dose vials).[74] In the case of a small number of deliveries within a given period, facility staff often wait to open multi-dose vials to avoid wastage. To address this issue, vaccine suppliers could consider making available a combination of single-dose and multidose vials, such that vial size would be appropriate for both smaller facilities with fewer daily deliveries and larger facilities with multiple daily deliveries. Facility staff should receive training on a protocol specific to their facility's volume of deliveries and vial sizes. Some would argue that vials should be opened regardless of concerns for wastage because the benefits of timely vaccination far outweigh the risk of wastage.

Short window for administering vaccine

The HepB-BD vaccine's short window for administration is perhaps its greatest implementation challenge. Administering timely vaccine is difficult for births that occur in facilities. It is even more pronounced for infants born outside of facilities (see discussion of at-home births in the community-level section). Maternal hesitancy and lack of awareness of HBV and the HepB-BD may further complicate efforts to administer timely infant vaccination in facilities. A mother's hesitancy may be due to general or HepB-BD-specific vaccine hesitancy, cost, or other factors, but the short window for vaccine administration requires an effective approach to educating mothers during pregnancy and generating maternal buy-in quickly.

The WHO suggests keeping mothers in the delivery ward for at least 24 after their child's birth, a practice not widely adopted in SSA health facilities.[19] A study in São Tomé and Príncipe reported combining two approaches: for mother-infant pairs to remain in the postnatal ward for longer than one day and to offer vaccines in the maternity ward for on-site vaccination. This joint approach yielded improved accessibility, greater convenience, and increased HepB-BD uptake.[19,21]

User fees

Cost is a critical barrier to consumer uptake (in addition to the previously discussed affordability consideration on a national level) that must be carefully addressed. User fees prevent families from taking their newborns to certain clinics or to be vaccinated at all. While vaccines in many countries are provided free-of-charge to facilities, most providers request a payment for a vaccination card to cover administrative and workforce costs for immunization services and monitoring during the infant's first year of life.[18]

Removing monetary barriers through small cash incentives or reducing user fees for immunization can improve uptake in the short-term,[18,78] though it may not be a sustainable long-term option. A study in the Democratic Republic of the Congo demonstrated that uptake of the rotavirus vaccine was 99% if the vaccine was provided free of charge.[11] In the long term, policymakers may consider using national- or district-level budgets to subsidize administrative costs accrued by facilities to improve regular immunization rates among infants.

Tracking systems

The current SSA practice for complete HBV immunization includes the monovalent HepB-BD vaccine followed by three additional doses of pentavalent vaccine at six, 10, and 14 weeks of life. A country's administrative capacity for tracking an infant's immunization progress may impede the vaccine's success.[2,19] A review including SSA countries that administer HepB-BD reported that the vaccine's documentation is suboptimal across the continent.[2] A lack of adequate reporting infrastructure (data health information systems)[67] and failure to comply with vaccine recording by facility staff may explain these findings.

The tracking system may be improved by standardizing all HepB-BD-related immunization-reporting tools, such as immunization cards, registers, and data management systems, to include HepB-BD-specific administration details. Tracking of doses administered also helps to inform supply management of HepB-BD at the facility level.[74] The use of standardized tools can calibrate and improve data monitoring efforts in LMICs.[67] Furthermore, monitoring and evaluation systems must be in place to

ensure that health workers are appropriately using the developed tracking tools. Training, protocol utilization, and regular assessment of health worker compliance in tracking vaccinations can increase compliance of vaccine documentation across the country.

Vaccine storage and stockouts

Health facility administrators should safeguard access to vaccines by addressing both limited storage space and stock-out determinants. Botswana, The Gambia, Mauritania, Namibia, and Nigeria reported stock-outs and limited vaccine sessions as barriers to timely access and administration of HepB-BD.[2,66] Poor communication between the immunization and maternity wards can further hinder vaccine logistics at the facility level.[66] A final logistical barrier is reaching remote rural villages with vaccines.[3,79]

Solutions to vaccine stock-outs and limited vaccine sessions include storing the vaccine in existing cold chains, preferably in labor wards, establishing standing orders for the vaccine, and leveraging partnerships with vaccine distributors.[11]Facilities can use existing storage space or store HepB-BD in the labor ward. Health officials in many SSA countries already recommend that infants receive the BCG and oral polio vaccines at birth, and both have achieved high rates of uptake.[18] Storage space in health facilities may therefore already exist, and introducing HepB-BD to the existing cold-chain storage unit may not prove to be a significant disruption.[19,68] One study in the Democratic Republic of the Congo leveraged the existing Expanded Programme on Immunization cold-chain infrastructure to provide HepB-BD but uncovered challenges in delivering the vaccine in a timely manner.[11] A São Tomé and Príncipe study demonstrated that storing the HepB-BD in labor wards is another effective approach to increase HepB-BD rates.[21] However, this may prove a challenge in some settings where maternity wards are not equipped for vaccine-specific storage requirements. Therefore, effective communication and coordination are needed between immunization clinic staff and maternity staff to ensure that infants receive timely vaccination. National mandates to vaccinate in maternity wards could help facilities and staff to shift birth-dose administration from immunization clinics to maternity wards.

SSA countries that currently administer HepB-BD also reported stock-outs as an implementation barrier. A solution to frequent stock-outs employed in the Western Pacific was establishing standing

orders for HepB-BD with the manufacturer.[45,67] Vaccine rates increased due to regular shipments of HepB-BD in place of need-based shipments.

Finally, a public-private partnership with Gavi can facilitate logistics, avoid stock-outs, and lower vaccine costs.[68] Gavi has overseen the distribution of many vaccines, including HepB-BD, across the globe and can therefore provide empirical knowledge of supply and logistics for recent adopters of HepB-BD. In addition, national vaccination initiatives are advised to partner with private facilities where a substantial portion of deliveries occur to allow private providers to obtain routine HepB-BD free-of-charge, in line with public providers. The DRC provides vaccines for free through public, private, and faith-based facilities to increase immunization reach.[80] In the Philippines, 20% of deliveries occur in private facilities, so private providers received free vaccines in exchange for data on doses administered.[81] This approach will increase the accessibility of the HepB-BD vaccine for mother-infant pairs who seek care across different types of facilities.

2.3.3 Community level

SSA countries are predominately rural, presenting a unique access-based barrier. In SSA, marginalized people who must travel more than two-hours to access emergency public hospital facilities makeup 29% of the population, of whom 28% are women of childbearing age. In fact, hospital facility access is only widely available in 16 of 48 African countries.[82] South Sudan presents the most extreme case globally, with 75% of its population living further than a two-hour walk away from a hospital facility.[82] Given these statistics, immunization system strengthening cannot happen solely at centralized health facilities. Instead, efforts must also extend to reach mothers and newborns at the community level.

A high proportion of SSA infants are born at home and therefore do not have access to HepB-BD.[19,83] Low HepB-BD adherence rates are largely due to the lack of formal outreach programs to vaccinate newborns at home or to refer mother-infant pairs to nearby facilities.[19,84] Another determinant is the lack of access to health facilities and trained CHWs to administer the vaccinations. Proposed solutions include improved maternal involvement, CHW involvement, and innovative technologies.

Maternal involvement

The mother-infant pair is integral to the success of any immunization implementation approach. Health officials often consider at-home births inadvisable. However, most home births occur not because the mother refuses to visit a health facility but because she lacks access to a facility.[85] Therefore, educating mothers about the importance of timely HepB-BD must occur at both the facility and the community levels. Decision-makers should consider community-level interventions focused on health behaviors. For instance, cultural barriers may impact the time taken to bring an infant to a facility after delivery. In The Gambia and Nigeria, where at-home birth rates are high, mothers wait seven days to name their infants before visiting a facility, hindering timely administration of HepB-BD.[67]

While the prevalence of home births may be attributed to cultural, religious, or access-related issues, most women eventually bring their newborns to facilities after birth. Health officials should consider leveraging these visits after a home birth to deliver HepB-BD as soon as possible and educate mothers about the importance of a timely visit.

Additional targeted interventions include raising awareness within communities and building trust by leveraging existing civil society networks, improving understanding, and reminding caregivers of the importance of HepB-BD.[75] These initiatives allow the most crucial contributors in the implementation formula, the mothers, to have the resources necessary to understand the importance of timely vaccination.

Antenatal care facilities are an essential resource to educate pregnant women about the importance of HepB-BD. More than 90% of SSA women have had at least one antenatal care visit; this is an opportune time to teach women about in-facility delivery benefits and the importance of timely HepB-BD.[19,67] However, community-based educational initiatives should be simultaneously promoted by establishing a gathering place within a community or using radio or social media campaigns to disseminate vaccination information to expectant mothers. Exposure to information during pregnancy has a positive impact on HBV knowledge and can be achieved by incorporating targeted education programs or improving existing educational material to include targeted HepB-BD information.[86] A Nigerian study delivered an educational initiative for expectant mothers, providing information on HBV burden in-

country and across SSA, vaccine benefits, and the timing of the HepB-BD vaccine.[66] The study found that immunization education and awareness successfully increased HepB-BD uptake. Information strategies should focus on the vaccine's safety and be delivered by CHWs to increase HepB-BD uptake.[87]

A final approach that is often overlooked in the HepB-BD-related literature is the use of home-based records as a potential solution to increase immunization coverage at the community level. Home-based records, vaccine records that mothers can carry out of the health facility with them, can facilitate mothers' knowledge and detection of health problems and can encourage continuity of care and completion of the four doses of HBV vaccine.[88]

Community health worker involvement

Significant vaccination obstacles exist during at-home births due in large part to fissures in communication between community members and health facilities. CHWs can bridge these fissures, improving vaccine awareness and knowledge in a community.

CHWs can act as intermediaries to provide relevant delivery and vaccination information to mothers, other family members, and health facilities. Notably, CHWs are a critical source of health information for pregnant women and mothers, as well as other community members, in rural locations. CHW-led home visits are vehicles for reaching women who do not have access to antenatal care in rural communities.[75] Home visits allow skilled birth attendants to educate expectant mothers, identify potential births in the communities, attend the deliveries,[67] promote institutional deliveries,[67,89] and refer the mother-infant pair to nearby facilities for vaccination and other services. In addition, many SSA countries have regular outreach services to provide vaccinations and other services to children living in hard-to-reach villages.[90] CHWs may even travel to remote communities for scheduled visits and to provide door-to-door immunization for infants.

Given that CHWs are the liaison between communities and a health facility, strong communication ties between CHWs and health facilities are crucial to vaccine uptake. This importance is highlighted by relevant SEA studies,[75,79] which reported a cost-effective and practical strategy through

regular district-level training. CHWs visit health facilities to receive regular training and share learnings with their communities.[75,79]A Republic of Kiribati study reported that educating CHWs led to an 18% increase in timely HepB-BD delivery across the island.[91] CHWs can further advocate for HepB-BD by involving religious and community leaders and by engaging men and other family members to influence community norms and acceptance.[74] CHWs play a vital role in the success of a vaccine intervention, and incentives to collaborate come either from having a stake in their community's well-being, from per-diems for vaccine interventions,[91] or encouraging referral of mother-infant pairs to health facilities.[74] CHWs are often the primary representative of the health care system at the community level. As such, their involvement is essential to ensure community buy-in of HepB-BD.

Evidence-based innovations to reach communities

Beyond knowledge barriers, logistical barriers to HepB-BD delivery exist at the community level. HepB-BD coverage in rural communities remains low due to HepB-BD's cold-chain storage requirements; the vaccine must be kept between 2°C and 8°C.[3,79] Increased vaccine coverage is now possible due to scientific (use of out-of-cold-chain or controlled- temperature chains) and technological (mHealth) innovations to address geographic barriers to access of HepB-BD.

Various studies have examined the advantages of vaccine storage at ambient temperature at the point of service delivery.[74] Studies in SEA exploring solutions to reach rural at-home births found that HepB-BD can be kept out-of-cold-chain (OCC) at a temperature of up to 37°C for one month without loss of potency.[2,3,92] While some countries have used OCC approaches to transport other vaccines,[93] this innovative approach is novel in SSA and has never been incorporated into a model to reach at-home births within a 24-hour window.

WHO recommends taking the OCC approach further by transporting and storing vaccines in stable temperature carriers—controlled-temperature chains (CTCs).[74] This approach increases coverage, reduces resource wastage, and increases the outreach of HepB-BD.[74] CTCs require several conditions to maintain the vaccine outside the traditional 2°C to 8°C cold chain, including single removal from the cold chain into temperatures not exceeding 40°C.[74] Compared with the OCC approach, this innovation halves

the cost, reduces the risk of freezing the vaccine, and more effectively protects vaccine quality.[74] However, unlike traditional OCC technology, CTCs require additional CHW training.[2] CTC trials conducted in Laos and the Solomon Islands tested the effect of CTCs for HepB-BD transport and storage and reported increases in vaccine uptake by 28%[94] (Laos) and 150%[95] (Solomon Islands). Delivering vaccines using CTCs has strong potential to increase vaccine coverage, especially in rural, hard- to-reach communities. CTCs are not currently available as licenses and pre qualifications are pending for HepB-BD.[45,74]

Studies have also reported coupling mHealth aspects with OCC methods for HepB-BD delivery. A Laotian study used mobile phones provided to CHWs to track at-home deliveries, real-time stock-outs, and to monitor cold-chain temperature following OCC vaccine delivery. The study demonstrated a significant improvement in the proportion of children receiving HepB-BD-related home visits.[91] Multifaceted innovations could im- prove HepB-BD coverage in rural villages.

2.4 Discussion

We summarize key determinants of HepB-BD implementation at the 3 levels of policy, facility, and community in SSA (Table 2.2). We highlight barriers to timely uptake of the vaccine at all levels, as well as evidence-based solutions to these barriers. Any implementation strategy for HepB-BD must consider all three levels and must be adapted to the local context. SSA countries should model their implementation strategies on the success stories of HepB-BD introduction in SEA.[52,79,87,91] There are a few key examples of successful HepB- BD introduction in SSA,[19,66,68] but there is much room for improvement since only 13 of 48 countries have incorporated HepB-BD into their routine vaccination schedules.

Several areas stand out as “low-hanging fruit” for further research and development. Although SSA countries acknowledge the need for buy-in for HepB-BD at the political and facility levels, health officials and researchers continuously understate the mother’s role in HepB-BD implementation approaches. In Nigeria, Botswana, and The Gambia, where HepB-BD policies exist,[21,91] the literature

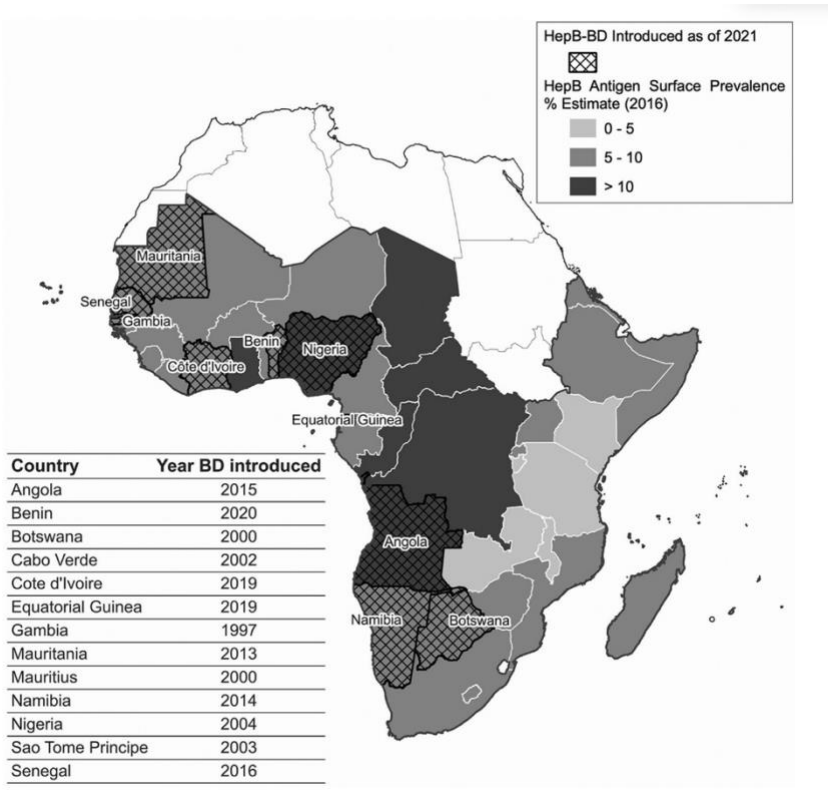
focuses predominately on results measured at the facility or national level, rather than at the community level. Notably, significant gaps exist in the literature when addressing the three sublevel themes discussed at the community level: maternal involvement, CHW involvement, and evidence-based innovations.

SSA is highly rural, and universal coverage of HepB-BD will prove impossible without reaching at-home births. We suggest future research be geared toward community-level HepB-BD implementation approaches leveraging CHWs and prioritizing mothers. Proposed research includes testing and leveraging evidence-based innovations already identified in SEA[3,45,67,79] to improve vaccine reach to home-births and involving mothers in the implementation process. Despite these potential benefits, existing literature does not address these service end-user approaches in a HepB-BD-specific context. Finally, scientific (OCC vaccines) and technological (mHealth) innovations can drastically improve vaccine uptake in at-home births.

2.5 Conclusion

Published literature on HepB-BD immunization implementation in SSA countries is limited, but success stories from diverse settings confirm that HepB-BD is feasible. Synergy must exist between the three levels of policy, facility, and community for SSA countries to effectively implement a universal HepB-BD immunization policy. Literature about the mother's role at the community level is strikingly scarce, and efforts to leverage community-level resources have been limited. To achieve successful HepB-BD introduction in African settings, more attention must be paid both by policymakers and researchers to the mother’s and the community's role in vaccine uptake.

Figure 2.1 Choropleth map demonstrating HepB-BD coverage and hepatitis B surface antigen prevalence in SSA[a]



Country	Year BD introduced
Angola	2015
Benin	2020
Botswana	2000
Cabo Verde	2002
Cote d'Ivoire	2019
Equatorial Guinea	2019
Gambia	1997
Mauritania	2013
Mauritius	2000
Namibia	2014
Nigeria	2004
Sao Tome Principe	2003
Senegal	2016

Abbreviations: HepB-BD, hepatitis B birth-dose; Hep B, hepatitis B; BD, birth-dose.

[a]This figure presents the countries in sub-Saharan Africa (SSA) that have introduced the birth-dose of HBV vaccine (HepB-BD) and estimates of HepB antigen surface prevalence by country. SSA islands not depicted in the map include Cabo Verde, Comoros, Mauritania, Mauritius, São Tomé and Principe, and Seychelles. The table lists the year of HepB-BD introduction for all SSA countries offering the vaccine by 2021. All classification intervals are left closed and right open. Geographical boundaries obtained from Global Administrative Areas version 3.6

Source: Razovi-Shearer et al.; Njuguna.

Table 2.1 HepB-BD uptake themes discussed in the empirical literature (N =42)

Author(s)	SSA Specific	Pol. Wil.: Advocacy	Pol. Wil.: Afford.	Effective Recs.	Knowledge / Training of HWs	Quick Vaccine Admin.	Tracking System	Vaccine Stockouts	Mother Involvement	CHW involvement	Evidence-Based Innovations
Anderson et al., 2018.	X		X								
Awuku, Yeboah-Afihene, 2018.	X	X				X					
Beigi et al., 2014.									X		
Boa et al., 2017.	X	X	X								
Breakwell et al., May. 2017.							X	X			X
Breakwell et al., Nov. 2017.	X	X	X	X	X	X	X	X	X	X	X
Centers for Disease Control and Prevention (CDC), 2013.					X			X		X	
Chang et al., 2019.						X					
Dionne-Odom et al., 2018.	X	X	X	X	X	X		X			X
Giao et al., 2019.									X	X	
Ginzberg, Wong, Gish, 2018.				X		X					
Hagan et al., 2019.			X				X				
Hambridge et al., 2019.	X			X							
Howell, Lemoine, Thursz, 2014.	X	X	X	X							
Jourdain, Ngo-Giang-Huong, Khamduang, 2019.				X							
Kolwaite et al., 2016.										X	X
Lemoine, Thursz, 2017.	X	X	X								
Li et al., 2017.					X			X		X	X
Mak et al., 2018.											
Miyahara et al., 2016.	X					X			X		
Moturi et al., 2018.	X					X				X	
Nayagam et al., 2016.		X	X	X							
Nayagam et al., 2016.		X	X	X							
McMahon, 2016.				X	X					X	X
Nguyen et al., 2019.									X		
Okenwa et al., 2019.	X	X		X	X	X		X	X		
Pham et al., 2018.					X	X					
Pham et al., 2014.									X		
Reardon et al., 2019.	X		X								
Scott et al., 2018.			X								
Sobel et al., 2011.				X	X			X			
Spearman, 2018.				X							X
Spearmen et al., 2017.	X				X		X	X	X	X	
Tamandjou et al., 2017.	X	X	X			X			X	X	X
Wiesen et al., 2014.					X		X	X	X	X	
Wiesen, Diorditsaa, Lib, 2016.				X							
Woodring et al., 2019.						X			X		X
(WHO), 2019.				X	X	X	X	X	X	X	X
Xeuatvongsa et al., 2016.										X	X

SSA Sub-Saharan Africa, Pol. Wil. Political Willingness, Recs. Recommendations, HW Health Worker, CHW Community Health Worker

Table 2.2 Potential barriers and solutions to HepB-BD uptake in SSA countries

Intervention Level	Determinant	Potential Barriers to Up-Take in sub-Sahara African Setting	Potential Solutions
Policy	Political willingness: advocacy	* Lack of awareness of importance of vaccine	* Engage relevant stakeholders (primary, minor, and private health sector) * Advocate alongside partners in accordant sectors
	Political willingness: affordability	* Lack of awareness of quantified impact of vaccine * Affordability of countrywide initiative	* Provide examples of cost effective studies * Draw on drug manufacturer or other donors for financial support
	Effective recommendations	* Lack of substantive research, literature or examples on vaccine significance	* Propose research-supported innovations * Draw from empirical past performance lessons * Develop strong implementation strategy
Facility	Knowledge and Training of Health Workers	* Lack of recognition of vaccine benefits and stigma among facility staff * Lack of training of health workers	* Educate facility staff * Foster provider buy-in and advocacy of vaccine * Regular training to all relevant staff * Completion of checklist form by staff before discharge of newborn * Couple immunization with BCG and OPV-0 * Provide performance-based financial incentives for staff
	Short Window for Administering Vaccine	* 24 hour administration window * Mother's hesitancy to vaccinate newborn due to vaccine acceptance or cost	* Keep mothers in delivery ward at least 24 hours after delivery * Administer vaccine in delivery ward * Educate mothers on importance of timely vaccination * Provide financial incentives for mothers
	Tracking System	* Lack of systems and documentation tools to record and track immunization	* Standardize all Hep B-BD immunization-reporting tools
	Vaccine Stockouts	* Vaccine stockouts and limited vaccine sessions	* Store the vaccine in existing cold chains and/or in labor wards * Develop standing orders for the vaccine * Create partnerships with vaccine distributor
Community	Mother Involvement	* Community level measures to target health behavior * Geographic distance inhibiting timely delivery of newborn to health facility	* Raise community awareness of vaccine * Establish a gathering place in the community to dissiminate information to mothers
	Community Health Worker (CHW) involvement	* Poor communication channels between CHWs and mothers * Poor communication channels between CHWs and health facilities	* CHWs to perform at-home-visits in rural communities to educate mothers and track pregnancies * Regular trainings and supervision of CHWs * Provide cash incentives for CHWs
	Evidence-Based Innovations	* Lack of rural distribution of the vaccine * Vaccine refrigeration requirements	* Use of out-of-cold-chain (OOC) or controlled temperature chains (CTC) to deliver vaccine to rural home-births * Mobile based devices to track pregnancies in rural areas

CHAPTER 3 : DETERMINANTS OF THE UPTAKE OF CHILDHOOD IMMUNIZATION IN KINSHASA PROVINCE, THE DRC : AN ORDERED LOGIT REGRESSION ANALYSES OF INFANT VACCINES ADMINISTERED AT BIRTH AND SIX-WEEKS OF AGE

3.1 Introduction

Childhood immunization against hepatitis B virus (HBV) was introduced to national vaccine schedules globally in the 1980s but not instituted in the African continent until the early 2000s.[96] Accordingly, the prevalence of chronic HBV and its complications is still unacceptably high in sub-Saharan Africa (SSA). The World Health Organization (WHO) estimates that chronic hepatitis infects over 60 million individuals in SSA,[2] and the majority are unaware that they are carriers.[3] If infected at birth via mother-to-child transmission (MTCT), an infant has a 70-90% chance of developing chronic HBV infection and a 25% chance of mortality.[7] The HBV birth-dose vaccine (HepB-BD) – administered within the first 24 hours after delivery and followed by additional vaccine doses – can prevent the overwhelming majority of MTCT cases.[8–10] Yet, in most of SSA, infants do not receive their first dose of the HBV vaccine series (HepB3) until six weeks, leaving them vulnerable to infection via MTCT. Timely receipt of HepB-BD is crucial in preventing MTCT. In a Cameroonian study of infants born to HBV surface antigen (HBsAg)-positive mothers, those who received HepB-BD within the first 24 hours were found to have a 1.4% lower prevalence of HBsAg than those who received it 24-47 hours after birth, and an 11.1% lower prevalence than those who received it 48-96 hours after birth.[97] In addition, the risk of transmission among infants born to HBsAg-positive mothers was found to be eight times higher for those who received HepB-BD more than seven days after birth compared to those who received it within the first three days of life,[98] highlighting the importance of timely uptake.

Such high-burden countries as the Democratic Republic of the Congo (DRC) are preparing to add HepB-BD in their national immunization schedule for administration alongside other routine birth-dose

(BD) vaccines–oral polio (OPV0) and tuberculosis (Bacille Calmette-Guérin [BCG]).[74] However, effective implementation of BD vaccination is challenging in the SSA context. Of the 14 countries in the region that have already introduced HepB-BD into national policy, the reported coverage within 24h after birth is only 10%.[99] A study in the Gambia found that despite the availability of HepB-BD between 2004 and 2014, only 1.1% of infants received the vaccine within 24 hours and only 5.4% by seven days after delivery.[64] These challenges are not unique to HepB-BD. A study in Kinshasa Province across health facilities highlighted significant challenges to the timely delivery of existing BD vaccines to newborns. Major determinants of the timely uptake of OPV0 and BCG included facility-level administration logistics, vaccine stockouts, and vaccine wariness and hesitation.[100] The current DRC national immunization schedule defines *timely delivery* of OPV0 and BCG BD vaccines as within the first seven days of life. Yet, ongoing challenges continue to impede timely BD delivery. Given these challenges, to introduce HepB-BD to the immunization schedule, facilities will require vaccine delivery strategies to proactively address barriers to administering three BD vaccines in an infant's first 24 hours of life. The DRC's national immunization schedule currently awaits the introduction of HepB-BD; for the time being, the first round of HepB3 is provided at six weeks of age.[101] In such contexts, identifying determinants of timely administration of current BD vaccines – especially BCG, which is administered by an injectable method like HepB-BD, rather than orally like OPV0 – can provide proximal and prospective insight into challenges to future timely HepB-BD uptake.

In the present study, I employ the Andersen Behavioral Health Model (BHM), used in previous immunization systems research, to categorize and understand the determinants of vaccine uptake.[36] The BHM addresses barriers to access and utilization at three levels: external environment, predisposing characteristics, and enabling resources, allowing me to investigate barriers to vaccine uptake at both the individual and facility levels. I must understand the determinants of infant receipt of timely vaccination to improve current and future BD immunization coverage. Therefore, I analyzed vital information about barriers and facilitators to the uptake of infant vaccines at multiple time points. To my knowledge, few

studies assess barriers to timely first-round immunization at both levels across multiple time points, and no study does so with the intent to improve future streamlined and timely uptake of HepB-BD.

3.2 Material and methods

3.2.1 Study design and setting

The assessment leveraged de-identified survey data collected during a continuous quality improvement (CQI) initiative study conducted at 105 maternity centers throughout the Kinshasa Province, DRC. The parent study was designed to assess the impact of continuous quality improvement interventions on long-term outcomes of antiretroviral therapy among pregnant and breastfeeding women. Therefore, eligible participants living with HIV were enrolled anytime during pregnancy, after delivery, or during well-child visits at the select facilities.

Mother-infant pairs were excluded from this analysis if the mother or infant died during the study period, or if the child was aborted during the study period. The original study sample included 2,875 expectant mothers enrolled in the cohort study from 2016-2020 during antenatal care (ANC) or postpartum visits. A face-to-face interview was conducted with all enrolled participants at registration and subsequent visits at the following time points: delivery (for pre-delivery enrolees), six weeks, six months, 12 months, 18-24 months, and 24+ months postpartum. The study staff collected information on the mother-infant pair at delivery. The infant's vaccination status was verified at each follow-up visit using vaccination cards and the vaccination registry in the clinic. Vaccine cards recorded the date of infant vaccines contemporaneously, so it was possible to calculate a precise number of days between the infant's birthday and vaccine date. Assessments about facility capacity and inventory were collected through interviews with facility managers and staff at each of the 105 facilities. Mothers were eligible for inclusion in this analysis if they were enrolled in the parent study.[39]

3.2.2 Dependent variables

The outcome measure of interest was infant vaccination status. I divided the outcome measure, BCG vaccine status, into four categories: within 24 hours of delivery, between one and seven days, or one week to 14 weeks; versus those who never received the BCG vaccine during the study period. The 14-

week mark represents the moment of advised completion of an infant's immunization schedule (**Figure 3.1**). HBV status is divided into three categories: within six weeks, six to 14 weeks, and no uptake during the study period. The study team verified the vaccine status of all infants during verbal interviews with mothers and per review of immunization cards.

3.2.3 Explanatory variables

Covariates were selected based on existing literature about determinants of vaccine uptake at the community and facility levels.[18,28,36] The framework for variable selection was based on Andersen's BHM to examine factors associated with vaccine utilization. The explanatory variables fell under the three BHM categories. (1) The external environment included the WHO Service Availability and Readiness Assessment (SARA),[102] the WHO immunization readiness assessment, facility size, ownership, and location – all assessed at the facility level. SARA was designed as a systematic survey to assess health facility service delivery, while the immunization service availability assessment was immunization service specific. (2) Predisposing characteristics included the infant's birth order, mother's age, marital status, and mother's education level. (3) Enabling factors included the mother's wealth index score and whether the mother traveled to the facility by foot or by transport**. Table 3.1** includes more information about the covariates and their distributions.

3.2.4 Statistical analysis

Regression models. I used multivariate ordered logistic regressions to run two versions of my analysis. Model I examined current BCG BD uptake, while Model II examined current HepB3 vaccine uptake. With Model I, I examined determinants of current BD vaccines to anticipate barriers to future HepB-BD uptake. BCG uptake was the chosen proxy rather than OPV0 uptake because the injectable method of administration of the vaccine more closely approximated that of future HepB-BD than the orally administered polio vaccine. Model II measured determinants of the uptake of the first dose of HepB3, currently administered at six weeks of age in the DRC.

Model fit statistics. Akaike's Information Criterion (AIC) was used to compare alternative functional forms and select the final model. Various functional forms of the continuous variables,

including quadratic and categorical forms, were compared through an iterative approach. If a functional form was selected for one variable, it was retained for subsequent comparisons. Model fit was examined for both models, and the best functional forms with the minimum AIC were selected independently, see **Appendix 3.1.** Findings were reported in average marginal effects with delta-standard methods.

Sensitivity analysis. Both human error by vaccine staff conducting the interviews and loss-to-follow-up (LTFU) led to missing vaccine information across all time points for BCG status (missing, n = 239; LTFU, n = 248) and HepB3 status (missing, n = 369; LTFU, n = 281). LTFU was only measured among the participants who had not yet vaccinated their infants. We conducted two sets of sensitivity analyses for each outcome variable, BCG and HepB3, (a total of four analyses) to assess the robustness of the results of a full-case analysis against the alternative scenarios, including those with all missing or LTFU-specific information. The first set of analyses was defined by increasing the sample size to include participants with missing vaccine information across all time points as 'not vaccinated' or as a distinct category. The second set of analyses included only the LTFU-specific observations as 'not vaccinated' or as a distinct category, see **Appendices 3.2, 3.3 and 3.4.** I found that a model with LTFU weights had directionality and magnitude in accordance with the majority of the models included in both sets of sensitivity analyses and therefore reported adjusted results accounting for LTFU.

3.3 Results

3.3.1 Sample characteristics

Between November 2016 and July 2020, the parent study enrolled 2,875 participants at 105 facilities. Of the enrolled participants, 56 mothers died, and 172 infants died or were aborted during the study period and were thus excluded from the analysis. A total of 239 mother-infant pairs did not provide BCG vaccine data, and 369 did not provide HepB3 vaccine information across any of the six follow-up visits after enrollment; these pairs were excluded from the analysis. The final sample with complete information included 2,398 (BCG analysis) and 2,268 (HepB3 analysis) women-infant dyads. Complete sample characteristics aggregated by the moment of the first infant vaccine can be found in **Table 3.2.**

3.3.2 First-dose vaccination coverage and timeliness

Of the participants with vaccine data, 82.6% received a BCG vaccine, and 68.4% received a HepB3 vaccine. Of those who received the BCG vaccine, 26.3% of the participants received it within 24 hours, 43.5% received it between one and seven days, and 12.8% received it between one and 14 weeks. Of infants who received the first dose of HepB3 vaccine, 22.4% received it within six weeks, and 46% between six and 14 weeks of life.

Predisposing characteristics. Overall, the mean age of the mothers was 31 years (S.D. = 6.099), and 1,705 (71.2%) mothers were married. Mothers had a median of four children (IQR: 2-5 children) and had 11 years of education (IQR: 9-12 years).

Enabling factors. Of the total eligible sample, 262 (11.1%) women fell within the lowest wealth quartile versus 523 (21.8%) who fell within the highest. 1,558 (65%) of the women traveled to the facility by taxi (or other forms of transportation) rather than by foot.

External environment. In terms of the external environment, overall, 1399 (58.3%) women sought care at health centers instead of hospitals, 1,349 (56.3%) women received care at a religiously-affiliated facility, and 1,457 (60.8%) women visited urban facilities. In addition, the median score for a mother's facility where she sought care was 6.75 (IQR: 6.12-7.39) on the general readiness scale and 6.11 (IQR: 5-6.67) on the immunization readiness scale.

3.3.3 Model I. Determinants of the uptake of BCG BD vaccine

Table 3 presents the results from the ordered logit analyses, which estimated how vaccine uptake at different time points was related to factors influencing the respondent at the predisposing, enabling, and external levels.

Predisposing factors. Every additional year of a mother's education was associated with a greater rate of earlier vaccination. For instance, an additional year of education was associated with a 0.48 percentage point increase in the probability that a mother would vaccinate her infant within 24 hours of delivery and a 0.52 percentage point decrease in the probability of never vaccinating her infant ($p < 0.05$).

Enabling factors. Household wealth index scores within the second quantile (compared to the fourth, and highest, wealth quantile) were associated with a 7.0 percentage point decrease in probability of timely uptake ($p < 0.001$) and a 7.9 percentage point increase in the probability of never vaccinating their infant ($p < 0.001$), see **Table 3.3.**

External environment. Higher general readiness scores were associated with timely uptake. A one-point increase in a facility's general readiness score was associated with a 1.7 percentage point increase in the probability of vaccination within 24 hours ($p < 0.01$) and a 2.6 percentage point decrease in the probability of never vaccinating an infant ($p < 0.01$). In addition, visiting religious-affiliated facilities compared to public facilities was significantly associated with receipt of timely BCG (4.2 percentage point increase in vaccination by 24 hours) ($p < 0.01$) and a 4.9 percentage point decrease in never receiving it ($p < 0.01$). In addition, religious-affiliated facilities were associated with an 8 percentage point decrease in the probability of vaccine uptake from one to seven days compared to private or other facilities ($p < 0.001$).

3.3.4 Model II. Determinants of the uptake of HepB vaccine

Similar to BCG vaccine uptake, factors that affected the timely uptake of the HepB3 vaccine varied across all three levels of the BHM.

Predisposing characteristics. Within the study sample, every additional year increase in a mother's age was associated with a 0.21 percentage point increase in the probability of an infant being vaccinated within six weeks and a 0.31 percentage point decrease in the probability of an infant not ever being vaccinated ($p < 0.05$). Every additional year of a mother's educational attainment was associated with a 0.77 percentage point increase in the probability that she would vaccinate her infant within six weeks of delivery ($p < 0.001$) and a 1.2 percentage point decrease in the probability of never vaccinating her infant ($p < 0.001$).

Enabling factors. Household wealth index scores within the second quantile, compared to the fourth and highest wealth quantile, were associated with a 5.3 percentage point decrease in the probability

of taking up timely vaccines ($p < 0.001$) and an 8.2 percentage point increase in the probability of never vaccinating their infant ($p < 0.001$). Further, among the study sample, using a form of transportation other than walking to travel to the facility was associated with a 2.5 percentage point decrease in the probability of vaccination within six weeks ($p < 0.05$) and a 3.7 percentage point increase in no vaccination ($p < 0.05$).

External environment. A one-point increase in a facility's immunization readiness score was associated with a 5.3 percentage point increase in the probability of vaccination within 14 weeks ($p < 0.01$). In addition, an additional point increase in a facility's general readiness score was associated with a 5.2 percentage point decrease in the probability of an infant never having been vaccinated ($p < 0.001$). Finally, visiting religious-affiliated facilities, compared to public facilities, was associated with an 8.9 percentage point decrease in the probability of vaccine uptake at 6 weeks ($p < 0.001$).

3.4 Discussion

In this study, I investigated the factors associated with timely infant immunization in 105 facilities in Kinshasa Province using a cohort of HIV-positive pregnant women and their infants. I observed similar immunization coverage for BCG (82.6%) and the first dose of HepB3 (68.4%) compared to the WHO/UNICEF estimates of national immunization coverage averaged from 2017-20 (84.5% and 71.3%, respectively).[103]

I employed the Andersen BHM to categorize factors that impacted vaccine uptake within three categories: predisposing characteristics (infant's birth order, mother's age, mother's year of educational attainment, and her marital status), enabling factors (household wealth index and form of transportation to the facility), and external environment (general readiness, immunization readiness, type, ownership, and urban status of the facility where the mother-infant pair sought care). I observed a strong positive association of factors across all three categories with timely uptake of both vaccines, BCG and HepB3. My analyses highlight the importance of considering the effect of determinants at different levels and time intervals. The implication is that policymakers in the DRC can be more focused on

implementing vaccine uptake strategies depending on their target group. For example, I identified significant determinants of timely uptake of both BCG and HepB3 at the external environmental level, focusing on intervenable facility characteristics.

Higher general readiness scores and attending a religiously affiliated facility were independently associated with both BCG and HepB3 timely uptake, a finding that aligns with previous studies highlighting vaccine storage and stockout challenges in the DRC.[100,104] In prior work, lower general facility readiness scores have been reported as barriers to timely immunization.[105] Therefore, new vaccine introduction strategies at the facility level should prioritize contributions to general readiness, such as workforce and operations, and immunization readiness, such as reliable availability of vaccines at each facility. Ensuring adequate supply prevents stockouts, which in turn prevents unnecessary/unproductive visits to a facility. This could also bring more equity as it reduces costs for families who live further away from the facility.

In addition, visits to public facilities were negatively and independently associated with timely uptake of BCG compared with visits to religiously-affiliated facilities. In contrast, visits to private, non-religious facilities, as compared to religious facilities, were positively associated with timely uptake of both BCG and HepB3. Previous studies on immunization uptake in SSA have cited a facility's religious affiliation driving a mother's choice to seek care there.[100] In terms of private facilities, studies show that mothers visiting private facilities tend to be of higher income levels,[106] a factor that was positively associated with timely vaccine uptake and may explain our findings. Future research could examine the reasons that vaccination rates are higher among those who select private facilities.

Within the category of predisposing characteristics, I found that the mother's educational attainment and age at the time of enrollment were positively associated with the timely uptake of vaccines, which indicated that knowledge, awareness, and experience with preventative care were vital for timely vaccine uptake. A mother's education level is an established predictor of infant immunization in low- and middle-income countries [29,36,107,108] and education is a valuable solution to overcome challenges to vaccine uptake.[80,109] Mothers primarily receive healthcare information from two sources:

health workers during ANC visits, and their families and communities. Previous studies have shown that knowledge about HBV risk and the vaccines' protection is low among Congolese individuals,[86,100] with one study finding a basic knowledge of HBV among only 33.2% of healthcare workers[86] and another finding that only 31.2% (87/280) of pregnant knew how HBV was transmitted.[110] To increase a mother's knowledge, initiatives to disseminate vaccine knowledge could be targeted to the mother's two primary sources of information, the facilities during ANC visits and their communities. In terms of the facility, training that includes vaccine information needs to be geared towards not only vaccine staff, but also the ANC staff who are disseminating information to pregnant women.[100] At the community level, approaches to address the knowledge barrier could be targeted towards the mother's complete social network of family and friends.[86]

Household wealth status was positively associated with timely BCG vaccination, consistent with other studies.[36,111,112] A possible explanation for this observation is the cost of the vaccinations. Although vaccinations are technically free in the DRC, facilities often require vaccination fees for a vaccine card and well-baby consultation. In addition, indirect costs such as transportation and income loss may act as economic burdens obstructing vaccine uptake.[36,113] The economic burden was further substantiated by our finding that mothers were more likely to vaccinate their infants on time, or ever, if they lived within walking distance to the facility. This finding was confirmed by earlier studies in SSA that distance to facility, travel time, and need for transport were negatively associated with immunization uptake;[36,107] one such study found that traveling a distance of over 30 minutes by foot compared to a shorter distance reduced vaccine uptake by one-third.[107] These implications for the enabling factors require policy intervention to reduce the economic burden of infant vaccines, such as transparency and standardization of vaccine costs across facilities and incentives for mothers living beyond walking distance from facilities.

A significant strength of this study was the aggregation of facility-level and individual-level longitudinal data across many facilities. Few studies have looked at a combination of the individual-level determinants of the mother-infant pair and the facility-level determinants of vaccine uptake. The study

employs a unique approach to controlling for confounding by using data from both the supply (environment) and demand (mother-infant pair) side. This study's access to longitudinal panel data of over 2,000 women and inventory data about each of the study facilities allowed me to evaluate a comprehensive list of determinants across the BHM levels that determine timely uptake of vaccines. Beyond the unique challenge of administering the vaccine within 24 hours of birth, these determinants highlight the need for an implementation strategy to be rolled out alongside universal HepB. Previous studies demonstrate that timely uptake remains low in countries that have previously adopted HepB-BD because there is no clear guidance to overcome individual- and facility-level challenges.[19,114] Our study's main policy implication was to highlight the barriers to current BD vaccines – and HepB3 vaccine – in a context that strives to include the HepB-BD vaccine in its national immunization schedule. Policymakers may use these findings as evidence when developing a future implementation strategy streamlining all three BD vaccines – HepB-BD, OPV0, and BCG – within the first 24 hours of life. Findings from this study can help national, sub-national, and facility-level stakeholders to strengthen the uptake of both BD vaccines and other available vaccines for infants across the DRC and SSA.

Despite the study's strengths, it was not without limitations. Our assessment leveraged sample participants from a cohort of women already enrolled in an HIV continuous quality improvement study, which impacted the generalizability of this study. However, vaccine uptake in this population was similar to the national average, and factors influencing vaccine uptake were aligned with other infant immunization studies in the Congo and elsewhere in SSA.[36,80,107–109,111,112,115] The measure of the outcome variables, vaccine uptake status and timing, may have suffered from recall bias because of the contemporaneous approach of capturing vaccine dates during study interviews. The study staff reviewed infants' vaccine records to correct any errors in logging the vaccine dates to help alleviate any errors. Another limitation of this study is that estimates are not causal but associations. In addition, only mothers recruited pre-delivery (approximately half of the sample) responded to a question regarding how many ANC visits they had attended because study staff dropped the question among mothers recruited post-delivery. Finally, while the parent study did experience significant rates of LTFU, study staff followed up

with respondents to understand reasons for LTFU and recapture some of the data otherwise lost. I was able to weigh LTFU within the 'never vaccinated' rate to represent more accurate rates of failure to vaccinate.

3.5 Conclusions

My findings reveal the factors that most influence timely vaccine uptake of BCG and HepB3 among a cohort of mother-infant pairs across 105 facilities in the Kinshasa Province. I found that higher educational attainment, age, and level of wealth among mothers were positively associated with timely vaccination. In addition, a mother's proximity/ability to walk to a facility and her choice of facility impacted the status of her infant's vaccine uptake. A mother visiting a facility with higher general and immunization readiness and religious affiliation led to a higher probability of timely infant immunization. Policymakers can use these findings to develop implementation guidance to ameliorate the timely delivery of current BD vaccines and to anticipate potential factors that may impact the future distribution of HepB-BD in the DRC.

Figure 3.1 Current routine immunization schedule from birth to 14 weeks, DRC 2022

		Age			
Vaccine	Disease	Birth	6 weeks	10 weeks	14 weeks
Bacille de Calmette et Guérin (BCG) vaccine	Tuberculosis				
Oral Polio Vaccine (OPV)	Poliomyelitis				
Pentavalent vaccine	Diphtheria, Pertussis, Tetanus, H. influenza type b, Hepatitis B				

**grey cells indicate vaccination is currently available on the national immunization schedule at the indicated time point.*

Table 3.1 Explanatory variables for timely vaccine utilization, their operational definitions, and measures

Variable	Operational Definition	Measure Type
Predisposing characteristics		
Infant's birth order	Number of infants birthed by the mother before the index infant	Continuous (children)
Mother's age	Age at time of enrollment	Continuous (years)
Mother's education	Educational level of the mother at time of enrollment	Continuous (years)
Mother's marital status	Marital status of mother is captured at enrollment divided into two categories, not married (separated, divorced, widowed, never married) or married	Dichotomous 0 = not married ; 1 = married
Enabling factors		
Household wealth index	Produced from existing variables (household assets ownership, household characteristics and access to utilities) from enrollment questionnaires through factor analysis using Principal Component Analysis (PCA)	Categorical 1 = low wealth ; 2 = mid-low wealth ; 3 = mid-high wealth ; 4 = high wealth
Transport to facility	Whether the mother traveled by foot or using transportation to the facility, captured at 6-week follow-up visit	Dichotomous 0 = walking ; 1 = taxi or other
External Environment		
General Service Readiness Assessment	Produced from existing variables (basic amenities, basic equipment, infection prevention, and diagnostic capacity) from the facility inventory questionnaires through factor analysis using PCA	Continuous (points)
Immunization Services and Availability Assessment	Produced from existing variables (staff guidelines, immunization equipment, medicine and commodities) from the facility inventory questionnaires also through factor analysis using PCA	Continuous (points)
Facility type	Health center or reference hospital, captured in facility inventory questionnaire	Dichotomous 0 = reference hospital ; 1 = health center
Facility Ownership	The gestational authority of the facility, captured in facility inventory questionnaire	Categorical 1 = public ; 2 = religious-affiliation ; 3 = private & other
Location	Urban versus rural/peri-urban status, captured in facility inventory questionnaire	Dichotomous 0 = rural/per-urban ; 1 = urban

Table 3.2 Characteristics of mother-infant pairs and facilities visited stratified by BCG vaccination status

	Overall		Vaccinated within 24 hours		Vaccinated within 1 week		Vaccinated with 14 weeks		Not vaccinated	
	N = 2398		N = 630		N = 1044		N = 307		N = 417	
	No	**(%)**	**No**	**(%)**	**No**	**(%)**	**No**	**(%)**	**No**	**(%)**
Mother's marital status										
Married	1705	(71.10)	452	(71.75)	753	(72.13)	207	(67.43)	293	(70.26)
Not married	691	(28.82)	178	(28.25)	290	(27.78)	99	(32.25)	124	(29.74)
Missing	2	(0.08)	0	(0)	1	(0.10)	1	(0.33)	0	(0)
Household wealth index										
Low wealth	262	(11.13)	86	(13.65)	106	(10.15)	33	(10.75)	42	(10.07)
Mid-low wealth	883	(36.82)	200	(31.75)	371	(35.54)	121	(39.41)	191	(45.80)
Mid-high wealth	725	(30.23)	194	(30.79)	325	(31.13)	93	(30.29)	113	(27.10)
High wealth	523	(21.81)	150	(23.81)	242	(23.18)	60	(19.54)	71	(17.03)
Transport										
Walking	839	(34.99)	215	(34.13)	322	(33.89)	363	(34.77)	114	(37.13)
Taxi and other	1558	(64.97)	415	(65.87)	628	(66.11)	680	(65.13)	193	(62.87)
Missing	1	(0.04)	0	(0)	0	(0)	1	(0.10)	0	(0)
Facility type										
Health center	1399	(58.34)	366	(58.10)	622	(59.58)	174	(56.68)	237	(56.83)
Reference hospital	999	(41.66)	264	(41.90)	422	(40.42)	133	(43.32)	180	(43.17)
Facility ownership										
Public	770	(32.11)	208	(33.11)	318	(30.46)	86	(28.01)	158	(37.89)
Religious-affiliation	1,349	(56.26)	338	(53.67)	599	(57.38)	100	(58.63)	232	(55.64)
Private & other	279	(11.63)	84	(13.22)	127	(12.16)	41	(13.36)	27	(6.47)
Location										
Urban	1457	(60.76)	397	(63.02)	635	(60.82)	183	(59.61)	242	(58.03)
Rural/peri-urban	941	(39.24)	233	(36.98)	409	(39.18)	124	(40.39)	175	(41.97)
	M	**(SD)**	**M**	**(SD)**	**M**	**(SD)**	**M**	**(SD)**	**M**	**(SD)**
Infant's birth order	4.06	(2.20)	4.09	(2.16)	4.041	(2.16)	4.21	(2.38)	3.94	(2.21)
Mother's education	10.6	(2.99)	10.700	(3.016)	10.74	(2.98)	10.438	(3.055)	10.25	(2.91)
Mother's age	31.252	(6.099)	31.33	(6.063)	31.451	(6.042)	31.20	(6.19)	30.68	(6.21)
General readiness	6.77	(0.91)	6.73	(0.88)	6.84	(0.90)	6.83	(0.89)	6.63	(1.00)
General readiness##General readiness	46.72	(12.40)	46.07	(11.83)	47.59	(12.26)	47.46	(12.15)	44.98	(13.50)
Immunization readiness	5.82	(1.52)	5.88	(1.50)	5.76	(1.54)	5.89	(1.51)	5.86	(1.49)

Table 3.3 Ordered logistic regression model results examining predisposing, enabling, and external predictors of infant vaccine uptake at different time points

Variable	Model I BCG Vaccine (birth-dose)				Model II HepB3 Vaccine (6 weeks)		
	Vaccinated within 24 hours	Vaccinated within 1 week	Vaccinated with 14 weeks	Not vaccinated	Vaccinated within 6 weeks	Vaccinated within 14 weeks	Not vaccinated
Infant's birth order	0.0058	0.0018	-0.00128	-0.0064	0.0020	0.0010	-0.0030
	(0.0040)	(0.0013)	(0.00087)	(0.0044)	(0.0036)	(0.0018)	(0.0054)
Mother's age	0.0018	0.00058	-0.00040	-0.0020	0.0021*	0.00106*	-0.0031*
	(0.0014)	(0.00045)	(0.00031)	(0.0015)	(0.0012)	(0.00065)	(0.0019)
Mother's education	0.0048*	0.00153*	-0.00100*	-0.0052*	0.0077***	0.0040***	-0.0117***
	(0.0027)	(0.00088)	(0.00060)	(0.0030)	(0.0024)	(0.0012)	(0.0035)
Mother's marital status							
Not married	0.0044	0.0014	-0.0010	-0.005	0.011	0.0053	-0.016
	(0.017)	(0.0051)	(0.0037)	(0.018)	(0.015)	(0.0072)	(0.022)
Household wealth index							
First	0.011	0.0014	-0.0025	-0.010	-0.024	-0.010	0.034
	(0.031)	(0.0041)	(0.0074)	(0.028)	(0.024)	(0.011)	(0.035)
Second	-0.070***	-0.0241***	0.0151***	0.079***	-0.053***	-0.0281***	0.082***
	(0.020)	(0.0069)	(0.0048)	(0.022)	(0.019)	(0.0096)	(0.028)
Third	-0.017	-0.0034	0.0039	0.016	-0.008	-0.0030	0.011
	(0.022)	(0.0043)	(0.0050)	(0.021)	(0.020)	(0.0073)	(0.027)
Transport							
Vehicle or other	-0.000	-0.0001	0.0001	0.000	-0.025*	-0.0124*	0.037*
	(0.016)	(0.0049)	(0.0034)	(0.017)	(0.015)	(0.0068)	(0.021)
General readiness	0.0166**	0.0122**	-0.0029**	-0.026**	0.0229***	0.0291***	-0.052***
	(0.0071)	(0.0050)	(0.0013)	(0.011)	(0.0061)	(0.0062)	(0.012)
Immunization readiness	0.0022	0.0007	-0.0005	-0.0024	0.0103**	0.0053**	-0.0156**
	(0.0048)	(0.0015)	(0.0010)	(0.0053)	(0.0046)	(0.0024)	(0.0069)
Facility type							
Reference hospital	-0.021	-0.0068	0.0046	0.023	0.001	0.0004	-0.001
	(0.016)	(0.0055)	(0.0035)	(0.018)	(0.015)	(0.0077)	(0.023)

Facility ownership							
Public	-0.042**	-0.0165**	0.0088**	0.049**	-0.009	-0.0055	0.015
	(0.017)	(0.0076)	(0.0035)	(0.021)	(0.015)	(0.0093)	(0.025)
Private & other	0.070***	0.0080***	-0.0159***	-0.062***	0.089***	0.0243***	-0.114***
	(0.026)	(0.0028)	(0.0060)	(0.021)	(0.024)	(0.0050)	(0.027)
Location							
Rural/peri-urban	-0.005	-0.0017	0.0012	0.006	-0.011	-0.0061	0.018
	(0.016)	(0.0051)	(0.0035)	(0.018)	(0.015)	(0.0079)	(0.022)

* = statistically significant at $p<0.05$, **=statistically significant at $p<0.01$, ***= statistically significant at $p<0.000$

CHAPTER 4 : BARRIERS AND FACILITATORS TO TIMELY BIRH-DOSE VACCINES IN KINSHASA PROVINCE, THE DRC: A QUALITATIVE STUDY

4.1 Background

Infant immunization is an effective strategy for reducing infectious disease morbidity and mortality. Since the 1990s, annual infant mortality from vaccine-preventable infectious diseases has decreased from 14 million to five million due to worldwide efforts by national policymakers to enforce recommended vaccination schedules.[116] In 2016, vaccine coverage across 152 high-burden countries for the first dose of Diphtheria Tetanus Toxoid and Pertussis (DTP) and measles-containing vaccine were 94% and 93%, respectively. Coverage falls short, however, for widely implemented birth-dose (BD) vaccinations—Bacillus Calmette-Guerin (BCG) and the first oral polio dose (OPV0)—with BCG coverage at only 37% in the same 152 countries.[117] While national policies have improved vaccine coverage, the next step is addressing the unique challenges of timely BD vaccine delivery.

The hepatitis B vaccine is the first cancer-preventing vaccine,[74] and is included in routine child immunization schedules globally—since the 1980s in high-income countries and 1997 in sub-Saharan Africa (SSA). The World Health Organization (WHO) recommended including the hepatitis B birth-dose vaccine (HepB-BD) in national guidelines in 2009. Historically, infants received the first dose of the vaccine at six weeks, which is too late to interrupt mother-to-child transmission (MTCT). If administered within 24 hours of delivery and followed by two or three additional doses, HepB-BD is >95% effective in preventing MTCT.[8–10] Countries like Democratic Republic of the Congo (DRC) are moving to include HepB-BD in their national immunization schedule.[74] However, without a clear implementation strategy, delivery of an additional BD only adds to the complexity of timely delivery.[118] Therefore, as countries streamline universal HepB-BD with existing BD vaccines, it is critical to explore the unique determinants to delivering timely BD vaccines.

To our knowledge, no qualitative studies have reported on determinants of BD vaccine uptake in a low-resource setting. This study aims to support decision-makers by identifying barriers and facilitators of timely BD vaccine delivery in Kinshasa Province, DRC through interviews with individuals across the vaccine care continuum.

4.2 Methods

4.2.1 Study design, setting, and patient population

We conducted semi-structured qualitative interviews in seven health facilities across Kinshasa Province, DRC. We purposefully sampled health facilities with maternity and vaccine wards. We chose the five most prominent facility types in the province—private, public, Catholic, Protestant, not-for-profit (NFP)—and selected a sample of seven facilities (**Figure 4.1**). Kinshasa Province is predominately urban, so we selected facilities accordingly - six urban and one rural of 983 facilities in the province.[119] Since Catholicism is the primary religion in the DRC, which represents a significant provider of health services, we selected two Catholic facilities. The facilities ranged in size and therefore experienced a range in volume of monthly deliveries, from 40 to 300. Vaccines in DRC flow from external donors—the Vaccine Alliance (Gavi), the United National Children's Fund (UNICEF), and the WHO—to the National Immunization Program (PEV) and the health zones, and finally to health facilities where vaccines reach the consumer—the mother-infant pair (**Figure 4.2**).[120,121] We invited a sample of up to two expectant mothers and three facility informants from each facility to participate, in addition to vaccine officials at the health zone and national levels. Eligibility requirements included: age ≥18 years and understanding of either French or Lingala, the two local languages in Kinshasa.

4.2.2 Data collection

Interviews were conducted using two semi-structured interview guides with open-ended questions, available in French and Lingala. The interview guides were developed using existing relevant literature[41,122–125] and reviewed and validated by the entire study team. To understand administrative barriers to HepB-BD, we interviewed decision-makers and/or providers (hereafter 'informants') from various levels of the health care continuum, including midwives, immunization staff, heads of maternity

and immunizations, and vaccine officials at the health zone and PEV. We interviewed primigravid (8) and multigravida (6) mothers to elicit perceptions about infant vaccination from new and experienced expectant mothers. The interviews were led by a bilingual (French/English) PhD candidate with education and experience interviewing study populations. Interviews were live translated from Lingala to French by a bilingual (French/Lingala) study team member with a medical doctorate and many years of experience interviewing study populations.

Staff working the day of the facility visit and mothers presenting for routine antenatal care (ANC) were approached for enrollment. Interviews were conducted in-person, in private rooms, in French or in Lingala, and on the same day as study enrollment. Interviews were audio-recorded and lasted 15-60 minutes.

4.2.3 Data analysis and framework

The audio-recorded interviews were transcribed and translated to English by a bilingual study member (AB); transcripts were then imported to MAXQDA2020 for coding and analysis. Deductive codes were generated using existing literature on vaccine uptake and administration barriers. Themes were established and harmonized through iterative analysis. AB coded and analyzed data alongside CEM. AB and CEM reviewed the transcripts for patterns and major sources of saturation to organize the findings into major themes as they were received. Theme saturation was reached when codes or categories described a similar phenomenon on repeated occasions across multiple respondents.[126] AB and CEM met regularly and compared and contrasted similarities and differences among the coded interviews. Finally, the study team reached consensus about what patterns of codes constituted a theme and the prevalence of the pattern required for saturation.

The data analysis was guided by the Consolidated Framework for Implementation Research (CFIR). The CFIR organizes key barriers and facilitators into five domains—intervention characteristics, inner setting, outer setting, staff characteristics, and the implementation process—of 37 measurable constructs.[127] Use of the CFIR framework allowed us to account for contextual factors.

4.2.4 Ethical considerations

Informants and expectant mothers provided written, informed consent. All consented to the audio recording of interviews. Data were de-identified prior to analysis and were stored on a secure server with copies of the recordings. Institutional Review Boards at UNC-Chapel Hill and the Kinshasa School of Public Health approved the study protocol [UNC IRB 21-0014; KSPH IRB 0001 1-04101-00001365292-20].

4.3 Findings

We approached 32 participants (17 informants and 15 expectant mothers) and conducted semi-structured interviews with 30 participants (16 informants and 14 expectant mothers) in June-July 2021 (**Table 4.1**). One informant declined due to medical reasons, and one mother declined due to wait time. Interviewees were recruited from seven health facilities, two health zones, and PEV. Our analysis identified 13 constructs related to the success of timely and streamlined vaccines (**Figure 4.3**). We organized the sections by CFIR domains (**Table 4.2**) and include additional quotes corresponding to the domains (**Appendix 4.1**).

4.3.1 Intervention characteristics

Evidence strength and quality

Many informants spoke to the effectiveness of the two existing BD vaccines, BCG and OPV0. In addition, many informants were aware of trials to pilot the HepB-BD vaccine in the DRC, such as a HepB-BD feasibility study conducted in Kinshasa-based maternity centers.[11] Further, a few informants mentioned inclusion of HepB-BD in WHO recommendations.[74]

Design quality and packaging

A critical barrier to BD vaccinations raised by informants was the design quality and packaging of BCG vaccine. In the DRC, BCG is only available in 20-dose vials, and opened vials have a six-hour shelf life. National policy states that a vial should be opened only when 10-20 newborns are present. In the words of one informant:

> "Yes…with the strategy, we need at least 20 newborns to open a vial, that's why we ask that they come back on Wednesdays. We have records of all of the newborns born. We call them every Wednesday and tell them to come back to the health facility as not to give it to them too long after birth" *Informant NFP 3*.

Further, a PEV informant described vaccine wastage as a provider-level performance gauge set by district-level health zones:

> "Beyond their day-to-day work, [the providers] have their performance metrics to consider and they don't want to inflate their rate of vaccine loss" *Informant PEV 1*.

Cost

Informants reported that mothers must buy a vaccine card to track infant immunizations. The card price varied between facilities from 1 USD in a rural facility to 15 USD in a private facility. All primigravid mothers reported not knowing about a fee for the vaccine card prior to delivery. For example:

> "They will give us a card after we deliver…for the payment, they haven't told us anything" *Mother NFP 2*.

All facilities but one reported transferring multiple complicated births to other facilities each month. Those mothers would pay for a vaccine card and begin infant vaccination at the facility where they delivered, and often returned to their preferred facility to continue infant vaccine visits. When asked whether the health facility would accept vaccine cards from other facilities, every informant except for one at a public health facility responded to the contrary:

> "No, if she begins her infant's vaccine care elsewhere, and decides to come here to continue it, she must repurchase a card here [but vaccines will not be repeated]." *Informant Catholic 4.*

4.3.2 Inner setting

Structural characteristics

Informants reported acquisition of vaccines in two ways: 1) daily retrieval by facility staff from vaccine storage at a health zone, and 2) storage at individual facilities in a solar fridge, provided through a selection process controlled by PEV and external donors. Facilities in the latter group may store monthly vaccine allotments for themselves and nearby facilities.

Four facility informants mentioned electricity outages posing a significant barrier to efficient vaccine storage; for example:

> "Now, vaccines are products that must be conserved in very specific conditions so that the antigen is active. If the required conditions are not reached, we stand the risk of providing placebo vaccines. So, even us here who have electricity, we realize that we stand the risk of experiencing electricity outages. These outages can alter the temperature at which the vaccines are kept" *Informant Public 3.*

A solution suggested by three informants was regular supervision of the cold-chain temperature to ensure vaccine viability:

> "Every morning I am obligated to travel and verify the temperature at which the vaccines are being stored and to record it, and to make sure that the health workers in the facility are doing this" *Informant Health Zone 1.*

A barrier to timely BD vaccination is that vaccines are stored in fridges near the vaccination ward of the facility, separate from the delivery/newborn wards. Six informants at the facility level reported a smaller fridge where vaccines may be kept near the delivery ward, but only three reported storing BD vaccines in these fridges. Informants reported a significant physical distance between the delivery and vaccination wards:

> "And for fridges... the maternity does not vaccinate, it is the vaccination nurse that oversees the number of children available for the vaccination…. the vaccines are kept in the fridge and the nurses are in charge of vaccinating*" Informant Protestant 1*.

Implementation climate

Mothers and informants expressed optimism for innovative vaccination techniques. Several informants shared exciting new approaches to increase vaccination rates and decrease loss-to-follow up, such as community health worker (CHW)[128] outreach programs, mHealth solutions, malaria prevention incentives, and the expansion of rural health posts:

> "Every time now that a mother comes in to have their child vaccinated, we register the moms, we collect their telephone number and their address, so every time they have an appointment coming up, they will receive a text message reminder of their appointment. This way, you will not be distracted and remember your date. Since we started this study, I would estimate though that we have decreased the loss to follow-up rate though, from 21% to 16-18%" *Informant Public 3.*

Learning climate

Some informants expressed a need for procedural training of staff across disciplines. Often midwives who care for infants in the first days of life do not receive guidance about vaccine administration. An informant suggested:

> "When we organize trainings or briefings about vaccination, we target vaccine providers from health facilities. We do not often see the midwives, even though they are the door for infants to enter into the [vaccine] system. So, it is really important to provide them too with briefings or trainings" *Informant PEV 1.*

4.3.3 Process of implementation

Planning

Many informants mentioned national immunization guidelines directing decision-making processes, but some provided inconsistent reports on several key aspects. For example, many informants referred to national immunization guidelines directing immunization policy, but some incorrectly interpreted these guidelines. When discussing BCG vials, one informant stated:

> "We are not obliged to vaccinate infants unless there are 15 of them. If 3 or 5 are born, then we do not vaccinate them" *Informant Catholic 1.*

While another stated:

> "The ideal is 20. But they have authorized us to provide the vaccine when there are 10 infants. So, when we have 10 infants, we administer 10 and lose the other 10 [doses]" *Informant Private 1.*

Clearer guidelines are needed to achieve timely and streamlined BCG, and ultimately HepB-BD, vaccine uptake.

Executing

A common barrier was the stockout of medicines, especially BCG vaccines. Regular stockouts of BD vaccines hinder timely vaccine uptake. All informants and many mothers mentioned stockouts:

> "There's a problem with the BCG. There aren't enough vaccines. Women who deliver here sometimes have to wait one month [for their infant] to receive the vaccine" *Mother Private 2.*

Informants described a nationwide stockout of BCG from May-July 2021. Stockouts are unpredictable, so facilities need to ensure adequate supplies.

External change agents

A few informants mentioned donors such as Gavi and UNICEF as providers of vaccines and solar fridges. For example, the health zone informant said:

> "UNICEF provided us with nine refrigerators—seven fridges in the facilities and two here in the health zone. They provided the new fridges in March" *Informant Health Zone 1*.

4.3.4 Characteristics of informants

Knowledge and beliefs about the intervention

Strong informant support for timely BCG and OPV0 vaccines was due to respect for PEV BD mandates. Many informants would welcome HepB-BD if research and policymakers supported it:

> "They told us that we should introduce that [HepB-BD] at birth. And we await the period that we begin introducing it. Because we were well informed by PEV that there will be an introduction but until today, nothing*" Informant Health Zone 2*.

Self-efficacy

During ANC visits, midwives focused more on maternal care than on infant vaccination. As a result, provider willingness to communicate with mothers about BD vaccines was low. Most providers expressed vaccine knowledge and confirmed dissemination to mothers during ANC visits, but none of the mothers supported these claims. Mothers only reported education about receiving tetanus vaccine themselves during pregnancy. One mother stated:

> "What is important is to help us understand. During the visits, [the midwives] need to go into more detail because here we are in the dark [about vaccines/diseases]" *Mother Catholic 1*.

4.3.5 Outer setting

External policy

All informants were aware of national guidelines to provide BCG and OPV0 at birth. All facility-level informants also stated willingness to accept inclusion of HepB-BD in the immunization schedule if PEV mandated it.

Mothers' needs & resources

Choice of health facility. Vaccine cost and availability played a minimal role in mothers' choice of facility. Many, even experienced, mothers did not know the cost of vaccine care and only vaguely

knew which facilities offered vaccines. Instead, mothers revealed that their choice of a health facility was based on three factors: quality of care provided, distance to the facility, and recommendations from their family/community:

> "[Seeking care at this facility] was my mom's advice. My mom delivered here, and my big sister delivered here too. My mom told me that there is good care for the sick and a good quality of health here" *Mother Catholic 4*.

Mothers mentioned distance to a delivery facility influencing their decision in two ways. They either chose the closest and most convenient facility, or a farther away but 'higher quality' facility (and may continue infant immunizations at a closer facility).

Many informants agreed with the first two motives—the quality of the facility and distance— in mothers' choice of facility. One informant cited another factor associated with facility choice: affiliation with a community and/or religion.

> "What motivates here is distance, that is an aspect but not the only aspect. The second aspect is partnership. Say the partnership to a community, or perhaps to a religion. You will see that a Catholic would like to visit a Catholic facility. The third is the perception by the community of the quality of service by the health facility… a woman would say that she wants to go in this facility because it is clean, because it is presentable, it is a bit of that" *Informant PEV 1*.

Knowledge about vaccines and diseases they prevent. Only five of 16 expectant mothers stated having knowledge of HBV. Mothers who indicated having knowledge about HBV understood it only as a disease and were unfamiliar with prevention measures. Further, one mother believed it to be a disease that mainly afflicts infants:

> "I don't know much [about HBV], but I've heard it talked about. It is more the children who suffer" *Mother NFP 1*.

Similarly, mothers generally knew little about infant vaccines. Most primigravid and multigravida mothers could not provide details about any vaccines received during infants' routine vaccine visits. Experienced mothers could name BCG or demonstrate where infants received the vaccines on the body but could not explain which diseases were prevented by specific vaccines:

> "Kids receive vaccines. I don't know the names of the vaccines, but one is given orally and the other in the arm" *Mother Public 2.*

When provided the chance to ask questions, many mothers asked for more information about HBV, the risk it poses to their babies, and prevention methods, suggesting openness to vaccine education:

> "I want to know what hepatitis B is and more about the vaccines" *Mother Protestant 1*.

Birth-dose vaccine acceptance. Every mother expressed comfort with the current immunization schedule, and vaccinating their newborns within 24 hours of delivery. None of the mothers reported hesitancy about vaccines for their infants. When prompted, a mother responded:

> "Yes, I would be very comfortable with [my child receiving a BD vaccine] because this vaccine will give my child force and strength. If there is a disease that attacks my child, they will be protected" *Mother Public 2.*

While the mothers did not express vaccine hesitancy themselves, seven mothers reported other family or community members expressing hesitancy:

> "My maternal aunt refused vaccines for her kids. She thought that vaccines are bad for kids" *Mother Catholic 4.*

In addition, while the primary focus of our exploration was to understand facility-level vaccine hesitancy, a comment by a health zone-level informant in relation to community uptake of vaccines offered during mass vaccine campaigns was a striking indicator of community level vaccine hesitancy that mothers inevitably experience:

> "Vaccines remain until now the best method for prevention. But the quality suffers because there are too many speculations, it is perhaps you—the whites—who are putting confusion into the heads of the blacks." *Informant, Health Zone 2.*

The informant believed that fake information and media arriving from exogenous sources are a serious risk to vaccine uptake across the DRC. He stated that this was evident by the consistent decrease in vaccine uptake during annual mass campaigns in the last few years.

4.4. Discussion

This study is one of the first to identify determinants of HepB-BD vaccine uptake reported through interviews with informants and expectant mothers. Applying the CFIR domains, we found significant barriers to timely BD vaccines in Kinshasa, DRC, including multi-dose vaccine vials which determined when facility staff could vaccinate newborns; logistical concerns with regular national vaccine

stockouts and storage issues; complex and unsynchronized vaccine fees across facilities; inadequate communication across delivery and vaccination wards; and limited and at times incorrect understanding of vaccines among mothers and other community members.

Many informants and mothers expressed a desire for change, progress, and learning, but within a top-down system in DRC, dissemination of HepB-BD and streamlining guidelines must begin at the national level. A study of five SSA countries that introduced HepB-BD found the weakness of national policies and lack of written guidelines to deliver timely HepB-BD a significant barrier.[19] Informants confirmed their willingness to adapt BD vaccine initiatives, if supported by research and policymakers. We recommend harnessing that enthusiasm by developing clear guidelines for HepB-BD implementation at each level and conducting multiple trainings across the healthcare delivery spectrum, beginning at the level of national decision-makers and external funders and continuing to midwives and staff who would administer vaccines.

Packaging of BCG vials has implications for streamlining BD vaccines. The DRC receives support from Gavi, which requests that countries reduce their wastage to 15% (3 doses) for every 20-dose BCG vial.[129] It is therefore standard across SSA facilities to conduct daily to monthly batching of doses, depending on the volume of births in the facility.[130] The low volume of deliveries at rural or smaller facilities poses a critical barrier to BCG vaccination. Like HBV, BCG is ideally administered within the 24-hour window following delivery, with reductions of neonatal mortality by more than 40% compared to outside the 24-hour window.[131,132] The balance between reducing wastage and increasing essential coverage is a barrier to BCG coverage.[130,133,134] A solution to reducing wastage is to make lower dosage vials available. In Zambia, facilities using 5-dose vials had 47% lower waste than those using 10-dose vials.[130] While HepB-BD is typically offered in a 10-dose vial, HepB-BD lasts up to one month after the vial is opened (unlike BCG, which only lasts 6 hours).[74] However, if facilities hope to streamline the delivery of all BD vaccines and discontinue the newborn-batching approach, the size of BCG vials must be revisited.

Storage across and within facilities was a significant barrier within the inner setting domain. If a facility did not have capacity to store vaccines, staff traveled daily to collect vaccines. In addition, the limited availability of other resources, such as fuel and vehicles, was a common barrier to collecting off-site vaccines. When facilities had vaccines on-site, cold chain temperature surveillance posed a threat to the effectiveness of the BD vaccines.[118] In addition, some informants reported only storing BD vaccines in the primary vaccine fridge, and not near the delivery ward. Midwives reported not having access to the fridge and needing to coordinate vaccine administration with vaccine staff. These administrative barriers can cause further delays in the timeliness of the BD vaccines. The WHO recommends storing HepB-BD in the delivery ward to facilitate timely vaccination, especially if the storage ward requires special access permission—which was often the case in the study facilities.[74] We recommend clear guidance for facilities in line with these recommendations on the adequate storage of vaccines.

Gavi and national-level co-financing cover the cost of infant vaccinations and staff administration fees in DRC.[135] Despite this financing, mothers have to pay prohibitive fees for services.[29] To improve vaccine access , WHO recommends that HepB-BD (and other vaccines) be supplied to facilities at no cost and that facilities should not charge families for vaccine administration.[74] Therefore, we recommend national policy mandating free vaccine services for mothers. At the same time, national programs and their partners should appropriately compensate health facilities for their efforts.

We endorse training facility staff (midwives and vaccine staff) and education for mothers about BD vaccines. Informants reported providing thorough education to mothers during ANC visits, though most mothers could not name infant vaccines. We recommend more explicit guidance and educational material to facilitate vaccine communication pre-delivery. The provision of communication tool-based training for health workers has been shown to have a positive impact on vaccine uptake.[136,137] Options may include employing audio-visual educational materials,[138] or utilizing social workers instead of midwives to present visual aid tools to parents.[139] Improving mothers' knowledge will help combat vaccine hesitancy and increase mothers' understanding of the benefits of timely and complete vaccination. Midwives should also receive training on vaccine delivery to streamline BD administration.

The outer setting factors of CFIR, such as mothers' socio-demographic factors, attitudes, and knowledge about vaccines on health-seeking behavior, are essential when considering BD vaccines. These factors influence the final link in the vaccine distribution process, consumer uptake. The literature suggests that the strongest predictor of not receiving timely BD vaccines is the cost of vaccines,[29] and we thus expected vaccine fees to influence a mother's health-seeking behavior. However, we found that mothers knew little about cost and availability, and instead based decisions about which facilities to attend on the facility's quality of care, distance from home, and recommendations by family and friends. In addition, contrary to national evidence suggesting a rise in vaccine hesitancy,[140] our findings indicated that, mothers were comfortable vaccinating their newborns more often than not. One facility informant suggested that vaccine hesitancy is not a problem upon initial delivery, but that hesitancy is fostered once the mother-infant pair leaves the facility and is influenced by community-level hesitancy. Increasing maternal health literacy can combat vaccine hesitancy at the individual and community levels to increase vaccine coverage.[141] Sensitization campaigns through social media, mass media, or CHWs should target not only mothers, but also community members.[136]

4.4.1 Limitations

Our study has a few limitations to note. First, as a typically sized qualitative study, a sample of 16 informants and 14 expectant mothers within a large urban area may not capture all viewpoints. We iteratively reviewed transcripts to ensure that we reached thematic saturation, which is a more valuable measure than sample size in the realm of qualitative research. Secondly, we recruited all mothers from ANC visits, and therefore the participants are predisposed to maternal and child healthcare—which includes immunization care—compared to mothers who deliver at home or who do not seek antenatal care. As homebirths are no longer legal in the DRC and an estimated 80% of births occur in facilities, this sample aligns with the setting of future HepB-BD implementation. Third, all participants were recruited in a predominately urban setting, and therefore the findings may be less generalizable to rural settings. Finally, some phrasing may have been lost in translation due multiple languages; this was countered by

the expertise of natively bilingual investigators who administered, interpreted, and analyzed the interviews.

4.5 Conclusions

Using the CFIR framework, this study integrates perspectives from facility informants and expectant mothers to inform future national policy and implementation of the HepB-BD in DRC. These stakeholder-driven findings should guide the streamlining of timely BD vaccinations upon HepB-BD implementation.

Figure 4.1 Participant sampling by health facility type

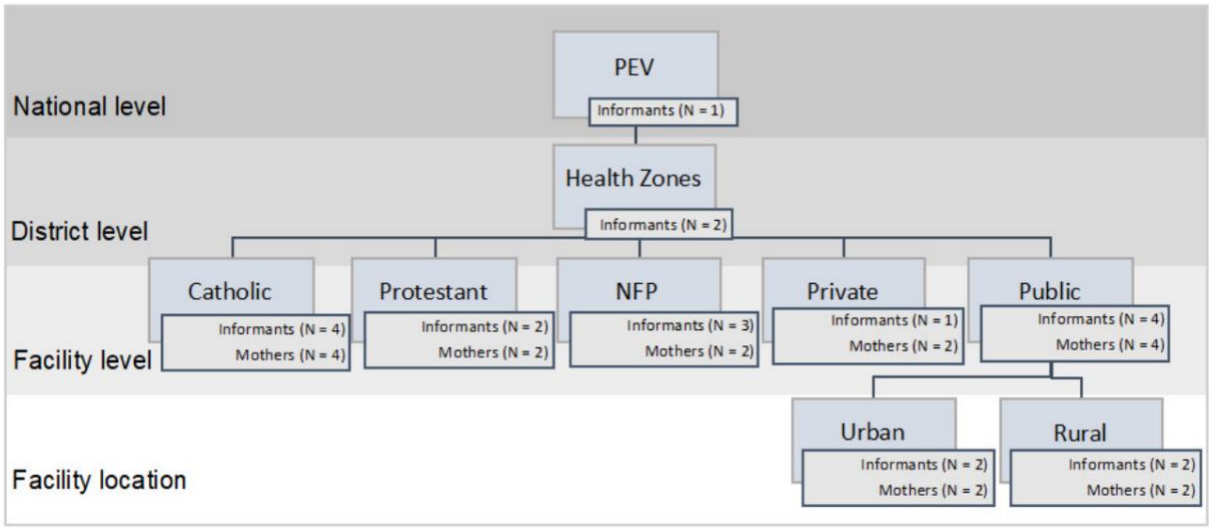
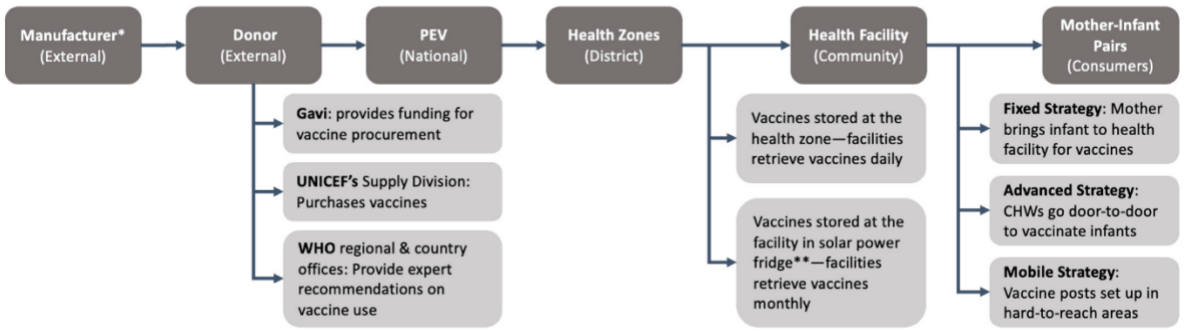


Figure 4.2 Illustration depicting hypothetical HepB-BD vaccine distribution system



*Manufacturer varies based on specific context and doses in vial (1-10 for HepB-BD)

**Solar power fridges provided by UNICEF and GAVI

Figure 4.3 CFIR constructs specific to timely delivery of streamlined birth-dose vaccines

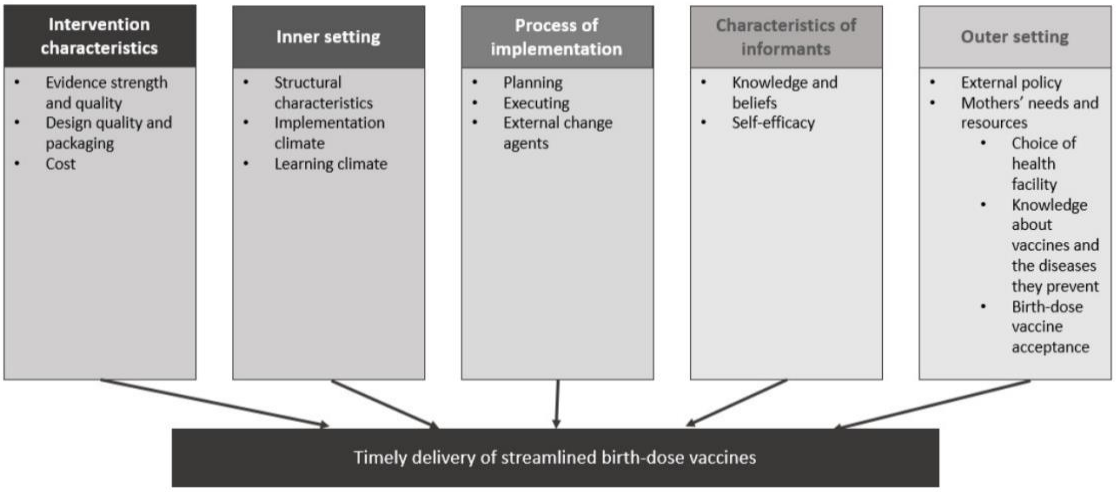


Table 4.1 Characteristics of study participants

Informants	N
Location	
Public Facility	4
Catholic Facility	4
Protestant Facility	2
Not-for-profit Facility	2
Health Zone	2
Private Facility	1
PEV	1
Region	
Urban	12
NA	3
Rural	2
Occupation	
Immunization Staff	5
Midwife	3
Head Nun/of Nursing/Midwives	3
Head of Vaccine Staff	2
Head of Vaccine Zone	2
Head of Facility	1
Head of National Vaccine	1
Mothers	N
Location	
Public Facility	4
Catholic Facility	4
Private Facility	2
Protestant Facility	2
Not-for-profit Facility	2
Region	
Urban	12
Rural	2
First Pregnancy	
Yes	8
No	6

Table 4.2 Facilitator and barriers to timely and streamlined BD vaccines presented within the CFIR construct

CFIR construct	Facilitators	Barriers
INTERVENTION CHARACTERISTICS - ***key attributes that influence the success of the intervention***		
Evidence strength & quality	Evidence based effectiveness of BD vaccines	
	Advocacy by global players, such as WHO	
Design quality & packaging	HepB-BD multi-dose vials viable < 28 days after opening	1-10 doses packaging options of HepB-BD
		BCG's 20-dose vials viable < 6 hours after opening
Cost	BD vaccines free-of-charge to facilities	Facilities require mothers to pay fee for vaccines (vaccine card)
		Infants' vaccine cards rarely accepted across facilities
INNER SETTING - ***attributes that interact with the facility***		
Structural characteristics	Many facilities reported small fridges near maternity ward	BD vaccines often kept in immunization ward and not near the maternity ward
	Some reported regular cold-chain supervision	Some small fridges were not used for BD vaccines/lacked space
	Some facilities have solar power fridges to maintain cold chain in case of electricity outage	Electricity outages pose risk to the cold-chain temperature
		Many facilities must retrieve BD vaccines daily at nearby reference facility
Implementation climate	Mothers and informants expressed optimism for BD innovation	
Learning climate		Need for BD vaccine training across disciplines
PROCESS OF IMPLEMENTATION - ***attributes that impact process***		
Planning	Plans for timely and streamlined BDs in the DRC underway	Clearer facility guidance on timely & streamlined BDs required

Executing		Regular national stockouts of BCG vaccine
External change agents	Donors help cover the cost of BD vaccines	
CHARACTERISTICS OF THE INFORMANTS - ***attributes rooted in the actions and behaviors of individuals***		
Knowledge & beliefs about the intervention	Informants support BD vaccines if PEV- and research-backed	
Self-efficacy		Need for stronger willingness by informants to communicate BD vaccine information to mothers
OUTER SETTING - ***exogenous attributes that influence the intervention***		
External policy	Health system top-down - informants would accept changes made to the national immunization schedule	
Patient needs & resources	Mothers sought information about HBV and other diseases	Vaccine availability did not influence mother's choice of facility
	Mothers were comfortable vaccinating newborns within 24-hours of delivery	Most mothers were not aware of risk, transmission, or of vaccine-preventable diseases
	Mothers did not report experiencing vaccine hesitancy themselves	Mothers reported vaccine hesitancy within their communities

CHAPTER 5 : USING INTERVENTION MAPPING TO FACILITATE THE ADOPTION AND IMPLEMENTATION OF TIMELY BIRTH-DOSE VACCINES IN KINSHASA PROVINCE, THE DEMOCRATIC REPUBLIC OF THE CONGO

5.1 Background

Birth-dose vaccines, such as the first oral polio dose (OPV0) and Bacillus Calmette- Guerin (BCG), play a critical role in protecting infants from life-threatening diseases and prevent severe morbidity for millions of children every year.[142–144] Likewise, hepatitis B vaccine (HepB-BD) has been shown to dramatically reduce mother-to-child transmission of hepatitis B virus if administered within 24 hours of an infant's birth (birth-dose), followed by the recommended subsequent doses.[97] This evidence led the WHO to recommend since 2009 that countries adopt the universal birth-dose vaccine, irrespective of maternal HBV serostatus.[97,145]

Despite the policy recommendation and effectiveness of administering timely HepB-BD to newborns to prevent mother-to-child hepatitis B transmission, timely HepB-BD implementation poses programmatic challenges. While 14 of 48 countries in SSA have introduced HepB-BD to their national immunization schedule,[47] timely uptake has remained strikingly low across the board. A 2022 study in Nigeria found that among the study sample, although 91% of infants received HepB-BD, only 33% received the vaccine within 24 hours of delivery.[146] A meta-analysis of 31 studies conducted in SSA found that the pooled rate of uptake of HepB-BD in the first 24 hours after delivery was 1.3%.[77] Even in high-income settings such as the United States, where HepB-BD was introduced in 1991, the complex challenge of timely delivery of HepB-BD led to high rates of delayed administration. A 2020 study in the US testing an intervention to improve timely administration through strategies such as staff education and guideline enforcement improved timely uptake from 40% to 92% of infants receiving HepB-BD.[147] As more SSA countries adopt the new birth-dose vaccine to their immunization schedules, the unique

challenges demonstrated by these anecdotes illustrate that implementation strategies are critical to introduction in a new context. A systematically developed implementation strategy—VANISH-BD (Vaccination of Newborns – Innovative Strategies to Hasten Birth-Dose vaccines' delivery)—will facilitate the adoption and implementation of timely birth-dose vaccine uptake.

I used intervention mapping (IM) to develop an evidence-based and theory-driven implementation strategy to facilitate the streamlined uptake of timely birth-dose vaccines. IM is a grounded approach that informs the use of implementation strategies to support the programmatic delivery of a health service intervention, further described below. Here I document the development of VANISH-BD, an implementation strategy to streamline birth-dose vaccine delivery in a timely manner using an IM approach. While I tailored the intervention development process to a DRC setting, my objective is to evaluate the implementation strategy's feasibility so that other researchers may adapt VANISH-BD to improve timely birth-dose vaccine uptake in other settings.

5.2 Methods

5.2.1 Setting

The intervention mapping process was set in Kinshasa Province, the DRC, a vast area with an estimated 15 million inhabitants.[148] The province encompasses urban, peri-urban, and rural areas, is one of the world's fastest-growing megacities, and is a contender as the most populous metropolitan area in Africa. Kinshasa Province is divided into 35 health zones with one reference hospital each; the number of facilities varies based on the size of the health zone.[149] The predominant facility ownerships in the DRC are religious, private, for-profit, and public.[149] In the DRC, the national vaccine program (Programme Élargi de Vaccination; PEV) selects facilities to provide vaccine services based on quality, and the number of individuals served rather than channeling vaccines only through publicly-owned facilities. For example, PEV may select a religious-based facility that reaches ample constituents to provide vaccination despite it not being government operated. Currently, PEV recommends two vaccines at birth, OPV0 and BCG. OPV0 is followed by additional doses at 6, 10, and 14 weeks of age, which are the same time points at which the pentavalent vaccine (which contains HepB3) is recommended. The final vaccine-

related setting consideration is that community health workers, employed at the health zone level, conduct vaccine outreach to improve uptake.

This study reports on the process of developing a theory-driven implementation strategy to improve the timely uptake of birth-dose vaccines in Kinshasa Province by using preliminary findings from this particular setting. A future study will evaluate the feasibility of VANISH-BD—an implementation strategy to improve timely and streamlined HepB-BD vaccine uptake developed using an IM approach – so that it can be scaled up or adapted by implementers in other similar settings.

5.2.2 Intervention mapping

Intervention mapping is a systematic approach that outlines a six-step process, using evidence and theory to introduce interventions and develop related implementation strategies for addressing health problems. Researchers and implementers have used intervention mapping in studies globally—and in sub-Saharan Africa specifically—to develop implementation strategies for introducing health interventions ranging from cancer management,[150] malaria elimination,[151] and improving antenatal care.[152] However, to our knowledge, studies have yet to employ an intervention mapping approach to developing an implementation strategy to improve the timely uptake of streamlined birth-dose vaccines.

IM is an iterative and cumulative process that uses outputs from previous steps to inform subsequent steps in the implementation process. The six steps of the IM process include:

(1) A needs assessment and logic model of the problem,
(2) Development of performance and change objectives,
(3) Selection of theory-based methods and strategies,
(4) Development of program components and materials,
(5) Development of the implementation and adoption plan, and
(6) Development of the evaluation plan.

Step 1 begins with an initial needs assessment focusing on the analysis of existing factors – both barriers and facilitators – related to the health problem. The analysis guides the development of a logic model of the problem. Step 2 integrates the findings from the needs assessment to select a target population, target performance and change objectives. Step 3 requires selecting theory-based methods and practical

strategies used in step 4 to design the intervention program and materials. Step 5 concentrates on program adoption and implementation, and step 6 generates the instruments to evaluate the intervention.[153]

An advantage of the IM process is its grounding in conceptual models, behavioral theory, and engagement with key stakeholders and community members to develop context-appropriate interventions. Community-based participatory research (CBPR) is an approach that ensures the use of bi-directional learning efforts to understand and improve intervention strategies.[154] CBPR provides a link through which evidence-based research, community members, and leaders can combine to develop sustainable and context-specific interventions. IM emphasizes applying CBPR principles by engaging community stakeholders throughout the intervention's development, implementation, and evaluation.

5.3 Results

5.3.1 Step 1. Needs assessment

In this step, I conducted formative research to define the priority population and environmental change agents using a literature review and qualitative and quantitative research approaches.

Literature review

Our assessment began with a literature review of barriers and facilitators to the timely uptake of HepB-BD in sub-Saharan Africa to review lessons learned from other similar contexts.[118]The review consisted of 49 articles and highlighted the need for a multi-level initiative to target factors impacting timely birth-dose vaccine uptake at the policy, facility, and community levels. The review also identified research supporting streamlined efforts of HepB-BD, polio, and BCG birth dose vaccines to improve timely uptake. At the time of the review's publication, four SSA-based studies assessed the effect of streamlined vaccines outside the 24-hour window. However, no study had evaluated the effect of streamlining the three vaccines at birth.[77] The WHO confirms that the three vaccines do not interfere with one another's immune response, and should be administered at birth.[74] Therefore, timely, streamlined birth-dose vaccines are a proven approach to improving infant health outcomes.

Qualitative research

I conducted interviews with expectant mothers and informants at the health facility, health zone, and national level (n = 30) across Kinshasa Province.[100] These interviews explored determinants to the uptake of currently available birth-dose vaccines – OPV0 and BCG – and perceived barriers to future uptake of HepB-BD vaccine from various perspectives. I conducted the interviews in seven health facilities, two health zone administration offices, and the national PEV offices. Facility staff working the day of and mothers visiting the center for a prenatal visit were approached and recruited for the study. Findings from this study highlighted significant barriers to the uptake of birth dose vaccines, including regular stockouts and lack of storage capacity, inconsistent vaccine fees across facilities, lack of communication between delivery and vaccine departments, and limited understanding of vaccines among mothers and communities.[100]

Quantitative research

I conducted regression analyses leveraging longitudinal data from a continuous quality improvement study (NCT03048669) to assess the barriers to the timely administration of currently available birth-dose vaccines, OPV0 and BCG.[155] I also evaluated the first dose of the pentavalent vaccine (including HBV) at six weeks. The study sample spanned 105 health clinics (currently unpublished). From the total study sample of 2,800 women, the sub-study included 2,398 eligible mother-infant dyads. The sub-study exclusion criteria included missing data about the infant's vaccine uptake, death of the mother or infant, and loss of follow-up before the study team could capture vaccination information. The longitudinal data analyzed the impact of factors such as a mother's socio-demographics and a health facility's general readiness score on an infant's timely receipt of vaccines. At the individual level, results showed that a mother's education, wealth, and proximity to a facility influenced the timely uptake of vaccines. A mother visiting a facility with religious affiliation and high general and immunization-specific readiness also impacted the timely uptake of vaccines.

Conceptual model

The PRECEDE (Predisposing, Reinforcing, and Enabling Constructs in Educational/Environmental Diagnosis and Evaluation) model guided our first step of IM. PRECEDE is a comprehensive structure often used in IM research to evaluate health needs to guide the design and implementation of health interventions.[156] PRECEDE categorizes factors influencing the health problem using three levels: individual (predisposing), interpersonal (enabling), and structural/ policy (reinforcing) factors inherent in health behaviors and interventions. Findings from the three parts of the needs assessment were categorized using the PRECEDE model in **Table 5.1**.

5.3.2 Step 2. Performance and change objectives

In the second step, I employed the main findings from the needs assessment to define birth-dose vaccine uptake behaviors for facility staff and mothers, defined our study objectives, described determinants of the identified behaviors, and developed matrices of change.

Our ultimate objective was to share findings with the national government to support modifying the national immunization policy and administration guidelines surrounding newborn immunization in Kinshasa Province, the DRC. Therefore, in this step, I aimed to develop, implement, and examine the feasibility of an intervention streamlining birth-dose vaccines, including HepB-BD, OPV0 and BCG, within 24 hours of delivery for newborns in Kinshasa. I achieved my objective by using a two-pronged approach targeting facilities and leveraging community outreach.

Change matrices help researchers determine the factors that must change to bring about each performance objective.[15] Using the findings from the needs assessment, I produced change matrices that combined factors likely to be associated with the achievement of our listed objectives. My change matrices included both performance objectives and the determinants of achieving each objective. I divided the matrices into two target groups, the adopters (**Appendix 5.1a**) –decision-makers at the health zone and facility levels, and the implementers (**Appendix 5.12b**) – health staff at the facility and community levels. Determinants included beliefs, behaviors, and expectations specific to the roles of

adopters and implementers. Any barrier determined through our needs assessment was therefore transformed into a change objective to achieve our desired outcome.[15,151]

To define the change objectives, I reported outcomes from needs assessment findings to community members. I held an open forum with health staff at the health zone and facility levels to elicit feedback and discuss reasonable change objectives. Each of the three sessions included approximately five participants and five study staff. Among the participants were a facility director, heads of vaccination, antenatal and maternity divisions, and a health zone representative. Sessions included dissemination of findings from the needs assessment, accompanied by an informative handout highlighting the critical determinants to timely birth-dose vaccine uptake. I then held group discussions to inform decisions on desired project outcomes for behavior change.

5.3.3 Step 3. Select theory-based methods and strategies

The objective of step 3 was to identify specific strategies to improve the determinants of success described in step 2. I therefore identified theoretical concepts and practical applications to guide the intervention's implementation. I identified methods for changing determinants from those outlined in step 2 and selected delivery strategies (**Appendix 5.2).** The community and health staff required sustained behavior change to improve timely birth-dose vaccine uptake. Therefore, I chose two relevant theories, the Theory of Planned Behavior [157] and the Social Cognitive Theory,[158,159] both widely employed to predict and explain health behavior in health-related interventions. The Theory of Planned Behavior states that behavior depends on an individual's motivation and ability to control behavior. The theory is categorized into three types of beliefs – behavioral, normative, and control.[157] The SCT suggests that bidirectional interaction between an individual and their behavior and environment leads to behavior change. The key components which impact behavior highlighted by the SCT include self-efficacy, behavioral capability, expectations, self-control, observational learning, and reinforcements.[158,159] Therefore, while I used the SCT to frame the macro-level factors influencing timely birth-dose vaccine uptake, the Theory of Planned Behavior focused on the micro-level components influencing the

individual's health behavior. Combining the two theories, I could predict and explain health behavior at various levels.

Using both theories, I successfully organized key determinants of behavior change and theory-based methods with practical application of behavior change techniques to overcome targeted barriers (**Appendix 5.3).** Using the theoretical frameworks, I grouped my strategies into three levels to impact sustained behavioral change: increasing knowledge, increasing self-efficacy, and changing outcome expectations. I employed the theory-based methods and linked each to practical application within the intervention's context.

Translating methods into applications required a sufficient understanding of the theory behind the method, leading to the theoretical change process. I constructed a logic model illustrating the potential relationships between theory and evidence-based methods and how they influenced determinants and outcomes (**Figure 5.1).** This model underpinned the intervention's planning, implementation, and evaluation.

5.3.4. Step 4. Develop the intervention

The next task for developing the intervention was to design educational and training materials and associated protocols for use by other policymakers and implementers aspiring to improve the uptake of timely and streamlined birth-dose vaccines. I assessed the existing resources at the facility and health zone levels, and examined how those resources, modified versions of the resources, or new assets could address our named program objectives. Based on the findings from the needs assessment, two program components were deemed important. First, a need to focus on behavioral aspects through individual and community awareness. Second, more buy-in from and guidance at the facility level are necessary to sustain a streamlined birth-dose vaccine approach. I employed implementation strategies to address the two components, including developing adopter and implementer relationships, identification of intervention champions, training sessions, and modification of educational materials, guidelines, and protocols (VANISH-BD). The two overarching components – updating material for individual and community awareness and training champions to ensure sustainability – are discussed below.

Updated material for individual and community awareness

Other relevant research and the needs assessment informed VANISH-BD's components for achieving specified program objectives. Our assessment found that mothers received little to no information about childhood vaccines during ANC visits, a missed opportunity to disseminate vaccine knowledge. In addition, the information shared varied across facilities, with no clear guidance on timely birth-dose vaccine uptake. Therefore, I developed new educational posters and scripts to be used by ANC staff to educate mothers about the risks of hepatitis B, polio, and tuberculosis and the benefits of the vaccines to prevent these diseases (**Appendix 5.4a., 5.4b. and 5.4c)**. In addition, my research suggested that the community plays a significant role in a mother's decision to vaccinate her infant. Therefore, I sought to leverage CHWs to partner with community leaders – through churches and schools – to further disseminate information about newborn vaccines. I developed specific guidelines and educational materials for this purpose (**Appendix 5.5a and 5.5b).** Finally, I found the following: only vaccine ward staff were administering the birth-dose vaccines, current guidelines did not ensure that delivery and vaccine ward staff communicate when newborns are born, and fridges in the maternity ward do not stock birth-dose vaccines. Each of these factors inhibited the timely uptake of streamlined birth-dose vaccines. Therefore, I developed updated protocols for birth-dose vaccine administration and a checklist outlining the guidelines for timely vaccine uptake to be administered by maternity ward staff for each newborn. All materials were translated into local languages and dialects and used pictures when possible to reach illiterate audiences.

Training champions to ensure a sustained initiative

In order to introduce a feasible and sustainable implementation strategy, our suggestion was to train community health workers and staff in the vaccine and delivery wards as champions to implement VANISH-BD in order to ensure that other health staff adhere to the initiative. The use of champions served three purposes: (1) to ensure day-to-day activities are maintained, (2) to hold recurring meetings with champions for continuous learning, and (3) to provide training to staff and incite buy-in to ensure the sustainability of VANISH-BD. Available evidence suggests that champions are facilitators of successful

change efforts and are crucial to practical implementation in health care.[160] Training, empowering, and leveraging champions is commonplace when implementing programs across global health systems. However, to date, most published research leveraging change champions is based on western research with scarce LMIC-based literature available.

The intervention planning group developed a two-day baseline training for champions and an additional two-days led by champions for relevant health staff. The training, which we will roll out during the trial phase, will consist of the study staff attending two days of onsite practice. The onsite practice will involve study staff visiting the facilities and supervising the implementation of VANISH-BD (**Appendix 5.6).**

In the future, every month during the study, the three levels of champions will then meet with study staff to debrief about challenges encountered and brainstorm potential solutions going forward. The champions will play a critical role during the study to help flesh out issues related to the implementation strategy. This step will ensure that the final implementation package, VANISH-BD, and associated training and education material and guidelines are field-tested, and feasibility verified for scale-up or use in other settings.

5.3.5 Step 5. Develop the implementation plan

Step 5 focused on developing an implementation plan to ensure the successful adoption and implementation of VANISH-BD across all study facilities. The objective was to implement the complete intervention in all facilities and achieve sustainability through the maintenance of champions and training. From this study's formative needs assessment step, and in response to the need for timely and streamlined birth-dose vaccines, I produced VANISH-BD's intervention plan and materials for all of these strategies (**Table 5.2**). The intervention plan has been discussed, and the adoption and implementation of VANISH-BD assured by leadership at the health zone and facility levels.

5.3.6 Step 6. Develop the evaluation plan

The final step was developing an evaluation plan, which ensured intervention feasibility measurement spanning the lifecycle of its implementation. During the future study, a continuous

evaluation will allow opportunities to amend the intervention and improve its adoption, impact, and sustainability. The evaluation plan will be finalized as part of the completed future study, but I present an overview below.

Study design and timing

I will evaluate the feasibility of VANISH-BD through a cluster-randomized controlled trial in Kinshasa Province, DRC, in 12 facilities. I will expose the treatment arm to VANISH-BD, and the control arm will receive the HepB-BD vaccine without the implementation package. The treatment and control facilities will be located in non-contingent catchment areas to ensure that community dissemination does not spill over to the control facility territory and to limit heterogeneity among the selected facilities.[161] I will organize an awareness session to inform the facility staff in the control arm that newborns will receive HepB-BD. I will divide the study period into two phases: a 12-month intervention and a three-month post-intervention follow-up phase. The 12-month intervention period of VANISH-BD will provide enough time for staggered facility roll-out, follow-up of enrolled mother-infant dyads, and time to deliver and follow the EPI schedule through 14 weeks. I will use the three-month post-intervention phase to clean and analyze study findings.

Outcomes

The primary outcome will be the proportion of newborns in facilities receiving timely birth-dose vaccines (within 24 hours of delivery) of all three vaccines, HepB-BD, OPV0, and BCG. The secondary outcome will be the number of children receiving a complete EPI schedule by 14 weeks of age. Both outcomes will be measured using birth and vaccine records at the facility and health zone levels. Health zone CHWs will help track down mother-infant dyads that leave or move from study facilities before completing their EPI schedule. A final outcome will be vaccine awareness and perceived benefit among health staff and mothers in the treatment and control groups. Awareness and perceived benefit will be measured using baseline and end-line questionnaires. The study staff will conduct a quarterly review of VANISH-BD's implementation and will make necessary adjustments to the study's approach.

5.4. Discussion

In this paper, I presented an intervention mapping approach to develop VANISH-BD, a strategy targeting health staff to equip them with the necessary tools to increase the uptake of timely birth-dose vaccines for newborns. VANISH-BD addresses the barriers to vaccine uptake using theory-based behavior change techniques to achieve the desired behavior outcome in health staff, mothers, and the community. In the future, I will conduct a randomized controlled trial to assess the feasibility of VANISH-BD. While this initiative was developed specific to the DRC, I intend for VANISH-BD to be adapted and used in other contexts.

Our initiative was based on formative research to define the priority population and environmental change agents using a literature review as well as qualitative and quantitative research. I categorized our assessment using the PRECEDE model to understand the individual, interpersonal, and environmental components that impact health behavior influencing the uptake of birth-dose vaccines. The needs assessment highlighted significant barriers at the individual level, such as lack of vaccine knowledge among mothers and health staff; at the interpersonal level, such as a lack of communication between EPI and maternity staff; and at the environmental level, such as an absence of consistent guidance about birth-dose vaccines across facilities.

Among our most significant challenges was the scarce literature on implementation strategies for effective rollout of timely HepB-BD in similar SSA settings. This gap in the literature pushed me to employ the IM approach to develop this initiative based on a needs assessment conducted in the DRC and to report on the findings so that other researchers and implementers may use the implementation strategy, VANISH-BD, in other vaccine uptake research. Through our decision to use an IM approach that is grounded in theory and evidence, I can proactively address multilevel barriers to timely streamlined BD vaccine uptake. As such, our intervention focuses on updating materials for individual and community awareness and training champions to foster internal ownership and leadership of VANISH-BD and, ultimately, its sustainability. Maternal education has been shown to positively contribute to child health and associated immunization service uptake.[162,163] A meta-analysis found that education about

vaccinations through counseling sessions and printable information materials increased overall vaccination coverage by 19%.[164] In the same meta-analysis, interventions for providers, such as training for health staff and reminders for end-users, were shown to improve vaccine coverage by 13%.[164] Finally, leveraging CHWs to engage and educate community and religious leaders is a commonly employed approach to increase vaccine uptake through information campaigns.[165–167] Given the unique challenge of administering the HepB-BD within the short window after birth, an intervention leveraging all of these evidence-based approaches has the best likelihood of increasing the uptake of timely birth-dose vaccines.

Our study's primary limitation is that scarce research exists on the novel approach of streamlining birth-dose vaccines within 24 hours of delivery. Our literature review found that despite WHO's recommendation of streamlined timely birth-dose vaccines, research studies applying this approach had yet to be conducted in SSA. However, this gap in the literature propelled me to develop VANISH-BD, an implementation strategy to improve the uptake of timely BD vaccines, so that future researchers and implementers may use our evidence-based approach in other settings.

5.4.1 Next steps

I will conduct an RCT to objectively assess VANISH-BD's feasibility and effect on the uptake of timely and streamlined BD vaccines for infants in Kinshasa Province, the DRC. The long-term objective is to (1) integrate this strategy alongside the roll-out of HepB-BD across the DRC to proactively improve timely HepB-BD and (2) improve the timely delivery of currently available OPV0 and BCG BD vaccines. Findings from this study can be used by policymakers in the DRC when developing an approach to revise the DRC national PEV schedule to include HepB-BD.

5.5 Conclusions

This study reports on developing VANISH-BD, an implementation strategy to improve the uptake of streamlined birth-dose vaccines within 24 hours of delivery. I developed VANISH-BD using an intervention mapping approach to ensure that it was grounded in theory. The intervention is contextually relevant, locally produced, sustainable, and designed to improve timely birth-dose vaccine uptake in the DRC. By providing a detailed, stepwise description of the intervention development process, other

researchers and implementers may use the findings to adopt the implementation strategy in other relevant settings to facilitate HepB-BD introduction and improve the uptake of streamlined birth-dose vaccines at the facility level.

Figure 5.1 Theory-driven logic of solution model for vaccine uptake

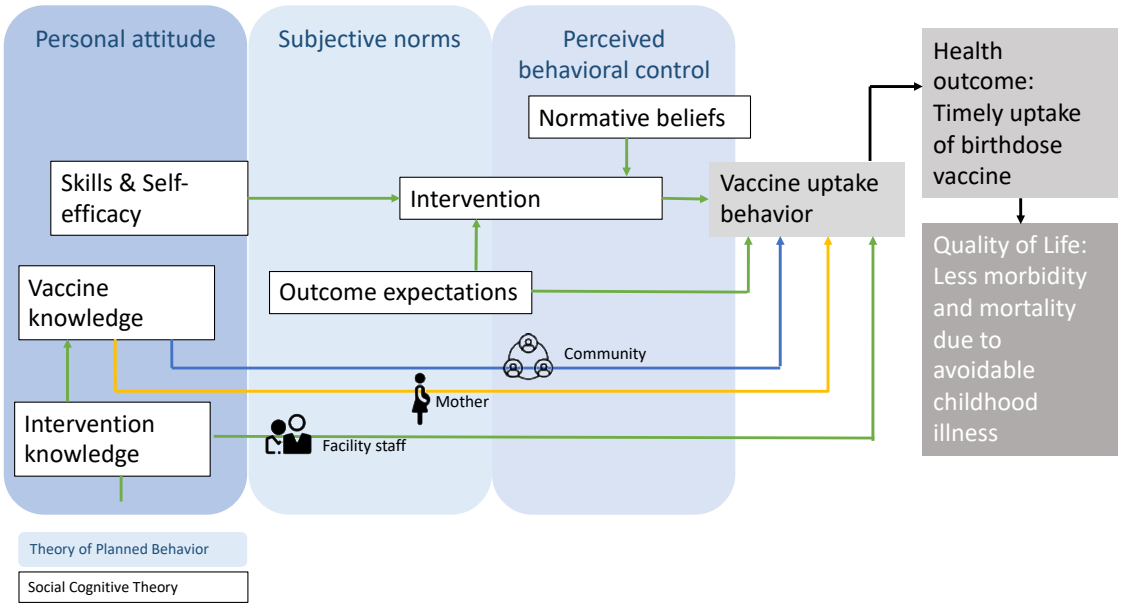


Table 5.1 Preliminary findings from need assessment

PRECEDE Construct		Preliminary Findings	Source
Individual (Predisposing)	Facilitators	Motivation to keep infant safe and protected	Qual
		More vaccine knowledge with more mature age and education	Qual & Quant
		Knowledge that vaccines can protect against seasonal diseases	Qual
	Barriers	Low socioeconomic status of mother	Quant
		Lack of knowledge about disease prevalence and vaccine benefits	Qual
		Delay seeking birth-dose vaccines	Quant
		Residing further than walking distance from a facility	Quant
Interpersonal (Reinforcing)	Facilitators	Opportunity exists to disseminate vaccine knowledge during ANC visits among mothers who seek antenatal care	Qual
		Opportunity exists to disseminate vaccine education to community by leveraging CHWs	Qual
		Physical space for posters and guidance in facilities	Qual
	Barriers	Collaboration and communication between midwives and vaccine staff	Qual
		Influence on vaccine hesitancy from families and friends (community)	Qual
		Clarity of vaccine education disseminated to mothers during ANC visits	Qual
Organizational (Enabling)	Facilitators	Existing guidelines and workflows in place for vaccine distribution	Qual & Quant
		Free vaccine services at public facilities	Qual
		Discussions at national level to include HepB-BD to national immunization schedule	Qual
	Barriers	Absence of guidelines about streamlining timely birth-dose vaccines across facilities	Qual & Quant
		Varying vaccine fees across facilities	Qual
		Stockouts of vaccines	Qual
		Absence of storage for birth-dose vaccines in delivery ward	Qual
		Absence of HepB-BD on national immunization schedule	Qual & Quant

Table 5.2 Specific implementation plans and materials for streamlining timely birth-dose vaccines

Implementation Strategy	Implementation Plan
Facility based education	• Development and dissemination of single-page infographic about HepB-BD for use during antenatal visits and at delivery by health staff to educate mothers and families about HBV risk and HepB-BD benefit. • Development and dissemination of educational posters about HepB-BD and other BD vaccines to be hung in facilities
Educational outreach program	• Creation of a community outreach initiative in schools and churches • Leverage CHWs to educate the community on HBV and other vaccine preventable diseases (tuberculosis and polio)
Champion approach	• Training of champions in the vaccine ward, the delivery ward, and community health workers • Champion supervision at the onset of the study
Champion learning collaborative	• Monthly joint meetings via a WhatsApp platform of each champion team to share experiences with the study and discuss challenges and solutions.
Written clinical guidelines	• Dissemination across all study facilities of written guidelines for the introduction of HepB-BD alongside streamlined OPV0 and BCG

CHAPTER 6 : CONCLUSION

6.1 Overview

Across sub-Saharan Africa (SSA), hepatitis B virus (HBV) prevalence is higher than anticipated, despite the widespread vaccination. The primary prevention tool is the three-dose HBV vaccine (HepB3), which has been available globally since 1982,[16] but only in the DRC since 2007. Likewise, the burden of infectious diseases such as tuberculosis, for which there is an established birth-dose vaccine, remains strikingly high in SSA.[168] This research advances our knowledge about the unique challenges to childhood vaccination uptake at the various socio-ecological levels, such as individual, facility, and national levels. My findings highlight the complexities of vaccine distribution systems and the comprehensive and detailed approaches to overcome these distribution challenges using methods such as implementation mapping guided by needs assessment and theory. This dissertation's findings are relevant to policymakers and implementers who aim to 1) better understand the unique determinants that impact timely birth-dose vaccine uptake and 2) introduce the HepB-BD vaccine to new contexts.

Here, I combined a scoping review of the literature, semi-structured interviews with expectant mothers and informants from the vaccine distribution system, and data analyses encompassing facility administration and individual care-seeking in order to provide a needs assessment of the birth-dose vaccine landscape. The needs assessment then played an integral role in an intervention mapping approach to develop an evidence- and theory-based approach to administering timely and streamlined vaccines. This study filled a gap in the current evidence in the following ways: Chapter 2 provided a literature review of determinants of HepB-BD uptake in SSA at three socio-ecological levels: national, facility, and community; Chapter 3 measured multi-level determinants of timely birth-dose vaccine by using a unique data source that combined longitudinal mother-infant dyad and facility inventory data;

Chapter 4 explored individual testimonies of the barriers and facilitators to infant vaccine uptake across the health system continuum; and Chapter 5 described the development of an implementation approach for introducing timely and streamlined birth-dose vaccines (OPV0, BCG, and HepB-BD) across maternity centers by employing an intervention mapping approach. To my knowledge, this was the first study of infant vaccine uptake that used an in-depth needs assessment, combining various methods, to proactively suggest an approach to overcoming wide-spanning and context-specific determinants across the socio-ecological levels.

The results of this study provided insight into vaccine distribution services in 105 maternity centers across Kinshasa Province, the DRC. Its focus on timely vaccine distribution and administration was timely and essential given the current worldwide epidemic and its impact on routine immunizations.[4,162,169] It is cited that the COVID-19 pandemic had disastrous effects on the uptake of childhood vaccines: in 2020, 17 million children globally did not receive any vaccines[170] and the rate of uptake for the first dose of the pentavalent vaccine (including HBV) declined by 41 % in SSA.[171] This underscored the imperative to better understand the complex determinants interplaying at all societal levels to disrupt timely vaccine and, more importantly, birth-dose vaccine uptake. Ultimately, this research contributed to the improvement of infant health outcomes against vaccine-preventable diseases by underscoring the unique vaccine confidence, immunization system management and administration, and access barriers that prevent infants in Kinshasa Province from receiving timely immunizations. This study provided context-specific and evidence-based solutions to overcoming these obstacles.

6.2 Summary of studies

The overarching goal of this research was to contribute to improved infant and population health by advancing understanding of the determinants and effects of timely infant vaccines; this dissertation work culminated in an implementation strategy for integrating a new vaccine – HepB-BD – while also improving the timely uptake of current birth-dose vaccines – OPV0 and BCG—in the DRC. I conducted four studies to meet this objective. My studies leveraged data and existing infrastructure across health

facilities in Kinshasa Province established by a DRC-based team and facilitated by faculty at UNC-Chapel Hill and Albert Einstein School of Medicine.

In the first study, I took a higher-level approach to explore existing challenges and real-world case studies of implementation challenges to introducing HepB-BD to new sub-Saharan African contexts by conducting a systematic literature review of published literature. I described barriers to the uptake of HepB-BD in SSA at the policy, facility, and community levels and proposed solutions relevant to stakeholders wishing to introduce HepB-BD to a new context. I highlighted the importance and challenge of reaching infants born outside of healthcare facilities (i.e., home deliveries) with HepB-BD in partnership with community health workers. I also discussed the critical role of maternal education and community engagement in future HepB-BD scale-up efforts.

The second study used two ordered regression models to assess barriers to and determinants of timely BCG and the first round of hepatitis B (HepB3) immunization across multiple time points using the Andersen Behavioral Model. Between 2016 and 2020, 1,981 infants (82.6%) received the BCG vaccine, and 1,551 (68.4%) received the first HepB3 vaccine. The distribution of timing of BCG uptake was as follows: 26.3% received BCG within 24 hours, 43.5% between one and seven days, and the remaining 12.8% between one and 14 weeks. Of infants who received the HepB3 vaccine, 22.4% received the first dose within six weeks, and 46% between six and 14 weeks. Many factors were positively associated with BCG uptake, including higher maternal education, household wealth, higher facility general readiness scores, and religious-affiliated facility ownership. The factors influencing HepB3 uptake included older maternal age, higher education level, household wealth, transport by taxi to a facility, higher facility general and immunization readiness scores, and religious-affiliated facility ownership. These findings suggest that investments to strengthen the vaccine delivery system might improve timely vaccine uptake and equity in vaccine coverage.

In the third study, I conducted semi-structured interviews in seven health facilities across Kinshasa Province from June to July 2021. The Consolidated Framework for Implementation Research (CFIR) guided my data analysis and I identified 13 constructs (2-3 per domain) related to the success of timely

and streamlined BD vaccines. I found significant barriers within and across each domain; most notably, the multi-dose vials of existing BD vaccines determining when facility staff could vaccinate newborns, often resulting in untimely vaccinations; logistical concerns with regular national vaccine stockouts and ability to store vaccines; complex and unsynchronized vaccine fees across facilities; inadequate communication across delivery and vaccination wards; and limited and at times incorrect understanding of vaccines among mothers and other community members.

In my fourth and final study, I employed an intervention mapping approach, using findings from my precursory chapters, to introduce HepB-BD and improve timely uptake of all birth-dose vaccines in Kinshasa Province. I described the development of the implementation strategy using intervention mapping, an evidence-based and theory-driven approach. I reported on the development of my intervention, beginning with the needs assessment based in Kinshasa Province, DRC, informing step 1 of intervention mapping. The intervention was contextually relevant, locally produced, sustainable, and designed to improve timely birth-dose vaccine uptake in the DRC. I intended to inform future implementers about improving timely and streamlined birth-dose vaccine uptake and for VANISH-BD to be adapted for similar contexts.

In sum, my findings presented unique determinants to timely vaccine uptake based on evidence from other countries, secondary data from a large-scale longitudinal study, and semi-structured interviews across the health system. The study also leverages an evidence-based and theory-driven approach, intervention mapping, to develop an implementation strategy to streamline timely birth-dose vaccines across maternity centers in the DRC. The process and results of this research highlight the need for more comprehensive, multi-dimensional, and context-specific approaches for improving vaccine distribution systems and introducing HepB-BD to new low-resource contexts.

6.3 Limitations

The studies described in the dissertation do have several limitations. First, the evidence review conducted during Chapter 2 and referenced throughout the dissertation studies is grounded in only a few examples of successful HepB-BD introduction in SSA.[19,66,68] The scarce literature, paucity of African

countries (13/48) that have introduced HepB-BD to date, and the poor uptake of the birth-dose vaccine where it has been introduced drove our DRC-based team to devise an implementation strategy to proactively improve timely HepB-BD uptake prior to its introduction.

Next, I collected data from participants during ANC care in a predominately urban setting. These expectant mothers are predisposed to maternal and child healthcare—including immunization care—compared to mothers who deliver at home or those who do not seek antenatal care. The findings, therefore, may be less generalizable to rural settings.

In addition, my assessment in Chapter 3 leveraged sample participants from a cohort of women already enrolled in an HIV continuous quality improvement study, which impacted the generalizability of this study. However, vaccine uptake in this population was similar to the national average, and factors influencing vaccine uptake were aligned with other infant immunization studies in the Congo and elsewhere in SSA.[36,80,107–109,111,112,115] The measure of vaccine uptake status and timing may have suffered from recall bias because of the contemporaneous approach of capturing vaccine dates during study interviews. The study staff reviewed infants' vaccine records to correct any errors in logging the vaccine dates to help alleviate any errors. Another limitation of the assessment detailed in Chapter 2 is that I could not infer causal estimates and instead presented associations. Finally, while the parent study did experience significant rates of LTFU, study staff followed up with respondents to understand the reasons for LTFU and recaptured some of the data that otherwise would have been lost. A weighted analysis including LTFU within the 'never vaccinated' category allowed me to calculate more accurate rates of failure to vaccinate.

The study described in Chapter 4 had a small sample size of 16 informants and 14 expectant mothers, which limited perspectives to those in Kinshasa's urban metropolis. However, I iteratively reviewed transcripts to reach thematic saturation. In addition, some phrasing may have been lost in translation due to multiple languages – Lingala, French, and English. This was countered by the expertise of natively bilingual investigators who administered, interpreted, and analyzed the interviews.

Finally, Chapter 5 focuses on the process of intervention mapping to develop an implementation strategy; therefore, the intervention has yet to be tested. However, the needs assessment, collaboration with national, facility, and community stakeholders, and evidence-based approaches in developing the intervention ensured that this intervention was context-specific and sustainable.

6.4 Implications for research

This research has important implications for research. First, in Chapter 2 I summarized research findings across various sub-Saharan African settings and developed a comprehensive list of solutions for overcoming barriers to HepB-BD uptake. Specifically, the review highlighted the scarce literature addressing the complexities of rural at-home births in many African settings. This is the first known review to provide future researchers and implementers with a blueprint for introducing the HepB-BD.

Chapter 3 evaluated the determinants of uptake of infant vaccines at different time intervals using ordered logit regression models. Data on timing of vaccine uptake for over 2,000 mother-infant dyads were available through a large-scale continuous quality improvement initiative across 105 maternity clinics in Kinshasa Province, the DRC. This study was unique due to the wealth of relevant data available at the mother-infant level and at the facility inventory and staffing levels. In addition, to my knowledge, this was the first study to use the employed method to highlight the unique determinants at various time intervals. Model I reported on determinants of BCG uptake within 24 hours of delivery, between one and seven days, or one week to 14 weeks; versus those who never received the BCG vaccine during the study period. Model II reported on uptake of HepB3 within six weeks, and at six to 14 weeks, compared to no uptake during the study period. These findings can be used to address specific determinants for targeted timing of uptake.

In Chapter 4, I addressed a research gap by reporting on the first qualitative studies that reported on determinants of BD vaccine uptake in a low-resource setting. While other research reported barriers and facilitators to infant vaccines, ours was the first to examine the unique challenges of introducing time-sensitive birth-dose vaccines. Further, my research was novel in combining results from testimonies of informants across the vaccine care continuum, from the national EPI schedule, through health zones, and

within various facility wards. In addition, I interviewed expectant mothers after finding that their voices and testimonies are often overlooked in related research in low-resource settings.

Finally, the research in Chapter 5 addresses the call to use evidence-based approaches and theory to underpin an intervention mapping approach for developing an implementation strategy to improve the timely uptake of streamlined birth-dose vaccines.

6.5 Implications for practice

In addition to contributing to the research in this field, the dissertation research results also have many practical applications. First, the results of these studies are drawn from real-world situations where teams are working to vaccinate infants and reduce infant morbidity and mortality. The findings can be used to identify solutions to common barriers to timely infant vaccines in the DRC and other similar settings. For instance, I identified significant determinants of timely uptake of both BCG and HepB3 at the external environmental level, focusing on intervenable facility characteristics. I found that infants are not receiving their birth-dose vaccines before they initially leave maternity centers due in part to a lack of communication between the maternity and EPI wards. Maternity wards do not have the ability to administer or store vaccines in their part of the maternity center. Therefore, when a mother-infant dyad leaves the facility, they are asked to return days later and visit the EPI ward. By improving inter-health staff communication, empowering the maternity staff to administer vaccines, and stocking birth-dose vaccines in already available refrigerators in the maternity ward, timely birth-dose vaccine uptake can be achieved in real-world settings in the DRC and elsewhere. In addition, these solutions culminated into an implementation strategy that may be uses by ministries of health in countries intending to introduce HepB-BD and improve timely and streamlined birth-dose vaccines.

6.6 Future directions

This research adds to the growing evidence base on the best practices for implementing evidence-based and context-specific interventions to improve health outcomes in low-resource settings. A few critical areas may be explored to continue contributing to this field of research. First, and critically, the implementation strategy developed in Chapter 5 should be piloted across facilities in Kinshasa Province,

the DRC. I intend to conduct an RCT to objectively assess the intervention's effect – comparing treatment clinics receiving the implementation strategy to control clinics that do not – on the uptake of timely and streamlined BD vaccines for infants in Kinshasa Province. The long-term objective is to (1) integrate this strategy alongside the future roll-out of HepB-BD across the DRC to proactively improve timely HepB-BD uptake, and (2) improve the timely delivery of already available BD vaccines, OPV0 and BCG. Findings from this study can be used by policymakers in the DRC when developing an approach to revising the DRC national EPI schedule to include HepB-BD.

Second, researchers can continue to study the determinants of timely birth-dose vaccine uptake. While Chapter 3 identified determinants of BCG uptake, I could not investigate the determinants of uptake of HepB-BD because the DRC has yet to introduce the vaccine. Future research may be conducted in similar contexts that have already introduced HepB-BD, using the same ordered logit regression approach to highlight determinants at various time points. Otherwise, a follow-up study re-examining determinants of HepB-BD in Kinshasa Province may be conducted as part of a pilot study introducing this vaccine.

Finally, literature both about reaching rural, hard-to-reach home births and about the mother's involvement is scarce within the vaccine uptake research field in SSA. In the DRC, this dissertation research--identifying determinants of timely vaccine uptake at the facility level and developing an implementation strategy to be utilized throughout facilities--may be used as a gateway to begin conversations with policymakers about reaching at-home deliveries with birth-dose vaccines and improving rural infant health outcomes. Future research may include testing and leveraging evidence-based innovations already identified in SEA,[3,45,67,79] such as OOC vaccines and mHealth innovations, to improve vaccine reach to home births. There is also a need for more research incorporating the mother's perspective and role in timely vaccine uptake. Although SSA countries acknowledge the need for buy-in for HepB-BD at the political and facility levels, health officials and researchers continuously understate the mother's and community’s role in HepB-BD implementation approaches. Crowd-sourcing is a

potential solution that would incorporate the voices of all stakeholders, from political players to mothers/caregivers, in a context-specific strategy to introduce timely HepB-BD.[172–174]

6.7 Concluding remarks

I leveraged multiple methods to identify challenges to introducing timely birth-dose vaccines, especially HepB-BD, in the DRC and throughout SSA. I then used the needs assessment to develop a proposed implementation approach to improving timely, streamlined birth-dose vaccines. An intervention mapping approach underpinned my needs assessment. I examined barriers to uptake related to the individual – vaccine confidence and knowledge; facility – administration barriers such as lack of communication between vaccine and maternity wards; and national – updating the EPI schedule and improving guidelines for timely birth-dose vaccine uptake—levels. This method allowed me to develop an implementation approach targeting every level of the socio-ecological model. Attention to the multi-level implementation determination of timely birth-dose vaccine uptake is critical to introducing and accelerating uptake in new contexts such as the DRC. Providing an intervention tool kit that will be piloted and adapted to similar contexts can help future implementers and policymakers in their efforts to improve childhood health outcomes against preventable diseases.

APPENDIX 3.1 MODEL I AND MODEL II SPECIFICATIONS

Model I	AIC	AIC [weighted]	Variable										
			Birth order	Age	Education	Marital	Wealth Index	Transport	Facility Readiness	Immunization Readiness	Facility type	Ownership	Urban
Model I.A	5107.446	6982.055	Linear	Linear	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model I.B	5108.343	6981.075	Quadratic	Linear	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model I.C	5109.336	6983.984	Linear	Quadratic	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model I.D	4951.815	6977.715	Linear	Linear	Linear	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model I.E	4953.564	6978.56	Linear	Linear	Quadratic	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model I.F	4954.756	6988.408	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model I.G	**4951.641**	6989.533	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Categorical	Binary	Categorical	Binary
Model I.H	4954.647	6977.053	Linear	Linear	Linear	Binary	Categorical	Binary	Categorical	Linear	Binary	Categorical	Binary
Model I.I	4956.521	6987.418	Linear	Linear	Quadratic	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model I.J	4954.847	6990.344	Quadratic	Linear	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model I.K	4956.742	6989.289	Linear	Quadratic	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model I.L	4952.726	**6969.91**	Linear	Linear	Linear	Binary	Categorical	Binary	Quadratic	Linear	Binary	Categorical	Binary
Model 1.M	4956.376	6990.264	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Quadratic	Binary	Categorical	Binary
Model 1.N	4954.624	6971.812	Linear	Linear	Linear	Binary	Categorical	Binary	Quadratic	Quadratic	Binary	Categorical	Binary

Model II	AIC	AIC [weighted]	Variable										
			Birth order	Age	Education	Marital	Wealth Index	Transport	Facility Readiness	Immunization Readiness	Facility type	Ownership	Urban
Model II.A	4006.155	5373.696	Linear	Linear	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model II.B	4008.155	5375.517	Quadratic	Linear	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model II.C	4007.579	5374.651	Linear	Quadratic	Categorical	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model II.D	3882.626	5365.971	Linear	Linear	Linear	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary
Model II.E	3883.884	5367.922	Linear	Linear	Quadratic	Binary	Categorical	Binary	Categorical	Categorical	Binary	Categorical	Binary

Model II.F	3882.698	5386.044	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model II.G	3885.882	5387.82	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Categorical	Binary	Categorical	Binary
Model II.H	3880.814	5366.406	Linear	Linear	Linear	Binary	Categorical	Binary	Categorical	Linear	Binary	Categorical	Binary
Model II.I	3883.904	5387.984	Linear	Linear	Quadratic	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model II.J	3884.537	5387.841	Quadratic	Linear	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model II.K	3884.528	5387.187	Linear	Quadratic	Linear	Binary	Categorical	Binary	Linear	Linear	Binary	Categorical	Binary
Model II.L	**3874.183**	**5352.979**	Linear	Linear	Linear	Binary	Categorical	Binary	Quadratic	Linear	Binary	Categorical	Binary
Model II.M	3882.259	5384.918	Linear	Linear	Linear	Binary	Categorical	Binary	Linear	Quadratic	Binary	Categorical	Binary
Model II.N	3875.091	5354.367	Linear	Linear	Linear	Binary	Categorical	Binary	Quadratic	Quadratic	Binary	Categorical	Binary

APPENDIX 3.2 MODEL I SENSITIVITY ANALYIS

Variables	Model 1. Complete Case	Model 2. Missing added as new category	Model 3. Missingness added to 'not vaccinated'	Model 4. LTFU added as category	Model 5. LTFU added with never
BIRTH ORDER					
First 24 hours	-0.0033731	0.0027309	0.0021107	0.0025946	0.0019172
1-7 days	0.0004969	0.000818	0.0006313	0.0003131	0.0002296
1-14 weeks	0.0016023	-0.0006384	-0.0004944	-0.0008616	-0.0006378
Not vaccinated	0.0012738	-0.0005758	-0.0022477	-0.0007775	-0.001509
Missing/LTFU		-0.0023347		-0.0012686	
AGE					
First 24 hours	0.0014175	.0027825*	.0028184*	0.0019638	0.0020484
1-7 days	-0.0002088	.0008335*	.000843*	0.000237	0.0002453
1-14 weeks	-0.0006734	-.0006505*	-.0006601*	-0.0006521	-0.0006814
Not vaccinated	-0.0005353	-.0005866*	-.0030013*	-0.0005885	-0.0016123
Missing/LTFU		-.0023788*		-0.0009602	
EDUCATION					
First 24 hours	0.0034582	.0063704**	.0063193**	0.0043431	0.0043906
1-7 days	-0.0005095	.0019082**	.0018902*	0.0005241	0.0005259
1-14 weeks	-0.0016427	-.0014892**	-.0014801**	-0.0014422	-0.0014606
Not vaccinated	-0.001306	-.0013431**	-.0067294**	-0.0013015	-0.0034559
Missing/LTFU		-.0054463**		-0.0021236	
MARITAL STATUS					
Not married					
First 24 hours	-0.0059991	-0.0017877	-0.0004628	0.002087	0.002614
1-7 days	0.0008531	-0.0005394	-0.0001387	0.0002472	0.0003058
1-14 weeks	0.0028629	0.0004178	0.0001084	-0.0006925	-0.0008688
Not vaccinated	0.0022831	0.0003773	0.0004931	-0.0006241	-0.0020511
Missing/LTFU		0.0015319		-0.0010175	
WEALTH INDEX					
First					
First 24 hours	0.015381	0.0270879	0.024699	0.0097373	0.0090706
1-7 days	-0.0041569	0.0034551	0.00312	-0.0003789	-0.0003613
1-14 weeks	-0.0064872	-0.0065663	-0.0059994	-0.0030923	-0.0028834

Not vaccinated	-0.0047368	-0.0052484	-0.0218197	-0.0025059	-0.0058259
Missing/LTFU		-0.0187282		-0.0037602	
WEALTH INDEX Second					
First 24 hours	-.0537647*	-.0462165*	-.0481882**	-.0659091**	-.0657557**
1-7 days	0.0077531	-.0146267**	-.0151531**	-.0091006*	-.008876*
1-14 weeks	.0256595*	.0108705*	.0113637**	.0221761**	.0221457**
Not vaccinated	.0203521*	.009871*	.0519776**	.020087**	.052486***
Missing/LTFU		.0401017**		.0327466***	
WEALTH INDEX Third					
First 24 hours	-0.0283561	-0.0217927	-0.0229156	-0.023584	-0.0246406
1-7 days	0.0055372	-0.005379	-0.005556	-0.0007491	-0.0007827
1-14 weeks	0.0129183	0.005228	0.005513	0.0077121	0.0080694
Not vaccinated	0.0099006	0.0045148	0.0229585	0.0065224	0.0173539
Missing/LTFU		0.0174289		0.0100987	
TRANSPORT Vehicle					
First 24 hours	0.0054138	0.0043194	0.00267	-0.000414	-0.0007484
1-7 days	-0.0007799	0.0013102	0.0008049	-0.0000498	-0.0000892
1-14 weeks	-0.0025794	-0.0010095	-0.0006252	0.0001375	0.0002489
Not vaccinated	-0.0020545	-0.0009126	-0.0028497	0.000124	0.0005887
Missing/LTFU		-0.0037075		0.0002023	
GENERAL READINESS First					
First 24 hours	-0.0139017	-.0615027***	-.0603473***	-.0641045**	-.0611563**
1-7 days	0.0025168	-.0229962**	-.0220538**	-0.0118278	-0.0106927
1-14 weeks	0.0064095	.0139956***	.0137981***	.0215785**	.0205858**
Not vaccinated	0.0049755	.0133493**	.068603**	.0202773**	.0512632**
Missing/LTFU		.0571539**		.0340765**	
GENERAL READINESS Second					
First 24 hours	-0.0306592	-0.0171755	-0.0193944	-0.0204916	-0.0219803
1-7 days	0.0045348	-0.004181	-0.0047563	-0.0014292	-0.0015881
1-14 weeks	0.0145671	0.0040938	0.0046242	0.0067364	0.0072391
Not vaccinated	0.0115574	0.0035403	0.0195265	0.0058693	0.0163293

Missing/LTFU		0.0137225		0.0093151	
IMMUNIZATION READINESS Second					
First 24 hours	.0466859*	0.014414	0.0152596	0.0257985	0.027133
1-7 days	-0.0089715	0.0042314	0.0044629	0.0025272	0.0026025
1-14 weeks	-.0213178*	-0.0033723	-0.0035779	-0.0084976	-0.0089519
Not vaccinated	-.0163965*	-0.0030297	-0.0161446	-0.007572	-0.0207836
Missing/LTFU		-0.0122434		-0.012256	
IMMUNIZATION READINESS Third					
First 24 hours	-0.0109091	0.0080171	0.008158	0.0012864	0.0012641
1-7 days	0.0008441	0.002495	0.0025457	0.0002037	0.0002019
1-14 weeks	0.0055143	-0.0018667	-0.0019027	-0.0004302	-0.0004239
Not vaccinated	0.0045506	-0.0016982	-0.008801	-0.000398	-0.0010421
Missing/LTFU		-0.0069472		-0.0006619	
FACILITY TYPE Ref. Hospital					
First 24 hours	0.0071325	-0.0184938	-0.0192418	-0.0019866	-0.0023708
1-7 days	-0.0010661	-0.0056884	-0.0059175	-0.0002413	-0.0002863
1-14 weeks	-0.0033808	0.0043133	0.0044968	0.0006598	0.0007889
Not vaccinated	-0.0026856	0.0039126	0.0206625	0.0005957	0.0018682
Missing/LTFU		0.0159562		0.0009724	
FACILITY OWNERSHIP Public					
First 24 hours	0.0217726	-.0320774*	-.0291441*	-0.0210431	-0.0182998
1-7 days	-0.0030966	-.0117456*	-0.010612	-0.0037415	-0.0031937
1-14 weeks	-0.0104026	.0073729*	.006717*	0.0071001	0.0061839
Not vaccinated	-0.0082733	.0069654*	0.0330391	0.0066228	0.0153096
Missing/LTFU		.0294847*		0.0110617	
FACILITY OWNERSHIP Private & Other					
First 24 hours	0.0478506	.0539294*	.0564223*	.0684677*	.0688202**
1-7 days	-0.00911	.0076499**	.0079964**	-0.0017608	-0.0016091
1-14 weeks	-0.0218565	-.0129513*	-.0135605*	-.0216198**	-.0217876**
Not vaccinated	-0.0168841	-.0104933*	-.0508582**	-.0178358**	-.0454235**

Missing/LTFU		-.0381348*		-.0272512**	
LOCATION					
Rural/peri-urban					
First 24 hours	-0.0059178	0.0006098	0.0009104	-0.0108173	-0.009731
1-7 days	0.0008563	0.0001824	0.0002718	-0.0013714	-0.0012188
1-14 weeks	0.002818	-0.0001426	-0.0002133	0.0036016	0.0032447
Not vaccinated	0.0022434	-0.0001285	-0.000969	0.0032595	0.0077051
Missing/LTFU		-0.0005211		0.0053277	

APPENDIX 3.3 MODEL II SENSITIVITY ANALYSES

Variables	Model 1. Complete case	Model 2. Missing added as new category	Model 3. Missingness added to 'not vaccinated'	Model 4. LTFU included as new category	Model 5. LTFU added to 'not vaccinated'
BIRTH ORDER					
Within 6 weeks	-0.0079183	0.0008473	-0.001527	0.0001156	-0.0020868
6-14 weeks	0.0012064	0.0004546	-0.0008181	0.0000265	-0.0004796
Not vaccinated	0.0067118	-0.0002682	0.0023451	-0.0000695	0.0025664
Missing/LTFU		-0.0010337		-0.0000726	
AGE					
Within 6 weeks	0.0021278	.0033554**	.0034782**	0.0021339	0.0023531
6-14 weeks	-0.0003242	.0018005**	.0018635**	0.0004892	0.0005408
Not vaccinated	-0.0018036	-.001062**	-.0053417**	-0.0012824	-0.0028938
Missing/LTFU		-.0040939**		-0.0013407	
EDUCATION					
Within 6 weeks	.0089197**	.0085256***	.0087671***	.007631**	.0082366**
6-14 weeks	-.001359*	.0045749***	.004697***	.0017495**	.001893**
Not vaccinated	-.0075607**	-.0026984***	-.0134641***	-.0045859**	-.0101296**
Missing/LTFU		-.010402***		-.0047945**	
MARITAL STATUS Not married					
Within 6 weeks	0.0014727	0.002642	0.0031351	0.0121547	0.0109403
6-14 weeks	-0.0002265	0.0014057	0.0016629	0.0025827	0.0023494
Not vaccinated	-0.0012462	-0.0008367	-0.004798	-0.0072436	-0.0132896
Missing/LTFU		-0.003211		-0.0074938	
WEALTH INDEX First					
Within 6 weeks	-0.0410075	-0.000012	-0.0018403	-0.0395753	-0.0397927
6-14 weeks	0.0074433	-5.29E-06	-0.0007904	-0.0062774	-0.0064248
Not vaccinated	0.0335641	3.94E-06	0.0026308	0.0232056	0.0462176
Missing/LTFU		0.0000134		0.0226471	
WEALTH INDEX Second					
Within 6 weeks	-0.0390085	-0.02981	-.0326354*	-.0587984**	-.0557818**
6-14 weeks	0.0072616	-.0164845*	-.0177915*	-.0130326**	-.0119052**
Not vaccinated	0.0317469	0.0094719	.0504269*	.0355003**	.067687**

Missing/LTFU		0.0368226		.0363307**	
WEALTH INDEX					
Third					
Within 6 weeks	-0.0277191	-0.0083576	-0.0123407	-0.0188254	-0.0217657
6-14 weeks	0.0058604	-0.0039281	-0.005762	-0.0018364	-0.0023508
Not vaccinated	0.0218587	0.0027198	0.0181027	0.0106847	0.0241164
Missing/LTFU		0.0095659		0.0099771	
TRANSPORT					
Vehicle					
Within 6 weeks	-.038293*	-0.0078994	-0.0144497	-0.0231418	-0.0259346
6-14 weeks	0.0068292	-0.0041639	-0.0074966	-0.0047992	-0.0053285
Not vaccinated	.0314638*	0.0025031	0.0219464	0.0137634	0.0312631
Missing/LTFU		0.0095602		0.0141776	
GENERAL					
READINESS					
Within 6 weeks	0.0143867	.0238745***	.0229138***	.030559***	.026866***
6-14 weeks	-0.0021919	.0128112***	.0122762***	.0070059***	.0061744**
Not vaccinated	-0.0121948	-.0075565***	-.0351899***	-.0183647***	-.0330404***
Missing/LTFU		-.0291292***		-.0192002***	
IMMUNIZATION					
READINESS					
Within 6 weeks	.0158745**	0.0005165	0.0027069	0.0077972	.0095666*
6-14 weeks	-.0024186*	0.0002771	0.0014502	0.0017876	0.0021986
Not vaccinated	-.0134559**	-0.0001635	-0.0041571	-0.0046858	-.0117652*
Missing/LTFU		-0.0006301		-0.004899	
FACILITY TYPE					
Ref. Hospital					
Within 6 weeks	.0362868*	0.0175745	0.0207477	.0331854*	.0354111*
6-14 weeks	-0.0058977	0.0092499	0.0108599	.0070907*	.0075509*
Not vaccinated	-.0303891*	-0.0055757	-0.0316076	-.0197962*	-.0429619*
Missing/LTFU		-0.0212487		-.0204799*	
FACILITY					
OWNERSHIP					
Public					
Within 6 weeks	.0609376**	-0.0107022	0.0031047	0.0097694	0.0205076
6-14 weeks	-0.0096336	-0.0063712	0.0018327	0.0027207	0.0055734
Not vaccinated	-.0513041**	0.0033442	-0.0049373	-0.0060334	-0.0260811
Missing/LTFU		0.0137292		-0.0064567	

FACILITY OWNERSHIP					
Private & Other					
Within 6 weeks	.093413**	.0488338*	.0657572**	.0843308***	.0911123***
6-14 weeks	-.0207703*	.0186441**	.0244596***	0.0058462	0.0069159
Not vaccinated	-.0726427***	-.0159671*	-.0902167***	-.0466218***	-.0980282***
Missing/LTFU		-.0515108**		-.0435552***	
LOCATION					
Rural/peri-urban					
Within 6 weeks	-.0376704*	-0.0095144	-0.01891	-0.0276105	-.0333973*
6-14 weeks	0.0049858	-0.0052003	-0.0105321	-0.0069689	-0.0086272
Not vaccinated	.0326846*	0.0030123	0.0294421	0.016876	.0420245*
Missing/LTFU		0.0117025		0.0177034	

APPENDIX 3.4 CQI LTFU SUB-STUDY RESULTS

Reason for LTFU	N			
Voluntary withdrawal	51			
Official transfer	26			
Voluntary transfer	78			
Dead	12			
True LTFU	150			
Travel	23			
Refused interview	15			
Still in care	97			
Resumed care after withdrawal	21			
		Model I	**Model II**	**Weight**
LTFU - not vaccinated	216	115	129	= .4547
LTFU - total	475	248	281	**46%**

APPENDIX 4.1 THEMES AND REPRESENTATIVE QUOTES

INTERVENTION CHARACTERISTICS	
Evidence strength and quality	
"I know that in our [DRC] immunization schedule, [HepB-BD] is not a vaccination that exists. If we were able to administer birthdose vaccine here [alluding to AVERT study], it is because a study was done here. But the others [facilities], so that they accept, they will need to have information and formation."	Informant Catholic 2
"I think that .. ahhh. That the study is shared. We are waiting for the findings from your first study, it will be very interesting. That way we can begin to share the message and there will be no fears or worries among the population. Because there are already vaccines given at birth, so this will be welcome given the study results."	Informant Protestant 1
Design quality and packaging	
"Yes… with the strategy, we need at least 20 newborns to open a vial, that's why we ask that they come back on Wednesdays. We have records of all of the newborns born. We call them every Wednesday and tell them to come back to the health facility as to not give it to them too long after birth."	Informant NFP 3
"They find it bad to open a vial of 20 doses to simply vaccinate seven children. So, the rest of the doses must be thrown away is a loss... vaccines are.. are.. are.. an important antigen, we cannot vaccinate 7 kids and lose 13 doses. It's a loss."	Informant Public 3
"Beyond their day-to-day work [the providers] have their performance metrics to consider and they don't want to inflate their rate of vaccine loss"	Informant PEV 1
Cost	
"They will give us a card after we deliver the payment, they haven't told us anything"	Mother NFP 2
"No, if she begins her infant's vaccine care elsewhere, and decides to come here to continue it, she must repurchase a card here[but vaccines will not be repeated]"	Informant Catholic 4
INNTER SETTING	
Structural characteristics	
"But those who do not have refrigerators, the vaccines are kept at a site like [a reference hospital] where they keep their vaccines and come and pick them up as needed. But us here, we have a fridge and so our delivery is monthly"	Informant Protestant 1
"Now, vaccines are products that must be conserved in very specific conditions so that the antigen is active. If the required conditions are not reached, we stand the risk of providing placebo vaccines. So, even us here who have electricity, we realize that we stand the risk of experiencing electricity outages. These outages can alter the temperature at which the vaccines are kept."	Informant Public 3
"First, we have a cold chain here where we can keep vaccines in the condition that they require. And we have a system of solar energy, we also have a temperature flier on the fridge, every morning we evaluate the fridges temperature and record it."	Informant Public 3
"Every morning I am obligated to travel and verify the temperature at which the vaccines are being stored and to record it, and to make sure that the health workers in the facility are doing this."	Informant Health Zone 1
"And for fridges... the maternity does not vaccinate, it is the vaccination nurse that oversees the number of children available for the vaccination…. the vaccines are kept in the fridge and the nurses are in charge of vaccinating."	Informant Protestant 1
Implementation climate	
"Generally, once we see that a child did not come into be vaccinated, the CHWs go that day to retrieve the child the next day to have them vaccinated."	Informant Protestant 1

"Every time now that a mother comes in to have their child vaccinated, we register the moms, we collect their telephone number and their address, so every time they have an appointment coming up, they will receive a text message reminder of their appointment. This way you will not be distracted and remember your date. Since we started this study, I would estimate though that we have decreased the lost to follow up rate though, from 21% to 16-18%."	Informant Public 3
Learning climate	
"When we organize trainings or briefings about vaccination, we target vaccine providers from health facilities. We do not often see the midwives, even though they are the door for infants to enter into the [vaccine] system. So, it is really important to provide them too with briefings or trainings."	Informant PEV 1
PROCESS OF IMPLEMENTATION	
Planning	
"Yes. We are not obliged to vaccinate infants unless there are 15 of them. If 3 or 5 are born, then we do not vaccinate them." *So if there are fewer than 10 infants born, then you do not open the vial?* "No."	Informant Catholic 1
"The ideal is 20 [infants]. But they have authorized us to provide the vaccine when there are 10 infants. So, when we have 10 infants, we administer 10 and lose the other 10."	Informant Private 1
Executing	
"The moms would call and call.. where's the BCG. It was a national stockout."	Informant NFP 1
"There's a problem with the BCG. There aren't enough vaccines. Women who deliver here sometimes have to wait one month [for their infant] to receive the vaccine."	Mother Private 2
External change agents	
"UNICEF provided us with nine refrigerators—seven fridges in the facilities and two here in the health zone. They provided the new fridges in March."	Informant Health Zone 1
CHARACTERISTICS OF INFORMANTS	
Knowledge and beliefs about the intervention	
"They told us that we should introduce that [HepB-BD] at birth. And we await the period that we begin introducing it. Because we were well informed by PEV that there will be an introduction but until today, nothing."	Informant Health Zone 2
Self-efficacy	
"What is important is to help us understand. During the visits, [the midwives] need to go into more detail because here we are in the dark [about vaccines/diseases]."	Mother Catholic 1
OUTER SETTING	
External policy	
"If the protocol from PEV changes, then we will change. We will adapt."	Informant Catholic 1
Mothers' needs and resources	
Choice of health facility	
".. The staff here are serious about their work and they take good care of the sick."	Mother NFP 2
"[Seeking care at this facility was my mom's advice. My mom delivered here, and my big sister delivered here too. My mom told me that there is good care for the sick and a good quality of health here"	Mother Catholic 4
"My older sister delivered here and had good memories, so she recommended I come here."	Mother Private 1
"Members of my family delivered here and told me that they had a good experience."	Mother Catholic 1

Do you expect to follow care at this facility all the way through your infant's routine vaccine care? "No." *Why?* "The distance." *You live far away?* "Yes and I will deliver here but follow care closer to home."	Mother Catholic 4
"What motivates here is distance, that is an aspect but not the only aspect. The second aspect is partnership. Say the partnership to a community, or perhaps to a religion. You will see that a Catholic would like to visit a Catholic facility.. The third is the perception by the community of the quality of service by the health facility… a women would say that she wants to go in this facility because it is clean, because it is presentable, it is a bit of that"	Informant PEV 1
Knowledge about vaccines	
"I don't know much [about HBV] but I've heard it talked about. Its more the children who suffer [from HBV]"	Mother NFP 1
"Kids receive vaccines. I don't know the names of the vaccines, but one is given orally and the other in the arm."	Mother Public 2
"My maternal aunt refused vaccines for her kids. She thought that vaccines are bad for kids"	Mother Catholic 4 Mother Catholic 3
In your community, have you noticed any vaccine hesitation? "The majority of my community."	
"Vaccines remain until now the best method for prevention. But the quality suffers because there are too many speculations, it is perhaps you—the whites—who are putting confusion into the heads of the blacks."	Informant Health Zone 2
Birth-dose vaccine acceptance	
"Yes, I would be very comfortable with it because this vaccine will give my child force and strength. If there is a disease that attacks my child, they will be protected"	Mother Public 2
"Because [the vaccines] protect the baby against diseases and epidemics. When the epidemic arrives, the baby has the protection necessary to be safe against the epidemic."	Mother NFP 3

APPENDIX 5.1A MATRIX OF CHANGE FOR ADOPTERS

		Determinants			
Target : role	**Performance objectives**	**Knowledge**	**Skills & Self-efficacy**	**Outcome expectations**	**Normative beliefs**
Health zone & facility decision-maker and leaders : adopter	PO1. Agree to participate in the study	K1.a. Describe the components of the study	SSE1.a. Expresses confidence in the ability to do what is expected of the study	OE.1.a. Expect that the study intervention development partners will provide support with program implementation and resources	NB.1. Express belief that other facilities like theirs are agreeing to implement the study
		K1.b. Describe the rates of timely birthdose vaccine uptake and HBV prevalence as problems that need to be addressed	SSE1.b. Perceives that the facility is capable of change	OE1.b. Expect this program will provide streamlined/timely birth-dose vaccine uptake	
			SSE1.c. Describes the facility as ready and able for change		
	PO2. Agree to expand vaccine services to include HepB-BD	K2.a. Express the unmet vaccine need among infants	SSE2.a. Express confidence in ability to work with partners and decision-makers to expand birth-dose vaccine service.	OE2.a. Expect that expanded birth-dose vaccine services will decrease infant morbidity and mortality rates	NB2.a. Express belief that other facilities are agreeing to expand birth-dose vaccine services
		K2.b. Describe the steps needed to expand birth-dose vaccine services	SSE2.b. Express confidence in facility's ability to arrange workflow to incorporate study		NB2.b. Express belief that leaders and decision-makers will encourage expansion
	PO3. Agree to participate in evaluation	K3.a. Describe the expected outcomes of the study	SSE3.a. Express confidence in ability to create records for evaluation	OE3.a. Expect the evaluation will add value to facility reporting	NB3. Express belief that other facilities in the study will participate in the evaluation

	K3.b. Describe the procedures for participating in the evaluation	SSE3.b. Believe facility is a learning environment	OE3.b. Expect that evaluation results will add value and status as compared to other competing facilities	
			OE3.c. Believe evaluation results will help facility support program and garner future funding	
PO4. Provide a program champion for the study	K4. Explain the responsibilities of the program champions in study	SSE4. Express confidence in the ability to recruit a program champion from each sub-group (midwives, vaccine staff, CHW)	OE4. Expect the program champion will enable the study to be implemented and maintained	NB4. Lists other clinics like theirs that use champions to assist in practice change
PO5. Assure procedures are in place for study implementation	K5. Describe process for ensuring study implementation procedures	SSE5. Demonstrate administrative ability to facilitate study implementation procedures	OE5. Expect that workflow procedures will improve staff engagement and efficiency	NB5. Express belief that other facilities in the study are also following implementation procedures
PO6. Oversee that procedures remain in place for sustained study implementation and workflow procedures	K6. Describe steps to assure sustained study implementation workflow and procedures	SSE.6. Demonstrate administrative ability to maintain ongoing program implementation	OE6. Expect that sustained workflow procedures will improve sustained study implementation	NB6. Express belief that sustaining the study is good for the facility

APPENDIX 5.1B MATRIX OF CHANGE FOR IMPLEMENTERS

		Determinants			
Target : role	**Performance objectives**	**Knowledge**	**Skills & Self-efficacy**	**Outcome expectations**	**Normative beliefs**
Health staff : implementer *All*	PO1. Facility staff agree to implement the program and attend 2-day study training.	K1.a. Describe the components of the study as easy to use and implement	SSE1. Demonstrate confidence in ability to attend and learn from training	OE1.a. Expect participating in training will ensure readiness to successfully implement the program	NB1. Expresses belief that their colleagues and other facility staff will attend trainings
		K1.b. Describe process for using guidelines and materials		OE1.b. Expect champion and facility leadership will praise/acknowledge them for completing the training successfully	
	PO2. Educates mothers about disease risk and vaccine benefits during ANC visits	K2. Awareness of study implementation procedures, guidelines, and workflows	SSE2.a. Demonstrate ability to deliver and maintain use of education material	OE2.b. Expect to make a difference and disseminate knowledge	NB2. Express belief that educating mothers makes a difference in infant morbidity and mortality
			SSE2.b. Demonstrate ability to adhere to study workflow procedures	OE2.b. Expect that workflows and procedures will aid study implementation	
Midwife : implementer	PO3. Coordinates with vaccine staff	K3. Awareness of study implementation procedures, guidelines, and workflows	SSE3.a. Demonstrate ability to coordinate vaccine administration	OE3.a. Expect that coordination between vaccine and delivery staff will improve timely birth-dose uptake	NB3. Express belief that midwives taking on additional step of coordinating vaccines for newborns will increase timely birth-dose vaccine uptake
			SSE3.b. Demonstrate ability to adhere to study workflow procedures	OE3.b. Expect that workflows and procedures will aid study implementation	

	PO4. Uses barrier scripts to respond to mother concerns about vaccination	K4. Awareness of study implementation procedures, guidelines, and workflows	SSE4.a. Express confidence using strategies to increase vaccine uptake	OE4.a. Expect to make a difference and disseminate knowledge	NB4. Express belief that educating mothers makes a difference in avoidable infant morbidity and mortality
			SSE4.b. Demonstrate ability to adhere to study workflow procedures	OE4.b. Expect that workflows and procedures will aid study implementation	
Vaccine staff : implementer	PO5. Captures infants' immunization status	K5. Awareness of study implementation procedures, guidelines, and workflows	SSE5.a. Demonstrate ability to regularly capture vaccine status at the end of every day	OE5.a. Expect to improve facility and study tracking of infants' vaccine information	NB5. Express belief that their role capturing infant vaccine status every day improves vaccine tracking and monitoring
			SSE5.b. Demonstrate ability to adhere to study workflow procedures	OE5.b. Expect that workflows and procedures will aid study implementation	
Community health worker : implementer	PO6. Partner with community leaders to improve preventable disease and vaccine awareness in community	K6. Awareness of study implementation procedures, guidelines, and workflows	SSE6.a. Demonstrate ability to recruit willing community leaders	OE6. Expect that community awareness of vaccines will improve over time through community-leadership involvement	NB6. Expresses belief that they are able to recruit community leaders to support VANISH-BD
			SSE6.b. Demonstrate ability to disseminate vaccine education to community leaders		NB6.b. Expresses belief that involving community leaders will make a difference in avoidable infant morbidity and mortality
Champion: implementer	PO7. Champions oversee implementation efforts and provide feedback to facility staff	K7.a. Awareness of daily and weekly activities associated with champion's role	SSE7. Demonstrates confidence and ability to oversee implementation of the study	OE7. Expect that through continuous monitoring and communication, the study will be implemented effectively	NB7. Believes that other champions in other clinics are conducting the same role

	K7.b. Awareness of steps needed to monitor implementation			
PO8. Champions identify barriers and provide suggestions for overcoming them	K8. Provides a list of potential barriers to implementation and solutions to address them	SSE8. Expresses confidence in their ability to identify problems and respond to them during implementation	OE8. Expects that timely identification of problems will facilitate addressing the barrier	NB8. Believes that other champions in other clinics have a role that includes identification of barriers and development of solutions

APPENDIX 5.2 DETERMINANTS, THEORETICAL-BASED METHODS, AND PRACTICAL APPLICATION FOR EACH STUDY ACTOR

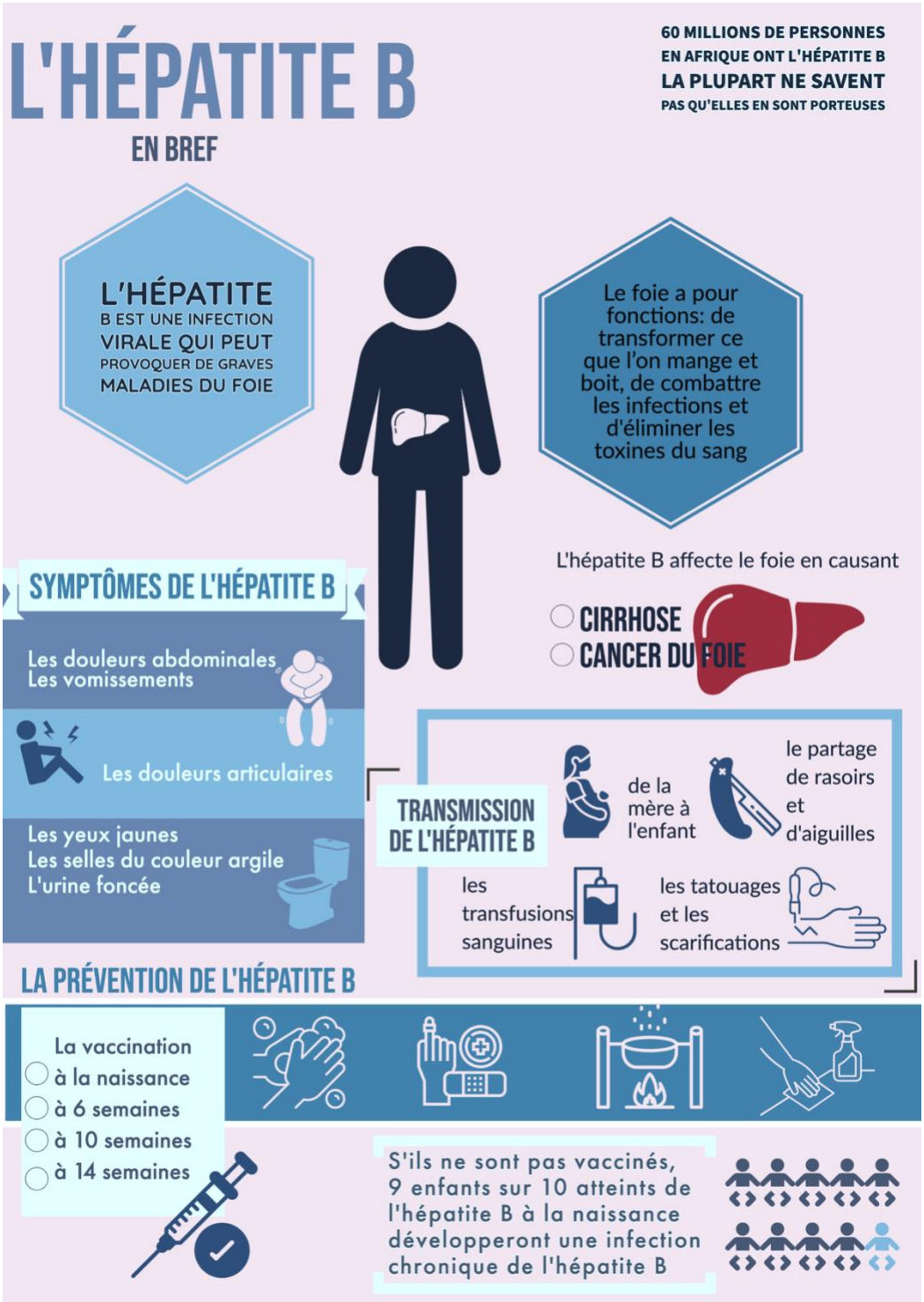
Determinants	Theory-based method	Study Actors					
		Implementer	Decision-makers	Vaccine staff	Midwives	CHWs	Champions
Knowledge	Technical assistance	Provide ongoing assistance to facilities					
	Organization planning		Hold meetings to discuss maintaining the intervention and work flow maintenance				Hold meetings to discuss lessons learned through modeling guideline-based practices
	Perceived severity / instruction	Develop educational material and script for midwives to use in order to disseminate information about vaccines			Disseminate instruction about severity of diseases to mothers	Disseminate instruction about severity of diseases to community	
	Information delivery and processing	Face to face training held over two days with champions Develop and share evidence-based protocol, training materials, educational materials, and facility guidelines					Conduct training with relevant facility staff

	Discussion			Discuss problems encountered collaborating for newborn vaccination or inputting vaccine data with champions	Discuss problem encountered during ANC to delivery visits with champions	Discuss problems encountered when conducting outreach visits with champions	
Skills & Self-efficacy	Skill building & guided practice	Administer skills training in how to use guidelines and incorporate active learning during champion training modeling intervention scenarios		Role play to practice conducting intervention during training	Role play to practice conducting intervention during training	Role play to practice conducting intervention during training	Administer skills training in how to use guidelines and incorporate active learning during staff training
	Reinforcement		Reinforce the use of the new facility guidelines and intervention materials				Reinforce the use of the new facility guidelines and intervention materials
	Monitoring and feedback						Regularly monitor and provide feedback to facility staff about skills observed
	Environmental restructuring	Alter vaccine fees to be low (free) and consistent across facilities	Integrate guidelines and materials into a workflow that prompt facility staff to apply guidelines to every mother-infant pair	Facility staff will round together to review new guidelines and protocols with champions Provide transportation vouchers for mothers who used public transportation to	Facility staff will round together to review new guidelines and protocols with champions	Facility staff will round together to review new guidelines and protocols with champions	

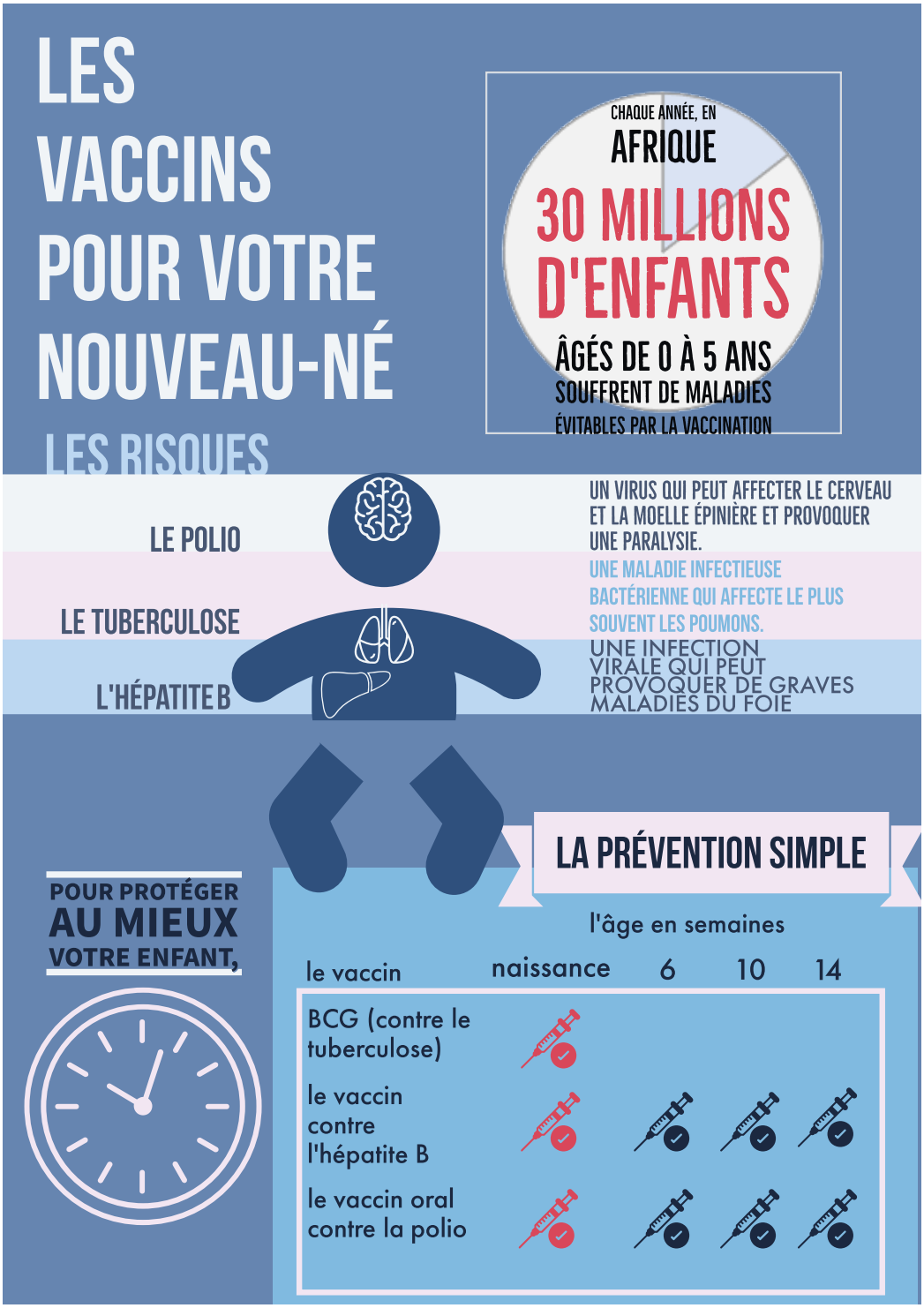
				attend vaccine appointment		
	Persuasion	Invite facility decision-makers to participate in intervention Train champions in the benefit of guideline-based practice	Select one champion from each of the three facility staff levels (vaccines, midwives, CHWs) to act as champion from their department		Disseminate vaccine information effectively during ANC clinics	Train facility staff in the benefit of guideline-based practice
	Modeling	Provide feedback to champions about regular modeling of guideline-based practice				Model the guideline-based practice on an ongoing basis with implementers
Outcome expectations & Normative beliefs	Cultural relevance	Translate training materials, educational materials, and facility guidelines to contextual languages				
	Evaluation	Oversee baseline and endline evaluation of intervention Use evaluation findings to advocate to policy-makers for HepB-BD introduction and subsidies for vaccines and transportation vouchers	Support process collecting baseline and endline evaluation of intervention	Monitor infant vaccine rates regularly to facilitate evaluation		

***** *Methods derived using Social Cognitive Theory and Theory of Planned Behavior*

APPENDIX 5.3A EDUCATIONAL MATERIAL: HEPATITIS B POSTER



APPENDIX 5.3B EDUCATIONAL MATERIAL: BIRTH-DOSE VACCINES POSTER



APPENDIX 5.3C EDUCATIONAL MATERIAL: HEPB-BD INFORMATIONAL GUIDE

Hepatitis B birth-dose vaccine informational guide

This guide summarizes the risk of hepatitis B transmission from mother to child and the benefits of the hepatitis B birth-dose (HepB-BD) vaccine. It provides direction for properly administering, storing, and managing HepB-BD. Information about the disease and the vaccine should guide responses to any questions that new mothers, fathers, and other family members may have about HepB-BD.

Amendment to the EPI schedule

The new approach will deliver streamlined HepB-BD alongside the standard OPV0 and BCG birth-dose vaccines to newborns *within the first 24 hours of delivery*. The below EPI schedule demonstrates the change to the EPI schedule, highlighted in yellow.

		Age			
Vaccine	Disease	Birth	6 weeks	10 weeks	14 weeks
Bacille de Calmette et Guérin (BCG) vaccine	Tuberculosis				
Oral Polio Vaccine (OPV)	Poliomyelitis				
Hepatitis B Birth-Dose (HepB-BD) vaccine	Hepatitis B				
Pentavalent vaccine	Diphtheria, Pertussis, Tetanus, H. influenza type b, Hepatitis B				

What is hepatitis B?

Hepatitis B is a virus that affects the liver. It is known as a 'silent epidemic' because many people who are infected are unaware because they do not experience symptoms until later in life (decades later) when they experience inflammation of the liver, cirrhosis (severe liver disease), and cancer of the liver. The Hepatitis B virus can even lead to death. Newborns and infants are at much higher risk of chronic hepatitis B virus if exposed to the disease.

How is hepatitis B spread?

Hepatitis B is 100 times more infectious than HIV and is also spread through contact with blood and other body fluids. Below is a list of ways that hepatitis B is spread:

	From mother to baby		By sharing razors and needles		Through unprotected sex with an infected person
	Through unsafe injections and transfusions		Through tattoos and scarification		

Hepatitis B *is not spread* through the air, water, or by food.

Is there a cure for hepatitis B?

There is currently no cure available for hepatitis B, but treatment with Tenofovir can manage a flare-up of the disease. Vaccines to protect your baby against hepatitis B are the surest way to protect your newborn against hepatitis B.

Why is HepB-BD so important?

Currently, the national immunization schedule begins vaccination against hepatitis B at six weeks of age. The WHO now recommends that HepB-BD be administered *within the first 24 hours of a newborn's life*, followed by additional doses at 6, 10, and 14 weeks. Timely administration of HepB-BD prevents mother-to-child transmission of hepatitis B and induces immunity to the hepatitis B virus.

Why is the timing of HepB-BD so important?

An infant should receive the HepB-BD within the first 24 hours of life so that a mom does not pass on hepatitis B to her newborn. Because hepatitis B is highly transmissible, a baby receiving HepB-BD within 24 hours of birth also protects them from potential exposure in their homes and communities during their first six weeks of life before they receive the next round of the hepatitis B vaccine

Administering HepB-BD *as early as possible* is critical for protecting a newborn against hepatitis B.

What are the potential side-effects of HepB-BD?

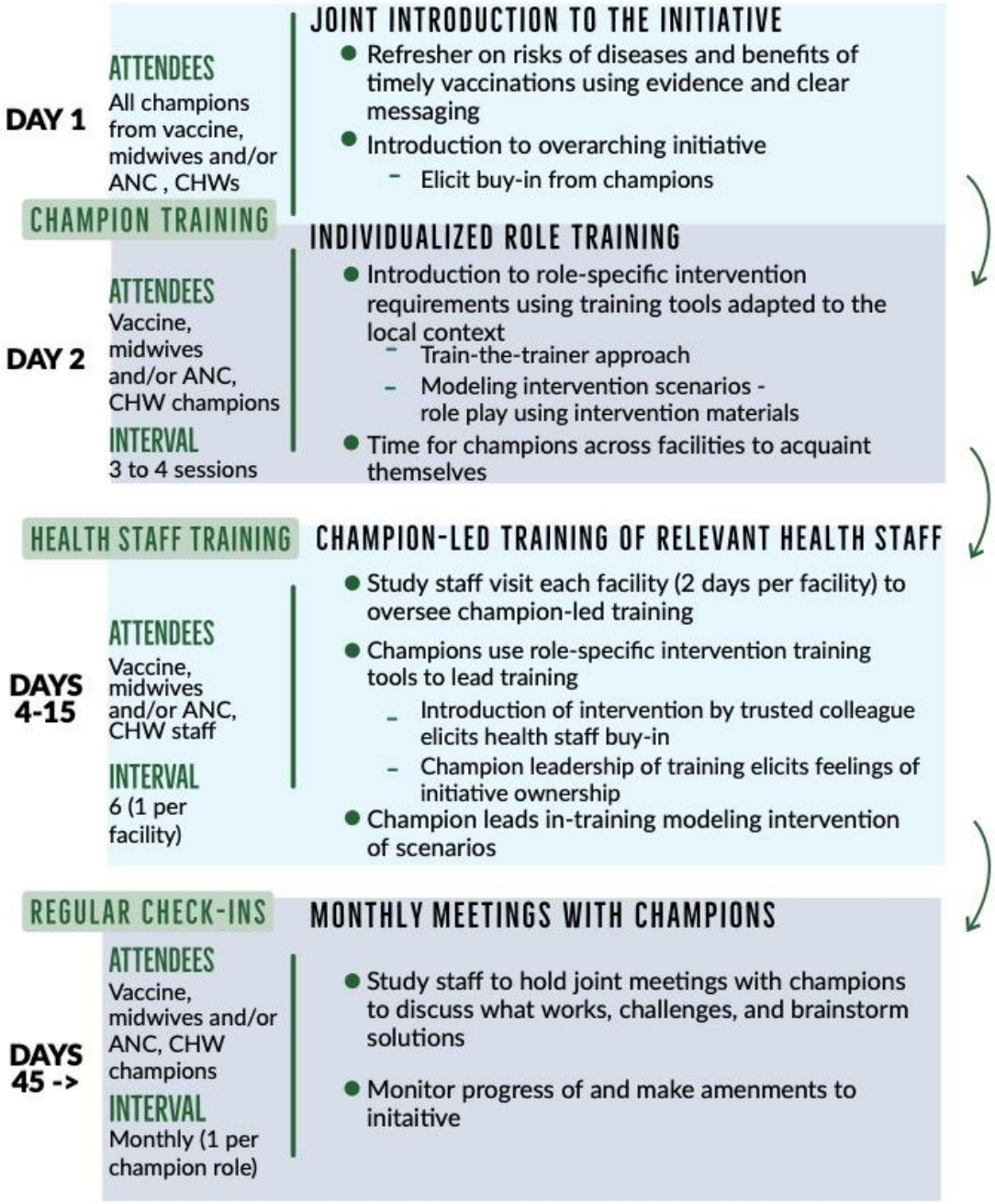
Side effect	Defined	How frequent?
	The most common side-effect to the vaccine is redness and swelling where the vaccine was injected.	Occurs in 1 in every 11 infants vaccinated lasting between 1 and 3 days.
	Less commonly, a fever may occur after the vaccine is administered.	Occurs in 1 in ever 14 infants vaccinated.
	More serious allergic reactions, which cause hives and difficulty breathing, are rare.	Occurs in only 1 in every 600,000 infants vaccinated. Nonetheless, an EpiPen should be kept nearby when injecting an infant.

Are there reasons why an infant should not receive HepB-BD?

Unlike other vaccinations, there are no contraindications for administering HepB-BD within the first 24 hours of delivery. There are also no contraindications for administering all three BD vaccines (HepB-BD, OPV0, and BCG) at the same time.

Low birthweight, premature delivery, Caesarian sections, and HIV infections are *not* reasons a newborn should not receive the hepatitis B vaccine. The only case in which an infant should delay receiving HepB-BD is if it would interfere with the treatment of urgent neonatal care. In such cases, the infant should receive HepB-BD once they are stable.

APPENDIX 5.4 TRAINING MATERIAL



APPENDIX 5.5A NEWBORN VACCINE CHECKLIST

Newborn BD vaccine checklist

Date:

Mother's name:

Mother's PID:

Infant's name:

Infants birthday:

No	Directive	Responsible	Completed	Completed by						Notes
BD administration										
1.01	Ask the mother and family if they have questions, respond to all questions using HepB-BD guide	Midwife	□ Y □ N	Name: Position:	□ Mother asked questions	□ Family asked questions	□ No questions			
1.02	Administer HepB-BD in left thigh	Midwife*	□ Y □ N	Name: Position:	□ < 24 hrs	□ > = 24 hours	□ Other: _ days	□ NA		
1.03	Administer BCG in upper left arm	Midwife, not EPI staff	□ Y □ N	Name: Position:	□ < 24 hrs	□ > = 24 hours	□ Other: _ days	□ NA		
1.04	Administer polio 0 orally	Midwife, not EPI staff	□ Y □ N	Name: Position:	□ < 24 hrs	□ > = 24 hours	□ Other: _ days	□ NA		
1.05	All injection equipment is safely disposed of	Midwife	□ Y □ N	Name: Position:						
1.06	Monitor newborn for adverse side-effects	Midwife	□ Y □ N	Name: Position:	□ Redness or swelling	□ Fever	□ Other: _____	□ No side effects		
Date recording & reporting										

2.01	Shared infant records with EPI staff	Midwife	□	Y	□	N	Name: Position:
2.02	Recorded infant BD information in database	EPI staff	□	Y	□	N	Name: Position:
2.03	Mother is given an at home based record (vaccination card) before leaving the facility	EPI staff	□	Y	□	N	Name: Position:
2.04	Mother is notified of follow-up EPI visit date before leaving	EPI staff	□	Y	□	N	Name: Position:

APPENDIX 5.5B CHAMPION SUPERVISION CHECKLIST

Health-Facility Supervision Checklist for Champions

Date:

Name of Champion:

Champion department:

Health facility:

No	Directive	Responses	Supervision Frequency	Notes
BD administration				
Supervised by : Midwife champion				
1.01	Total number of infants born during the week	Total :	Weekly	
1.02	Total number of mother and/or families who requested information about BD vaccines	# mothers: ___ # families: ___ # neither : ___	Weekly	
1.03 A	Total infants that received HepB-BD	# that received HepB-BD : ____	Weekly	
1.03 B	*Administered vaccine in left thigh*	# in left thigh : ___ # elsewhere & where : ___ NA : ____	Weekly	
1.03 C	*Timing of the vaccine*	< 24 hrs : __ > = 24 hours : ___ NA :	Weekly	
1.03 D	*Administered by maternity staff*	# administered by maternity staff : ___ # administered by other & who : ___ NA : ____	Weekly	
1.04 A	Total infants that received BCG	# that received BCG : ____	Weekly	
1.04 B	*Administered vaccine in left upper arm*	# in right thigh : ___ # elsewhere & where : ___ NA :	Weekly	

1.04 C	*Timing of the vaccine*	< 24 hrs : __ > = 24 hours : ___ NA : ____	Weekly
1.04 D	*Administered by maternity staff*	# administered by maternity staff : ___ # administered by other & who : ___ NA :	Weekly
1.05 A	Total infants that received OPV0	# that received OPV0 :	Weekly
1.05 B	*Timing of the vaccine*	< 24 hrs : __ > = 24 hours : ___ NA : ____	Weekly
1.05 C	*Administered by maternity staff*	# administered by maternity staff : ___ # administered by other & who : ___ NA :	Weekly
1.06	Monitor newborn for adverse side-effects	# with redness/welling : ___ # with fever : ____ # with other & what side effect : ____ # not monitored : _____ NA :	Weekly
1.07	All midwife staff on duty are trained and able to administer BDs	# of midwives on duty : ____ # of midwives trained : ____	Weekly
Vaccine handling, storage & management			
Supervised by : Midwife champion			
2.01	Delivery ward fridge stocked with appropriate number of BD vaccines		
2.01 A	*Unvaccinated newborns in postnatal ward*	# of unvaccinated newborns: Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7.	Daily

2.01 B	*HepB-BD vaccines*	# of HepB-BD vaccines: Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7. __ # of days since vial was opened : __/28 days Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7. __	Daily
2.01 C	*BCG vaccines*	# of BCG vaccines: Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7. __ # of hours since vial was opened: __/6 hours Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7.	Daily

2.01 D	*OPV0 vaccines*	# of OPV0 vaccines: Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7. __	Daily
2.02	Fridge temperature between +2 ˚C and +8 ˚C	Temperature AM/PM: Day 1. AM : __ PM: __ Day 2. AM : __ PM: __ Day 3. AM : __ PM: __ Day 4. AM : __ PM: __ Day 5. AM : __ PM: __ Day 6. AM : __ PM: __ Day 7. AM : __ PM: __	2x Daily
2.03	All vaccines kept on top shelf	# of vaccines not on top shelf: Day 1. __ Day 2. __ Day 3. __ Day 4. __ Day 5. __ Day 6. __ Day 7. __	Daily
2.04	Epinephrine is stored in delivery or postnatal ward	Is epinephrine available in delivery ward? Day 1. □ Yes □ No Day 2. □ Yes □ No Day 3. □ Yes □ No Day 4. □ Yes □ No Day 5. □ Yes □ No Day 6. □ Yes □ No Day 7. □ Yes □ No	Daily
2.05	Any required vaccine orders have been placed with EPI	Day 1. □ Yes □ No Day 2. □ Yes □ No Day 3. □ Yes □ No Day 4. □ Yes □ No Day 5. □ Yes □ No Day 6. □ Yes □ No Day 7. □ Yes □ No	Daily

Date recording & reporting			
Supervised by : EPI champion			
3.01	Mothers are provided at home-based record (vaccination card)	# of mothers given vaccination card : __ # of mothers not given a vaccination card : __	Weekly
3.02	Mothers are notified of follow-up EPI visit date before leaving	# of mothers given follow-up date : __ # of mothers not given follow-up date : __	Weekly
3.03	Birth-dose information recorded in database	# of infants born in the facility : ___ # of infants recorded in database : ___ Is all timing of HepB-BD captured : □ Yes □ No (If no, amend)	Weekly
3.04	Any required vaccine orders have been placed with health zone	Day 1. □ Yes □ No Day 2. □ Yes □ No Day 3. □ Yes □ No Day 4. □ Yes □ No Day 5. □ Yes □ No Day 6. □ Yes □ No Day 7. □ Yes □ No	Daily
Facility-based education			
Supervised by : Midwife champion			
4.01	Health staff runs through full script using informative poster during antenatal visit	□ Yes □ No Comments:	Weekly
4.02	Health staff is interactive and responds to mother's questions	□ Yes □ No Comments:	Weekly
Community-based education			
Supervised by : CHW champion			
5.01	CHWs to visit schools and share educational material	# of schools visited: __ # of schools returned to: __ Comments:	Weekly

		# of churches visited: __ # of churches returned to: __ Comments:	
5.02	CHWs to visit churches and share educational material		Weekly
5.03	CHWs to track down mother-infant dyads that leave or move from facility before completing their EPI schedule	# of children lost to follow up: ___ # of children tracked down: ___ # of children missing vaccine information/ not tracked down:	Weekly

REFERENCES

1. World Health Organization (WHO). Hepatitis B. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. Published 2020. Accessed October 8, 2020.

2. Breakwell L, Tevi-Benissan C, Childs L, Mihigo R, Tohme R. The status of hepatitis B control in the African region. *PanAfrican Med J*. 2017;27(Supp 3):17. doi:10.11604/pamj.supp.2017.27.3.11981

3. Tamandjou CR, Maponga TG, Chotun N, Preiser W, Andersson MI. Is hepatitis B birth dose vaccine needed in Africa? *Pan Afr Med J*. 2017;27(Supp 3:18):1-3. doi:10.11604/pamj.supp.2017.27.3.11546

4. World Health Organization (WHO). *Global Progress Report on HIV, Viral Hepatitis and Sexually Transmitted Infections, 2021*. Vol 53.; 2021. https://www.who.int/publications/i/item/9789240027077.

5. Keane E, Funk AL, Shimakawa Y. Systematic review with meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa. *Aliment Pharmacol Ther*. 2016;44(10):1005-1017. doi:10.1111/apt.13795

6. Thompson P, Parr JB, Holzmayer V, et al. Seroepidemiology of hepatitis B in the Democratic Republic of the Congo. *Am J Trop Med Hyg*. 2019;101(1):226-229. doi:10.4269/ajtmh.18-0883

7. Edmunds WJ, Medley GF, Nokes DJ, O'Callaghan CJ, Whittle HC, Hall AJ. Epidemiological patterns of hepatitis B virus (HBV) in highly endemic areasr. *Epidemiol Infect*. 1996;117(2):313-325. doi:10.1017/s0950268800001497

8. Poovorawan Y, Sanpavat S, Pongpunlert W, Chumdermpadetsuk S, Sentrakul P, Safary A. Protective Efficacy of a Recombinant DNA Hepatitis B Vaccine in Neonates of HBe Antigen—Positive Mothers. *JAMA*. 1989;261(22):3278-3281. doi:10.1001/jama.1989.03420220092033

9. Wong VCW, Reesink HW, Ip HMH, et al. Prevention of the HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis-B vaccine and hepatitis-B immunoglobulin. Double-blind randomised placebo-controlled study. *Lancet*. 1984;1(8383):921-926. doi:10.1016/S0140-6736(84)92388-2

10. Reardon JM, O'Connor SM, Njau JD, Lam EK, Staton CA, Cookson ST. Cost-effectiveness of birth-dose hepatitis B vaccination among refugee populations in the African region: a series of case studies. *Confl Health*. 2019;13(1). doi:10.1186/s13031-019-0188-y

11. Thompson P, Morgan CE, Ngimbi P, et al. Arresting vertical transmission of hepatitis B virus (AVERT-HBV) in pregnant women and their neonates in the Democratic Republic of the Congo: a feasibility study. *Lancet Glob Heal*. 2021;(21):1-10. doi:10.1016/s2214-109x(21)00304-1

12. Kagina BM, Abel B, Bowmaker M, Scriba TJ, Gelderbloem S, Smit E. Delaying BCG vaccination from birth to 10 weeks of age may result in an enhanced memory CD4 T cell response. *Vaccine*. 2009;27(40):5488-5495. doi:10.1016/j.vaccine.2009.06.103.

13. Lund N, Andersen A, Hansen ASK, et al. The Effect of Oral Polio Vaccine at Birth on Infant Mortality: A Randomized Trial. *Clin Infect Dis*. 2015;61(10):1504-1511. doi:10.1093/cid/civ617

14. Highfield L, Valerio MA, Fernandez ME, Eldridge-Bartholomew LK. Development of an implementation intervention using intervention mapping to increase mammography among low income women. *Front Public Heal*. 2018;6(300):1-12. doi:10.3389/fpubh.2018.00300

15. Fernandez ME, ten Hoor GA, van Lieshout S, et al. Implementation mapping: Using intervention mapping to develop implementation strategies. *Front Public Heal*. 2019;7(158):1-15. doi:10.3389/fpubh.2019.00158

16. Spearman CW, Afihene M, Ally R, et al. Hepatitis B in sub-Saharan Africa: strategies to achieve the 2030 elimination targets. *Lancet Gastroenterol Hepatol*. 2017;2(12):900. doi:10.1016/S2468-1253(17)30295-9

17. The Coalition for Global Hepatitis Elimination/TFGH (CGHE). HepB Birth Dose Introduction in AFRO: Community of Practice. In: ; 2021.

18. Zivich PN, Kiketa L, Kawende B, Lapika B, Yotebieng M. Vaccination Coverage and Timelines Among Children 0–6 Months in Kinshasa, the Democratic Republic of Congo: A Prospective Cohort Study. *Matern Child Health J*. 2017;21(5):1055-1064. doi:10.1007/s10995-016-2201-z

19. Moturi E, Tevi-Benissan C, Hagan J, et al. Implementing a Birth Dose of Hepatitis B Vaccine in Africa: Findings from Assessments in 5 Countries. *J Immunol Sci*. 2018;2(SI1):31-40. doi:10.29245/2578-3009/2018/si.1104

20. Hambridge T, Nartey Y, Duah A, Plymoth A. Hepatitis B mother-to-child transmission in the eastern region of Ghana: A cross-sectional pilot study. *Pan Afr Med J*. 2019;33:1-9. doi:10.11604/pamj.2019.33.218.17242

21. Hagan JE, Carvalho E, Souza V, et al. Selective hepatitis b birth-dose vaccination in São Tomé and príncipe: A program assessment and cost-effectiveness study. *Am J Trop Med Hyg*. 2019;101(4):891-898. doi:10.4269/ajtmh.18-0926

22. Gambarin-Gelwan M. Hepatitis B in Pregnancy. *Clin Liver Dis*. 2007;11(4):945-963. doi:10.1016/j.cld.2007.08.004

23. Mpody C, Thompson P, Tabala M, et al. Hepatitis B infection among pregnant and post-partum women living with HIV and on antiretroviral therapy in Kinshasa, DR Congo: A cross-sectional study. *PLoS One*. 2019;14(5):1-14. doi:10.1371/journal.pone.0216293

24. Kose S. Efficacy and safety of lamivudine treatment in late pregnancy with high HBV DNA: a perspective for mother and infants. *J Infect Dev Ctries*. 2011;5(4):303-306. doi:10.3855/jidc.1398

25. Xu H, Zeng T, Liu JY, et al. Measures to reduce mother-to-child transmission of hepatitis B virus in China: A meta-analysis. *Dig Dis Sci*. 2014;59(2):242-258. doi:10.1007/s10620-013-2918-0

26. Shi Z, Yang Y, Ma L, Li X, Schreiber A. Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B virus: A systematic review and meta-analysis. *Obstet Gynecol*. 2010;116(1):147-159. doi:10.1097/AOG.0b013e3181e45951

27. Wolfson LJ, Gasse F, Lee-Martin SP, et al. Estimating the costs of achieving the WHO-UNICEF Global Immunization Vision and Strategy, 2006-2015. *Bull World Health Organ*. 2008;86(1):27-39. doi:10.2471/BLT.07.045096

28. Wiysonge CS, Uthman OA, Ndumbe PM, Hussey GD. Individual and contextual factors associated with low childhood immunisation coverage in Sub-Saharan Africa: A multilevel analysis. *PLoS One*. 2012;7(5). doi:10.1371/journal.pone.0037905

29. Zivich PN, Kiketa L, Kawende B, Lapika B, Yotebieng M. Vaccination Coverage and Timelines Among Children 0–6 Months in Kinshasa, the Democratic Republic of Congo: A Prospective Cohort Study. *Matern Child Health J*. 2017;21(5):1055-1064. doi:10.1007/s10995-016-2201-z

30. Bangura JB, Xiao S, Qiu D, Ouyang F, Chen L. Barriers to Childhood Immunization in Sub-Saharan Africa: A Systematic Review. *BMC Public Health*. 2020;20(1108):1-15. doi:10.21203/rs.3.rs-17855/v1

31. Malande OO, Munube D, Afaayo RN, et al. Barriers to effective uptake and provision of immunization in a rural district in Uganda. *PLoS One*. 2019;14(2):1-15. doi:10.1371/journal.pone.0212270

32. Obasohan PE, Mustapha MA, Makada A, Obasohan DN. Evaluating the Reasons for Partial and Non-immunization of Children in Wushishi Local Government Area, Niger State, Nigeria: Methodological Comparison. *Afr J Reprod Health*. 2018;22(4):113-122. doi:10.29063/ajrh2018/v22i4.12

33. Babirye JN, Rutebemberwa E, Kiguli J, Wamani H, Nuwaha F, Engebretsen IMS. More support for mothers: a qualitative study on factors affecting immunisation behaviour in Kampala, Uganda. *BMC Public Health*. 2011;11(1):723. doi:10.1186/1471-2458-11-723

34. Tadesse T, Gelaw B, Haile Y, et al. Immunization service availability and readiness in primary health care in pastoral and semi-pastoral CGPP Ethiopia implementation districts. *Ethiop J Heal Dev*. 2019;33(Special issue):7.

35. Miyahara R, Jasseh M, Gomez P, et al. Barriers to timely administration of birth dose vaccines in The Gambia, West Africa. *Vaccine*. 2016;34(29):3335-3341. doi:10.1016/j.vaccine.2016.05.017: 10.1016/j.vaccine.2016.05.017

36. Sarker AR, Akram R, Ali N, Chowdhury ZI, Sultana M. Coverage and determinants of full immunization: Vaccination coverage among senegalese children. *Med*. 2019;55(8). doi:10.3390/medicina55080480

37. Soi C, Gimbel S, Chilundo B, Muchanga V, Matsinhe L, Sherr K. Human papillomavirus vaccine delivery in Mozambique: Identification of implementation performance drivers using the Consolidated Framework for Implementation Research (CFIR). *Implement Sci*. 2018;13(1):1-12. doi:10.1186/s13012-018-0846-2

38. Yotebieng M, Mpody C, Ravelomanana NLR, et al. HIV viral suppression among pregnant and breastfeeding women in routine care in the Kinshasa province: a baseline evaluation of participants in CQI-PMTCT study. *J Int AIDS Soc*. 2019;22(9):1-12. doi:10.1002/jia2.25376

39. Yotebieng M, Behets F, Kawende B, Ravelomanana NLR, Tabala M, Okitolonda EW. Continuous

quality improvement interventions to improve long-term outcomes of antiretroviral therapy in women who initiated therapy during pregnancy or breastfeeding in the Democratic Republic of Congo: Design of an open-label, parallel, group randomized . *BMC Health Serv Res*. 2017;17(1):1-7. doi:10.1186/s12913-017-2253-9

40. Peterson HB, Haidar J, Fixsen D, Ramaswamy R, Weiner BJ, Leatherman S. Implementing innovations in global women's, children's, and adolescents' health: Realizing the potential for implementation science. *Obstet Gynecol*. 2018;131(3):423-430. doi:10.1097/AOG.0000000000002494

41. Li AJ, Tabu C, Shendale S, et al. Qualitative insights into reasons for missed opportunities for vaccination in Kenyan health facilities. *PLoS One*. 2020;15(3):1-15. doi:10.1371/journal.pone.0230783

42. Kajungu D, Muhoozi M, Stark J, Weibel D, Sturkenboom MCJM. Vaccines safety and maternal knowledge for enhanced maternal immunization acceptability in rural Uganda: A qualitative study approach. *PLoS One*. 2020;15(12):1-17. doi:10.1371/journal.pone.0243834

43. World Health Organization Regional Office for Africa. Hepatitis. https://www.who.int/health-topics/hepatitis#tab=tab_1. Accessed December 26, 2021.

44. World Health Organization Regional Office for Africa. *Regional Strategic Plan for Immunization 2014-2020*.; 2015.

45. Dionne-Odom J, Njei B, Tita ATN. Elimination of Vertical Transmission of Hepatitis B in Africa: A Review of Available Tools and New Opportunities. *Clin Ther*. 2018;40(8):1255-1267. doi:10.1016/j.clinthera.2018.05.016

46. Nelson NP, Easterbrook PJ, McMahon BJ. Epidemiology of Hepatitis B Virus Infection and Impact of Vaccination on Disease. *Clin Liver Dis*. 2016;20(4):607-628. doi:10.1016/j.cld.2016.06.006

47. Njuguna H. Building Toward a Future of African Children Free of HBV Infection: Hepatitis B Virus infection in Africa. In: ; 2021.

48. Razavi-Shearer D, Gamkrelidze I, Nguyen MH, et al. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. *Lancet Gastroenterol Hepatol*. 2018;3(6):383-403. doi:10.1016/S2468-1253(18)30056-6

49. Boa A, Douba A, N Guessan TB, et al. A plea for introduction of hepatitis B vaccination at birth in Côte d'Ivoire. *Sante Publique*. 2017;29(5):751-760. doi:10.3917/spub.175.0751

50. Nayagam S, Thursz M, Sicuri E, et al. Requirements for global elimination of hepatitis B: a modelling study. *Lancet Infect Dis*. 2016;16(12):1399-1408. doi:10.1016/S1473-3099(16)30204-3

51. Nguyen Si Anh H, Vo HL, Hoang Bao L, Tran Minh H, Tran Thi Thu H, Kien VD. Hepatitis B Birth Dose Vaccination among Vietnamese Children: Implications for the Expanded Program on Immunization. *Biomed Res Int*. 2019;2019:198. doi:10.1155/2019/3453105

52. Pham TTH, Le TX, Nguyen DT, et al. Knowledge, attitudes and medical practice regarding hepatitis B prevention and management among healthcare workers in Northern Vietnam. *PLoS*

One. 2019;14(10):1-15. doi:10.1371/journal.pone.0223733

53. Scott N, Palmer A, Morgan C, et al. Cost-effectiveness of the controlled temperature chain for the hepatitis B virus birth dose vaccine in various global settings: a modelling study. *Lancet Glob Heal*. 2018;6:e659-e667. doi:10.1016/S2214-109X(18)30219-5

54. Sobel HL, Mantaring JB 3rd, Cuevas F, et al. Implementing a national policy for hepatitis B birth dose vaccination in Philippines: lessons for improved delivery. *Vaccine*. 2011;29(5):941-945. doi:10.1016/j.vaccine.2010.11.047

55. Spearman CW. Towards the elimination of hepatitis B and hepatocellular carcinoma. *S Afr Med J*. 2018;108(8b):13-16. doi:10.7196/SAMJ.2018.v108i8b.13496

56. Pham TT, Le HM, Nguyen DT, et al. Assessment of the timely administration of the hepatitis B and BCG birth dose and the primary infant vaccination schedule in 2015-2016 in the Mekong Delta, Viet Nam. *Vaccine*. 2018;36(38):5760-5765. doi:10.1016/j.vaccine.2018.08.002

57. World Health Organization. Hepatitis B vaccines: WHO position paper, July 2017 - Recommendations. *Vaccine*. 2019;37(2):223-225. doi:10.1016/j.vaccine.2017.07.046

58. Chang M-H, Fischler B, Blauvelt B, et al. Survey of Impediments to Prevention of Mother-to-infant Transmission of Hepatitis B Virus by International Societies. *J Pediatr Gastroenterol Nutr*. 2019;69(6):648-654. doi:10.1097/MPG.0000000000002483

59. Ginzberg D, Wong RJ, Gish R. Global HBV burden: guesstimates and facts. *Hepatol Int*. 2018;12:315-329. doi:10.1007/s12072-018-9884-8

60. Howell J, Lemoine M, Thursz M. Prevention of materno-foetal transmission of hepatitis B in sub-Saharan Africa: The evidence, current practice and future challenges. *J Viral Hepat*. 2014;21(6):381-396. doi:10.1111/jvh.12263

61. Jourdain G, Ngo-Giang-Huong N, Khamduang W. Current progress in the prevention of mother-to-child transmission of hepatitis B and resulting clinical and programmatic implications. *Infect Drug Resist*. 2019;12:977-987. doi:10.2147/IDR.S171695

62. Kolwaite AR, Xeuatvongsa A, Ramirez-Gonzalez A, et al. Hepatitis B vaccine stored outside the cold chain setting: a pilot study in rural Lao PDR. *Vaccine*. 2016;34(28):3324-3330. doi:https://doi.org/10.1016/j.vaccine.2016.03.080

63. Mak L-Y, Seto W-K, Fung J, Yuen M-F. Novel developments of hepatitis B: treatment goals, agents and monitoring tools. *Expert Rev Clin Pharmacol*. 2019;12(2):109-120. doi:10.1080/17512433.2019.1567327

64. Miyahara R, Jasseh M, Gomez P, et al. Barriers to timely administration of birth dose vaccines in The Gambia, West Africa. *Vaccine*. 2016;34(29):3335-3341. doi:10.1016/j.vaccine.2016.05.017

65. Nayagam S, Conteh L, Sicuri E, et al. Cost-effectiveness of community-based screening and treatment for chronic hepatitis B in The Gambia: an economic modelling analysis. *Lancet Glob Heal*. 2016;4(8):e568-e578. doi:10.1016/S2214-109X(16)30101-2

66. Okenwa UJ, Dairo MD, Uba B, Ajumobi O. Maternal reasons for non-receipt of valid Hepatitis B

birth dose among mother-infant pairs attending routine immunization clinics, South-east, Nigeria. *Vaccine*. 2019;37(46):6894-6899. doi:10.1016/j.vaccine.2019.09.056

67. Breakwell L, Anga J, Dadari I, et al. Evaluation of storing hepatitis B vaccine outside the cold chain in the Solomon Islands: Identifying opportunities and barriers to implementation. *Vaccine*. 2017;35(21):2770-2774. doi:10.1016/j.vaccine.2017.04.011.

68. Awuku YA, Yeboah-Afihene M. Hepatitis B At-Birth dose vaccine: An urgent call for implementation in Ghana. *Vaccines*. 2018;6(1):8-11. doi:10.3390/vaccines6010015

69. UNICEF. *Hepatitis B (HepB) Vaccine Price Data*.; 2022. https://www.unicef.org/supply/documents/hepatitis-b-hepb-vaccine-price-data.

70. Anderson S, Harper LM, Dionne-Odom J, Halle-Ekane G, Tita ATN. A decision analytic model for prevention of hepatitis B virus infection in Sub-Saharan Africa using birth-dose vaccination. *Int J Gynaecol Obstet*. 2018;141(1):126-132. doi:10.1002/ijgo.12434

71. NITAG. The unique database on National Immunization Technical Advisory Groups. https://www.nitag-resource.org/. Published 2020.

72. The National Organisation for People Living with Hepatitis B. https://noplhb.org/our-story/. Published 2020.

73. World Health Organization (WHO). The WHO strategy on research for health. *World Heal Organ*. 2012:53. https://www.who.int/phi/WHO_Strategy_on_research_for_health.pdf.

74. World Health Organization. Preventing Perinatal Hepatitis B Virus Transmission : A Guide for Introducing and Strengthening Hepatitis B Birth Dose Vaccination. 2015:1-112. http://www.who.int/iris/handle/10665/208278.

75. Adamu AA, Adamu AL, Dahiru AI, Uthman OA, Wiysonge CS. Mainstreaming implementation science into immunization systems in the decade of vaccines: A programmatic imperative for the African Region. *Hum Vaccines Immunother*. 2018;14(10):2443-2446. doi:10.1080/21645515.2018.1473682

76. Beigi RH, Fortner KB, Munoz FM, et al. Maternal immunization: Opportunities for scientific advancement. *Clin Infect Dis*. 2014;59(Suppl 7):S404-S414. doi:10.1093/cid/ciu708

77. Bassoum O, Kimura M, Dia AT, Lemoine M, Shimakawa Y. Coverage and timeliness of birth dose vaccination in sub-Saharan Africa: A systematic review and meta-analysis. *Vaccines*. 2020;8(2):1-16. doi:10.3390/vaccines8020301

78. Merten S, Schaetti C, Manianga C, et al. Sociocultural determinants of anticipated vaccine acceptance for acute watery diarrhea in early childhood in katanga province, democratic republic of congo. *Am J Trop Med Hyg*. 2013;89(3):419-425. doi:10.4269/ajtmh.12-0643

79. Li X, Heffelfinger J, Wiesen E, et al. Improving hepatitis B birth dose coverage through village health volunteer training and pregnant women education. *Vaccine*. 2017. doi:10.1016/j.vaccine.2017.06.056

80. Mwamba GN, Yoloyolo N, Masembe Y, et al. Vaccination coverage and factors influencing

routine vaccination status in 12 high risk health zones in the Province of Kinshasa City, Democratic Republic of Congo (DRC), 2015. *Pan Afr Med J*. 2017;27(Supp 3):7. doi:10.11604/pamj.supp.2017.27.3.11930

81. Patela MK, Z. CR, Ducusin JU, Castrod M de Q, Garciae LC, Hennessey K. Findings from a hepatitis B birth dose assessment in health facilities in the Philippines: opportunities to engage the private sector. *Vaccine*. 2014;32(39):5140-5144. doi:10.1016/j.vaccine.2013.11.097.

82. Ouma PO, Maina J, Thuranira PN, et al. Access to emergency hospital care provided by the public sector in sub-Saharan Africa in 2015: a geocoded inventory and spatial analysis. *Lancet Glob Heal*. 2018;6(3):e342-e350. doi:10.1016/S2214-109X(17)30488-6

83. Lemoine M, Thursz MR. Battlefield against hepatitis B infection and HCC in Africa. *J Hepatol*. 2017;66(3):645-654. doi:10.1016/j.jhep.2016.10.013

84. Centers for Disease Control and Prevention (CDC). Hepatitis B vaccine birthdose practices in a country where hepatitis B is endemic - Laos, December 2011-February 2012. *Morb Mortal Wkly Rep*. 2013;62(29):587-590.

85. Odutola A, Afolabi MO, Ogundare EO, et al. Risk factors for delay in age-appropriate vaccinations among Gambian children. *BMC Health Serv Res*. 2015;15(1):1-9. doi:10.1186/s12913-015-1015-9

86. Shindano TA, Bahizire E, Fiasse R, Horsmans Y. Knowledge, Attitudes, and Practices of health-care workers about viral hepatitis b and C in South Kivu. *Am J Trop Med Hyg*. 2017;96(2):400-404. doi:10.4269/ajtmh.16-0287

87. Giao H, Vinh BQ, Huynh Tam Lang N, Le An P. Parents' Attitude about Hepatitis B Disease and Practice of Hepatitis B Vaccination among Children in Ho Chi Minh City, Vietnam. *Biomed Res Int*. 2019;2019:1-7. doi:10.1155/2019/9323814

88. World Health Organization (WHO). *Packages of Interventions for Family Planning, Safe Abortion Care, Maternal, Newborn and Child Health*.; 2010. doi:WHO.FCH/10.06

89. Woodring J, Pastore R, Brink A, Ishikawa N, Takashima Y, Tohme RA. Progress Toward Hepatitis B Control and Elimination of Mother-to-Child Transmission of Hepatitis B Virus — Western Pacific Region, 2005–2017. *MMWR Morb Mortal Wkly Rep*. 2019;68(8):195-200. doi:10.15585/mmwr.mm6808a2

90. Périères L, Marcellin F, Lo G, et al. Hepatitis B Vaccination in Senegalese Children: Coverage, Timeliness, and Sociodemographic Determinants of Non-Adherence to Immunisation Schedules (ANRS 12356 AmBASS Survey). *Vaccines*. 2021;9(5):510. doi:10.3390/vaccines9050510

91. Xeuatvongsa A, Datta SS, Moturi E, et al. Improving hepatitis B birth dose in rural Lao People's Democratic Republic through the use of mobile phones to facilitate communication. *Vaccine*. 2016;34(47):5777-5784. doi:10.1016/j.vaccine.2016.09.056

92. Center for Disease Control. *Perinatal Quality Collaborative Success Story*.; 2016. https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pdf/ohio-success-story_508tagged.pdf.

93. Zipursky S, Djingarey MH, Lodjo JC, Olodo L, Tiendrebeogo S, Ronveaux O. Benefits of using vaccines out of the cold chain: Delivering Meningitis A vaccine in a controlled temperature chain during the mass immunization campaign in Benin. *Vaccine*. 2014;32(13):1431-1435. doi:10.1016/j.vaccine.2014.01.038

94. Thinking outside the Box : Innovations in Preventing Hepatitis B at Birth. CDC Global Health. https://www.cdc.gov/globalhealth/immunization/stories/laos-hep-b-vax.htm. Published 2017. Accessed September 28, 2021.

95. Wiesen E, Diorditsa S, Li X. Progress towards hepatitis B prevention through vaccination in the Western Pacific, 1990-2014. *Vaccine*. 2016;34(25):2855-2862. doi:10.1016/j.vaccine.2016.03.060

96. Nesbitt A, Heathcock R, Dunn J, Shukla R, Neal K. Integration of hepatitis B vaccination into national immunisation programmes. *Br Med J*. 1997;314:1030-1033. doi:10.1136/bmj.315.7100.121a

97. Shimakawa Y, Veillon P, Birguel J, et al. Residual risk of mother-to-child transmission of hepatitis B virus infection despite timely birth-dose vaccination in Cameroon (ANRS 12303): a single-centre, longitudinal observational study. *Lancet Glob Heal*. 2022;10(4):e521-e529. doi:10.1016/S2214-109X(22)00026-2

98. World Health Organization. *Practices to Improve Coverage of the Hepatitis B Birth Dose Vaccine*.; 2013. doi:WHO/IVB/12.11

99. Nayagam S, Shimakawa Y, Lemoine M. Mother-to-child transmission of hepatitis B: What more needs to be done to eliminate it around the world? *J Viral Hepat*. 2020;27(4):342-349. doi:10.1111/jvh.13231

100. Boisson A, Morgan CE, Fried B, et al. Barriers and facilitators to timely birth-dose vaccines in Kinshasa Province, the DRC: a qualitative study. *J Glob Heal Reports*. 2022;6:1-13. doi:10.29392/001c.35449

101. World Health Organisation (WHO). *National Immunization Schedule Democratic Republic of the Congo*.; 2018.

102. World Health Organization (WHO). *Reference Manual: Service Availability and Readiness Assessment (SARA) - An Annual Monitoring System for Service Delivery*.; 2015. http://www.who.int/healthinfo/systems/sara_reference_manual/en/.

103. World Health Organization. Hepatitis B Birth Dose vacination coverage. Immunization Data portal. https://www.who.int/data/immunization. Published 2020. Accessed December 20, 2021.

104. Lancione S, Alvarez JV, Alsdurf H, Pai M, Zwerling AA. Tracking changes in national BCG vaccination policies and practices using the BCG World Atlas. *BMJ Glob Heal*. 2022;7(1):1-8. doi:10.1136/bmjgh-2021-007462

105. Phillips DE, Dieleman JL, Shearer JC, Lim SS. Childhood vaccines in Uganda and Zambia: Determinants and barriers to vaccine coverage. *Vaccine*. 2018;36(29):4236-4244. doi:10.1016/j.vaccine.2018.05.116

106. Levin A, Munthali S, Vodungbo V, et al. Scope and magnitude of private sector financing and

provision of immunization in Benin, Malawi and Georgia. *Vaccine*. 2019;37(27):3568-3575. doi:10.1016/j.vaccine.2019.05.023

107. Ibnouf A, Van den Borne H, Maarse J. Factors influencing immunisation coverage among children under five years of age in Khartoum State, Sudan. *South African Fam Pract*. 2007;49(8):14-14f. doi:10.1080/20786204.2007.10873611

108. Bbaale E. Factors influencing childhood immunization in Uganda. *J Heal Popul Nutr*. 2013;31(1):118-127. doi:10.3329/jhpn.v31i1.14756

109. Desai S, Alva S. Maternal education and child health: is there a strong causal relationship? *Demography*. 1998;35(1):71-81.

110. Thahir S, Tulenko SE, Ngimbi P, et al. Low knowledge about hepatitis B prevention among pregnant women in Kinshasa, Democratic Republic of Congo. *PLOS Glob Public Heal*. 2022;2(9):e0000450. doi:10.1371/journal.pgph.0000450

111. Herliana P, Douiri A. Determinants of immunisation coverage of children aged 12-59 months in Indonesia: A cross-sectional study. *BMJ Open*. 2017;7(12):1-14. doi:10.1136/bmjopen-2016-015790

112. Fenta SM, Fenta HM. Individual and community-level determinants of childhood vaccination in Ethiopia. *Arch Public Heal*. 2021;79(1):1-11. doi:10.1186/s13690-021-00581-9

113. Lanaspa M, Balcells R, Sacoor C, Nhama A, Aponte JJ, Bassat Q. The performance of the expanded programme on immunization in a rural area of Mozambique. *Acta Trop*. 2015;149:262-266. doi:10.1016/j.actatropica.2015.06.007

114. Adjei CA, Stutterheim SE, Naab F, Ruiter RAC. Chronic Hepatitis B stigma in Ghana: A qualitative study with patients and providers. *BMJ Open*. 2019;9(6):1-12. doi:10.1136/bmjopen-2018-025503

115. Galadima AN, Zulkefli NAM, Said SM, Ahmad N. Factors influencing childhood immunisation uptake in Africa: a systematic review. *BMC Public Health*. 2021;21(1):1-20. doi:10.1186/s12889-021-11466-5

116. United Nations Children's Fund. *Levels & Trends in Child Mortality Report 2021*.; 2021. www.unicef.org.

117. Roy P, Vekemans J, Clark A, Sanderson C, Harris RC, White RG. Potential effect of age of BCG vaccination on global paediatric tuberculosis mortality: a modelling study. *Lancet Glob Heal*. 2019;7(12):e1655-e1663. doi:10.1016/S2214-109X(19)30444-9

118. Boisson A, Goel V, Yotebieng M, Parr JB, Fried B, Thompson P. Implementation Approaches for Introducing and Overcoming Barriers to Hepatitis B Birth-Dose Vaccine in sub-Saharan Africa. *Glob Heal Sci Pract*. 2020;10(1):1-14.

119. District Health Information System. District Health Information System (Version 2). https://www.dhis2.org. Accessed May 20, 2022.

120. United Nations Children's Fund. *HepB-Vaccines-Prices-27052021*.; 2021.

121. Gavi The Vaccine Alliance. Operating Model. https://www.gavi.org/our-alliance/operating-model. Published 2022. Accessed January 12, 2021.

122. Nganga SW, Otieno NA, Adero M, et al. Patient and provider perspectives on how trust influences maternal vaccine acceptance among pregnant women in Kenya. *BMC Health Serv Res*. 2019;19(1):1-13. doi:10.1186/s12913-019-4537-8

123. Fleming JA, Munthali A, Ngwira B, et al. Maternal immunization in Malawi: A mixed methods study of community perceptions, programmatic considerations, and recommendations for future planning. *Vaccine*. 2019;37(32):4568-4575. doi:10.1016/j.vaccine.2019.06.020

124. Hughes CC, Jones AL, Feemster KA, Fiks AG. HPV vaccine decision making in pediatric primary care: A semi-structured interview study. *BMC Pediatr*. 2011;11. doi:10.1186/1471-2431-11-74

125. Olaniyan A, Isiguzo C, Hawk M. The Socioecological Model as a framework for exploring factors influencing childhood immunization uptake in Lagos state, Nigeria. *BMC Public Health*. 2021;21(1):1-10. doi:10.1186/s12889-021-10922-6

126. Saunders B, Sim J, Kingstone T, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant*. 2018;52(4):1893-1907. doi:10.1007/s11135-017-0574-8

127. CFIR Consolidated Framework for Implemantion Research. CFIR Research Team-Center for Clinical Management Research. https://cfirguide.org/constructs/. Published 2022. Accessed January 18, 2022.

128. World Health Organization. *What Do We Know About Community Health Workers? A Systematic Review of Existing Reviews*. Vol 19.; 2020.

129. World Health Organization. *Monitoring Vaccine Wastage at Country Level*.; 2005. doi:WHO.V&B/03.18/Rev.1

130. Kanagat N, Krudwig K, Wilkins KA, et al. Health care worker preferences and perspectives on doses per container for 2 lyophilized vaccines in Senegal, Vietnam, and Zambia. *Glob Heal Sci Pract*. 2021;8(4):680-688. doi:10.9745/GHSP-D-20-00112

131. Schaltz-Buchholzer F, Frankel HN, Benn CS. The real-life number of neonatal doses of Bacille Calmette-Guérin vaccine in a 20-dose vial. *Glob Health Action*. 2017;10(1):1-4. doi:10.1080/16549716.2017.1267964

132. Aaby P, Roth A, Ravn H, et al. Randomized trial of BCG vaccination at birth to low-birth-weight children: Beneficial nonspecific effects in the neonatal period? *J Infect Dis*. 2011;204(2):245-252. doi:10.1093/infdis/jir240

133. Wallace AS, Krey K, Hustedt J, et al. Assessment of vaccine wastage rates, missed opportunities, and related knowledge, attitudes and practices during introduction of a second dose of measles-containing vaccine into Cambodia's national immunization program. *Vaccine J*. 2018;36(30):4517-4524. doi:10.1016/j.vaccine.2018.06.009.

134. Kristensen DD, Bartholomew K, Villadiego S, Lorenson K. What vaccine product attributes do immunization program stakeholders value? Results from interviews in six low- and middle-

income countries. *Vaccine*. 2016;34(50):6236-6242. doi:10.1016/j.vaccine.2016.10.057

135. Griffiths UK, Asman J, Adjagba A, Yo M, Oguta JO, Cho C. Budget line items for immunization in 33 African countries. *Health Policy Plan*. 2020;35(7):753-764. doi:10.1093/heapol/czaa040

136. Jarrett C, Wilson R, O'Leary M, et al. Strategies for addressing vaccine hesitancy - A systematic review. *Vaccine*. 2015;33(34):4180-4190. doi:10.1016/j.vaccine.2015.04.040

137. Hu Y, Chen Y, Wang Y, Song Q, Li Q. Prenatal vaccination education intervention improves both the mothers' knowledge and children's vaccination coverage: Evidence from randomized controlled trial from eastern China. *Hum Vaccines Immunother*. 2017;13(6):1477-1484. doi:10.1080/21645515.2017.1285476

138. Nkereuwem OO, Kochhar S, Wariri O, et al. The use of a speaking book® to enhance vaccine knowledge among caregivers in the Gambia: A study using qualitative and quantitative methods. *BMJ Open*. 2021;11(3):1-13. doi:10.1136/bmjopen-2020-040507

139. Mulumba JGT, Daoud S, Kabang B. Raising parents' awareness of the benefits of immunization by using a visual aid tool. *Trop Doct*. 2007;37(3):146-147. doi:10.1258/004947507781524638

140. Ditekemena JD, Nkamba DM, Mavoko AM; HM, et al. COVID-19 Vaccine Acceptance in the Democratic Republic of Congo: A Cross-Sectional Survey. *Vaccines*. 2021;9(2):153. doi:10.3390/vaccines9020153

141. Johri M, Subramanian S V., Sylvestre MP, et al. Association between maternal health literacy and child vaccination in India: A cross-sectional study. *J Epidemiol Community Health*. 2015;69(9):849-857. doi:10.1136/jech-2014-205436

142. Machingaidze S, Wiysonge CS, Hussey GD. Strengthening the expanded programme on immunization in Africa: looking beyond 2015. *PLoS Med*. 2013;10(3):e1001405. doi:10.1371/journal.pmed.1001405

143. Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet*. 2012;379(9832):2151-2161. doi:10.1016/S0140-6736(12)60560-1

144. Rainey JJ, Watkins M, Ryman TK, Sandhu P, Bo A, Banerjee K. Reasons related to non-vaccination and under-vaccination of children in low and middle income countries: Findings from a systematic review of the published literature, 1999–2009. *Vaccine*. 2011;29(46):8215-8221. doi:https://doi.org/10.1016/j.vaccine.2011.08.096

145. World Health Organization (WHO). *Prevention of Mother-to-Child Transmission of Hepatitis B Virus (HBV): Guidelines on Antiviral Prophylaxis in Pregnancy*.; 2020.

146. Bada FO, Stafford KA, Osawe S, et al. Factors associated with receipt of a timely infant birth dose of hepatitis B vaccine at a tertiary hospital in North-Central Nigeria. *PLOS Glob Public Heal*. 2022;2(9):e0001052. doi:10.1371/journal.pgph.0001052

147. Sarathy L, Cirillo C, Dehn C, Lerou PH, Prendergast M. Improving timeliness of Hepatitis B vaccine birth dose administration. *Hosp Pediatr*. 2021;11(5):446-453. doi:10.1542/HPEDS.2020-002766

148. The World Bank. Population in largest city - Congo, Dem. Rep. The World Bank Data. https://data.worldbank.org/indicator/EN.URB.LCTY?locations=CD. Published 2021. Accessed December 11, 2022.

149. Republique Democratique du Congo Ministere de la Santé et Hygene Publique. *Plan National De Developpement Sanitaire 2016-2020*.; 2016.

150. DeBoer RJ, Ndumbalo J, Meena S, et al. Development of a theory-driven implementation strategy for cancer management guidelines in sub-Saharan Africa. *Implement Sci Commun*. 2020;1(1):1-9. doi:10.1186/s43058-020-00007-7

151. Ingabire CM, Hakizimana E, Kateera F, et al. Using an intervention mapping approach for planning, implementing and assessing a community-led project towards malaria elimination in the Eastern Province of Rwanda. *Malar J*. 2016;15(1):1-12. doi:10.1186/s12936-016-1645-3

152. van Pelt S, Massar K, Shields-Zeeman L, et al. The Development of an Electronic Clinical Decision and Support System to Improve the Quality of Antenatal Care in Rural Tanzania: Lessons Learned Using Intervention Mapping. *Front Public Heal*. 2021;9(645521):1-14. doi:10.3389/fpubh.2021.645521

153. Kay Bartholomew Eldredge L, Markham CM, Ruiter RAC, Fernández ME, Kok G, Parcel GS. *Planning Health Promotion Programs: An Intervention Mapping Approach*. Jossey-Bass; 2016.

154. Israel BA, Schulz AJ, Parker EA, Becker AB. Review of community-based research: assessing partnership approaches to improve public health. *Annu Rev Public Health*. 1998;19:173-202. doi:10.1146/annurev.publhealth.19.1.173

155. Boisson A, Thompson P, Fried B, Shea C, Domino M, Yotebieng M. Determinants of the uptake of childhood immunization in Kinshasa Province, the DRC: ordered logit regression analyses to assess timely infant vaccines administered at birth and six-weeks of age. *BMC Glob Heal*.

156. Crosby R, Noar SM. What is a planning model? An introduction to PRECEDE-PROCEED. *J Public Health Dent*. 2011;71(SUPPL. 1). doi:10.1111/j.1752-7325.2011.00235.x

157. Ajzen I. The Theory of Planned Behavior. *Organ Behav Hum Decis Process*. 1991;50:179-211. doi:0749-5978/91

158. Bandura A. *Self-Efficacy: The Exercise of Control*. New York: Freeman; 1997.

159. Bandura A. Social Cognitive Theory : An Agentic Perspective. *Annu Rev Psychol*. 2001;52:1-26. doi:0066-4308/01/0201-0001

160. Miech EJ, Rattray NA, Flanagan ME, Damschroder L, Schmid AA, Damush TM. Inside help: An integrative review of champions in healthcare-related implementation. *SAGE open Med*. 2018;6:1-11. doi:10.1177/2050312118773261

161. Yotebieng M, Chalachala JL, Labbok M, Behets F. Infant feeding practices and determinants of poor breastfeeding behavior in Kinshasa, Democratic Republic of Congo: A descriptive study. *Int Breastfeed J*. 2013;8(1):1. doi:10.1186/1746-4358-8-11

162. Bobo FT, Asante A, Woldie M, Dawson A, Hayen A. Child vaccination in sub-Saharan Africa:

Increasing coverage addresses inequalities. *Vaccine*. 2022;40(1):141-150. doi:10.1016/j.vaccine.2021.11.005

163. Burroway R, Hargrove A. Education is the antidote: Individual- and community-level effects of maternal education on child immunizations in Nigeria. *Soc Sci Med*. 2018;213:63-71. doi:https://doi.org/10.1016/j.socscimed.2018.07.036

164. Siddiqui FA, Padhani ZA, Salam RA, et al. Interventions to Improve Immunization Coverage Among Children and Adolescents: A Meta-analysis. *Pediatrics*. 2022;149(s6). doi:10.1542/peds.2021-053852D

165. WHO/UNICEF. *The Role of Community Health Workers in COVID-19 Vaccination Implementation Support Guide*.; 2021. doi:WHO/2019-nCoV/NDVP/CHWs_role/2021.1

166. Banerjee P, Seth R, Dhaliwal BK, et al. Vaccine acceptance in rural India: Engaging faith leaders as vaccine ambassadors. *Front Public Heal*. 2022;10. doi:10.3389/fpubh.2022.979424

167. Wijesinghe MSD, Ariyaratne VS, Gunawardana BMI, et al. Role of Religious Leaders in COVID-19 Prevention: A Community-Level Prevention Model in Sri Lanka. *J Relig Health*. 2022;61(1):687-702. doi:10.1007/s10943-021-01463-8

168. The World Bank. *Tuberculosis Case Detection Rate (% All Forms) - Sub-Saharab Africa*.; 2023.

169. Boisson A, Morgan CE, Stover A, et al. Changes in hepatitis B vaccine perception in response to the COVID-19 pandemic: Development of the Shift in vaccine confidence (SVC) survey tool. *Vaccine J*. 2022:1-7. doi:10.1016/j.vaccine.2022.12.028

170. UNICEF. *COVID-19 Pandemic Leads to Major Backsliding on Childhood Vaccinations, New WHO, UNICEF Data Shows*.; 2021.

171. Buonsenso D, Cinicola B, Kallon MN, Iodice F. Child Healthcare and Immunizations in Sub-Saharan Africa During the COVID-19 Pandemic. *Front Pediatr*. 2020;8(August):6-9. doi:10.3389/fped.2020.00517

172. Bao H, Salisbury K, Chi BH, Tucker JD, Tang W. Research Mentorship Crowdsourcing Contest: Toward Global Health Good. *Am J Trop Med Hyg*. 2020;103(3):1270-1273. doi:10.4269/ajtmh.19-0945

173. Kpokiri EE, John R, Wu D, et al. Crowdsourcing to develop open-access learning resources on antimicrobial resistance. *BMC Infect Dis*. 2021;21(1):1-7. doi:10.1186/s12879-021-06628-0

174. Tang W, Ritchwood TD, Wu D, et al. Crowdsourcing to improve HIV and sexual health outcomes: A scoping review. *Curr HIV/AIDS*. 2019;16(4):270-278. doi:10.1007/s11904-019-00448-3.