Research priority setting on maternal, perinatal and newborn health in LMICs: Theory and practice in relation to preterm birth.

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy

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Research priority setting on maternal, perinatal and newborn health in LMICs: Theory and practice in relation to preterm birth

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Abstract

Background: Despite progress in reducing neonatal deaths, preterm birth (PTB) remains the leading cause, with millions of babies affected and significant survival gaps between high- and low-resource settings. Addressing the burden of PTB in resource-limited settings requires targeted research on its causes, mechanisms, and risks, along with cost-effective maternal and newborn health interventions. My PhD aimed to address this evidence gap and inform future recommendations regarding PTB in LMICs within the SDG era by: (i) identifying and prioritising research on PTB and pre-eclampsia and eclampsia (PE/E) (ii) conducting community-level exploration to identify gaps and opportunities for improving care for preterm babies among high-risk adolescents in rural Bangladesh.

Methods: I used an adapted Child Health and Nutrition Research initiative (CHNRI) method to determine research priorities on PTB in LMICs and Bangladesh, and PE/E in LMICs. Using qualitative research, I explored perception and experiences of adolescents and communities in caring for preterm babies in rural Bangladesh. This involved in-depth or key informant interviews with mothers of premature and term babies, family members and healthcare providers and focus groups with community members.

Results: In study 1 on PTB research priority setting, health systems and policy related research were prominent among the top 20 priorities for LMICs. These were related to facility and community-based Kangaroo Mother Care (KMC), breastfeeding, referral and transportation, use of skilled attendants, quality improvement, and antenatal steroid use. There was substantial overlap in research priorities for LMICs and Bangladesh.

In study 2 on PE/E priority setting, experts prioritised health systems and delivery research to enhance detection, transfer, and management of women with PE/E in LMICs. Topics were related to care delays, availability of supplies and quality of care in facilities, provider and facility readiness, guideline implementation, Magnesium Sulphate use, providers' knowledge gaps, referral systems, early identification and screening.

Study 3 examined two main themes: perception and understanding of preterm birth and care practices for preterm babies. The first theme revealed inconsistent knowledge about preterm birth's definition, appearance, causes, and associated problems. The second theme highlighted inappropriate care, multiple healthcare provider usage and delayed care-seeking due to factors like perceived illness severity, costs, and quality, including inadequate equipment and trained personnel. Adolescents showed significant knowledge gaps and relied on family members for baby's care.

Conclusions: My PhD systematically identifies and prioritises future research areas for preventing and managing PTB and PE/E in LMICs, particularly Bangladesh. By integrating research prioritisation with insights from high-risk groups, especially adolescents in low-resource settings, this study informs policy and practice to reduce maternal and newborn health disparities.

Declaration

I, the author, confirm that the Thesis is my own work. I am aware of the University's Guidance on the Use of Unfair Means (www.sheffield.ac.uk/ssid/unfair-means). This work has not previously been presented for an award at this, or any other, university.

Publication and conference presentations

Two original research papers have been published from the thesis in peer-reviewed journals. The manuscripts included in this thesis represent the authors' accepted versions after peer-review. Links to the publisher versions have been provided to adhere to the publishers' copyright policies and embargo restrictions, as outlined on sherpa.ac.uk/Romeo (accessed on March 4, 2024). Additionally data from the thesis has been presented, at national and international conferences throughout the duration of the PhD studies.

Published articles related to this work:

1. **Salam SS,** Ameen S, Balen J, Nahar Q, Jabeen S, Ahmed A, et al. Research prioritisation on prevention and management of preterm birth in low and middle-income countries (LMICs) with a special focus on Bangladesh using the Child Health and Nutrition Research Initiative (CHNRI) method. Journal of global health. 2023;13.

2. **Salam SS,** Rahman AE, Mhajabin S, Mazumder T, Majid T, Samad Talha MTU, et al. Perception and experiences of adolescent mothers and communities in caring for their preterm babies: findings from an in-depth study in rural Bangladesh. BMC pregnancy and childbirth. 2024;24(1):145.

During the course of the PhD studies, four additional papers were written and subsequently published in peer-reviewed journals. Although these papers are not included as part of the thesis, the insights gained from these experiences have informed the literature review, data collection, and writing of the thesis.

1. **Salam SS**, Mitchell C. "Evaluating Alcohol, Tobacco, and Other Substance Use in Pregnant Women". In: Anumba D, Jayasooriya S, editors. Evidence Based Global Health Manual for Preterm Birth Risk Assessment 2022.

2. **Salam SS,** Ramadurg U, Charantimath U, Katageri G, Gillespie B, Mhetri J, et al. Impact of a school-based nutrition educational intervention on knowledge related to iron deficiency anaemia in rural Karnataka, India: A mixed methods pre-post interventional study. BJOG. 2023;130 Suppl 3:113-23.

3. Gillespie B, Katageri G, **Salam S,** Ramadurg U, Patil S, Mhetri J, et al. Attention for and awareness of anaemia in adolescents in Karnataka, India: A qualitative study. PLoS One. 2023;18(4):e0283631.

4.   Campbell F, **Salam S,** Sutton A, Jayasooriya SM, Mitchell C, Amabebe E, et al. Interventions for the prevention of spontaneous preterm birth: a scoping review of systematic reviews. BMJ Open. 2022;12(5):e052576.

Conference presentations related to this work:

1.   Salam SS (on behalf of NIHR PRME research group), Research priority setting for prevention and treatment of pre-eclampsia and eclampsia in LMICs. RCOG; 2021; UK. (Oral presentation, Online)

2.   Salam SS (on behalf of NIHR PRME research group), Research priority setting for prevention and treatment of pre-eclampsia and eclampsia in LMICs. AFEMSON; 2021; Nigeria. (Oral presentation, Online)

3.   Salam SS (on behalf of NIHR PRME research group), Research priority setting for prevention and management of preterm births in LMICs. PTB Dialogues; 2022; UK. (Oral presentation, Online)

4.   Salam SS (on behalf of NIHR PRME research group), Perception and care practices of adolescent mothers about their preterm newborns. PTB Dialogues; 2022; UK. (Oral presentation, Online)

5.   Salam SS (on behalf of NIHR PRME research group), Respectful care for preterm newborns in rural Bangladesh, Implementing Respectful Care: Science and Practice, GLOW 2020; UK. (Oral presentation, online)

6.   Salam SS (on behalf of NIHR PRME research group), "I don't know why she was born early, it was God's will": an in-depth study exploring adolescents' perceptions and experiences in caring for preterm babies in rural Bangladesh, Sheffield Global Health Symposium; 2020; UK. (Oral presentation)

7.   Salam SS (on behalf of the NIHR PRIME research group), Perceptions and experiences of adolescent mothers in caring for their preterm babies in rural Bangladesh**:** Findings and Co-Development of Prioritised Interventions. 3rd International Conference on MNCH; 2022; India. (Oral presentation)

Acknowledgements

List of Figures (not related to the publications)

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Annexures (not related to the publications)

List of Abbreviations

AEA	Average Expert Agreement
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Care
CAM	Combined Approach Matrix
CHERG	Child Health Epidemiology Reference Group
CHNRI	Child Health and Nutrition Research Initiative
CHW	Community Health Worker
cKMC	Community based Kangaroo Mother Care
COHRED	Council on Health Research for Development
COVID-19	Coronavirus Disease 2019
CPAP	Continuous Positive Airway Pressure
CSR	Clinical Science Research
ENAP	Every Newborn Action Plan
ENHR	Essential National Health Research
EPI	Epidemiological Research
EPMM	Ending Preventable Maternal Mortality
3D CAM	Three-Dimensional Combined Approach Matrix
FGD	Focus Group Discussion
GlyFn	Glycosylated Fibronectin
HELLP	Hemolysis, Elevated Liver enzymes and Low Platelets
HIC	High Income Countries
HDP	Hypertensive Disorders of Pregnancy
HPSR	Health Policy and Systems Research
Iccdr,b	International Centre for Diarrhoeal Disease Research, Bangladesh
IDI	In-depth Interview
IUGR	Intra-uterine fetal growth restriction
JLA	James Lind Alliance
KII	Key informant Interview
KMC	Kangaroo Mother Care
LBW	Low Birth Weight
LSR	Laboratory Science Research
LMIC	Low-income and middle-income countries
MDG	Millenium Development Goal
MNCH	Maternal, Newborn and Child Health
MRI	Magnetic Resonance Imaging
NIHR	National Institute for Health and Care Research

NCD	Non-Communicable Disease
PE/E	Pre-eclampsia/Eclampsia
POC	Point-of-Care
PMTCT	Prevention of Mother-To-Child Transmission
PRIME	Prevention and Management of preterm birth
PROM	Premature Rupture of Membrane
PTB	Preterm Birth
QI	Quality Improvement
RDNI	Research to Develop New Interventions
RIEI	Research to Improve Existing Interventions
ROP	Retinopathy of Prematurity
RPS	Research Priority Scores
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SCANU	Specialised care newborn units
SCENE	Separation and Closeness Experiences in the Neonatal Environment
SDG	Sustainable Development Goal
SD	Standard Deviation
SGA	Small for Gestational Age
SQL	Structured Query Language
TB	Tuberculosis
WHO	World Health Organisation

1   Chapter 1: Introduction

Preterm birth (PTB), defined by the WHO as birth before 37 completed weeks of gestation, remains a significant global concern (1, 2). In 2020, an estimated 13.4 million babies (9.9% of all live births) were born prematurely, a slight decrease from 13.8 million in 2010 (9.8% of all live births) (1, 3). The annual rate of reduction was only -0.14%, indicating minimal progress in the last decade (3). Significant disparities in preterm birth incidence and survival exist between high- and low-resource regions and countries (1, 4). Southern Asia and sub-Saharan Africa, which together account for 55.6% of global live births, bear majority (65%) of the global preterm birth burden (1, 3). In 2020, over 50% of PTBs occurred in just eight countries, with India recording the highest number of preterm births (3.02 million, over 20% of global preterm births) (3). While most high PTB rates are observed in low- and middle-income countries, rates of 10% or higher were also seen in high-income countries like Greece and the USA, highlighting that preterm birth is a global issue (1, 3).

PTB continues to be the leading cause of neonatal and under-five mortality, as well as the fourth leading cause of loss of Disability-Adjusted Life Years (DALYs) worldwide across all age groups (2019) (5-7). In 2019, approximately 900,000 children died from PTB complications, accounting for 36.1% (0.88 million) of neonatal deaths and 7.7% (0.94 million) of under-five deaths (5). Ten countries contributed to 59.5% of global under-five deaths, with PTB complications responsible for 6.3%–25.7% of these deaths, and mortality rates ranging from 1.3 to 14.4 per 1,000 live births (5). The limited progress in reducing PTB rates, coupled with a lack of significant decline in related deaths, has resulted in a growing proportion of deaths attributed to preterm birth, rising from 14.5% to 17.6% among children under five between 2000 and 2019 (5, 6). If this trend persists, PTB complications will continue to be the leading cause of neonatal and under-five mortality by 2030, posing a significant obstacle to achieving the Sustainable Development Goals (SDGs) (5, 6, 8).

1.1   Evidence-based policies, strategies and interventions for PTB prevention and newborn survival

The achievement of the SDG targets for newborn mortality critically depends on the widespread implementation of evidence-based interventions that prevent PTB, enhance the survival of preterm newborns, and the adoption of policies that facilitate the implementation of these interventions starting at the national level (9). PTB has long been a focal point in maternal, newborn, and child health agendas across many countries and is increasingly being adopted into national and subnational policies. This has been possible due to global initiatives such as the Every Newborn Action Plan (ENAP) and the Ending Preventable Maternal Mortality (EPMM) in the last decade (9). These efforts, combined with the inclusion of newborn mortality reduction targets in the SDGs and the Global Strategy for Women's, Children's, and Adolescents' Health, have prompted action and helped adopt/refine healthcare

guidelines (such as those on preterm birth, antenatal care and sick newborn care) and interventions (9-14).

PTB is categorised based on gestational age as "moderately or late preterm" (32-36 weeks), "very preterm" (28-32 weeks), and "extremely preterm" (less than 28 weeks). Additionally, it can be classified as spontaneous or medically indicated. This level of specificity is essential for understanding the risk factors and necessary intervention strategies, which are addressed during the continuum of sexual, reproductive and maternal health and aimed at the individual, household, community, or health facility level (9, 15). Several evidence-based guidance and research studies have identified interventions or strategies for women to prevent and manage preterm birth primarily spontaneous PTB (11-14, 16-20). Focused during adolescence, pre-pregnancy, pregnancy, labour and birth, postnatal maternal and newborn stages, these are broadly categorised into: Preconception care, including ensuring women and adolescent girls can decide the number and spacing of their children; evidence-based, high-quality antenatal care to identify and reduce preterm birth risks during the antenatal period (e.g., advanced antenatal care, micronutrient supplementation, low-dose aspirin, progesterone provided vaginally, education for smoking cessation, malaria prevention, treatment of infection etc); providing respectful care and evidence-based care (e.g., skilled attendance at birth, antenatal corticosteroids, tocolytics, delayed cord clamping etc) during labour and childbirth; and high-quality respectful care for women, newborns (e.g., immediate newborn care, kangaroo mother care, CPAP for respiratory distress etc.), and families during the postnatal period (11-14, 16-23). With 80% of births now occurring in health facilities globally and neonatal mortality rates ranging from 16 to 30 deaths per 1,000 live births in majority of countries, improving the quality of inpatient care for small and sick newborns including preterm babies has become a priority (9). The World Health Organization has established standards to enhance the quality of care in health facilities, emphasising implementation of evidence-based interventions, a skilled workforce, access to essential equipment, family-centered care, a safe and hygienic environment, continuous monitoring and quality improvement, integrated referral systems, and supportive policies and leadership (14, 22). Additionally, emphasis is also placed on addressing intersectoral determinants such as equity and rights, economic stability, environmental conditions—including nutrition and climate—education, and the effects of emergencies which impact the health of women and newborns throughout the life cycle (9).

Although PTB rates do not differ significantly between high- and low-resource countries, there is a considerable survival gap for preterm newborns across these settings (1, 5, 24). In low- and middle-income countries (LMICs), substantial challenges in the coverage, quality, and equity of essential reproductive, maternal, newborn, and child health (RMNCH) services and interventions hinder effective prevention and management of PTBs (22, 23, 25, 26). Factors such as exposure to air pollution (26-28), low or advanced maternal age (29), poor maternal nutrition (30, 31), and infections (32, 33) that affect prematurity are also either higher or on the rise in these regions. Furthermore, new and escalating

challenges such as conflict, climate change, COVID-19, and the cost-of-living crisis are amplifying existing inequities in care for women and all small and vulnerable newborns particularly in regions with already fragile health systems (9).

1.2   Impact and challenges of pre-eclampsia and eclampsia in PTBs

While reducing PTB rates and associated morbidity and mortality remains a primary goal in obstetric practice, certain medical conditions still necessitate delivery before 37 weeks of gestation to prevent further maternal or foetal complications (34, 35). Medically indicated preterm births, account for 28% to 40% of all preterm births, with pre-eclampsia/eclampsia being a leading cause (35). Pre-eclampsia, a hypertensive disorder of pregnancy, contributes to 76,000 maternal deaths and 500,000 foetal and newborn deaths annually (36, 37). Pre-eclampsia and eclampsia (PE/E) affect 3–5% of pregnancies globally, with significant regional variations (38-40) with studies reporting rates of 5.7%, 4.3%, 4.7%, and 3% in India, Pakistan, Mozambique, and Nigeria, respectively PE/E (41).

Despite ongoing research, there is no cure for PE/E, and medical management focuses on prevention, early detection, risk stratification, and timely delivery to optimise maternal and foetal outcomes (18). Approximately 9% of preterm births each year result from labour induction or caesarean section due to severe PE/E (36). However, the success of interventions in reducing maternal and neonatal mortality has been significantly higher in high-income countries than in low- and middle-income countries (LMICs). Widespread prenatal screening, access to hospital care, and timely medical intervention have led to a 90% reduction in both eclampsia incidence and maternal case fatality in high-income countries (42, 43). In contrast, several challenges hinder effective PE/E management in LMICs. Delays in identifying at-risk mothers and initiation of treatment, limited healthcare access, and poor quality of care during labour and postpartum—due to shortages of essential medications, medical equipment, trained personnel, and implementation of standard management protocols—continue to contribute to high maternal and neonatal morbidity and mortality due to PE/E (44-49).

1.3   Adolescent pregnancy and motherhood: A modifiable risk factor for PTB

Adolescent pregnancy and motherhood, a modifiable risk factor for preterm birth, remain a significant public health and human rights concern due to their profound and long-term consequences on young individuals, families, and communities. Each year, 16 million adolescent mothers aged 15–19 years and 2 million under the age of 15 experience the physically and emotionally demanding process of pregnancy and childbirth (50, 51). Over 90% of these births occur in low- and middle-income countries (LMICs) and marginalized communities (52, 53).

Both hospital and population-based studies in high- and low-resource settings consistently show that adolescent mothers especially those below the age of 16 years face a higher risk of preterm birth (PTB) compared to mothers over the age of 19 (54-57). Preterm infants are high-risk neonates who require specialized care, making early recognition and timely healthcare-seeking essential to reducing

morbidity and mortality (22). Adolescent mothers, however, must balance the demanding role of motherhood while still undergoing their own biological, physical, emotional, and psychological development (58, 59). This added responsibility can be particularly challenging, and the extra care required for preterm infants may be difficult for these young mothers to provide. Consequently, the already elevated risks faced by adolescent mothers are often exacerbated by PTB, creating a cycle of increased vulnerability and distress for both mother and baby.

Despite high rates of adolescent pregnancies and preterm births in low-resource settings, there is a lack of in-depth studies on adolescent mothers' understanding and experiences in caring for their preterm infants. While research in countries like Malawi (60, 61), Uganda (62), and Ghana (63, 64) suggests factors like limited knowledge, poverty, and poor healthcare contribute to inadequate care, the specific challenges faced by adolescent mothers in many resource poor settings remain unclear. This highlights the need for more comprehensive research to explore the unique barriers adolescent mothers face and identify context specific interventions to support them in caring for their preterm babies

1.4   Prioritising research for effective preterm birth prevention and management in LMICs

Addressing the burden of PTB and its associated challenges, especially in resource-limited settings, requires both large-scale implementation of cost-effective, integrated adolescent, reproductive, maternal, and newborn health interventions, along with targeted research. Research into the causes, mechanisms, and risks before, during, and between pregnancies is essential for developing innovative prevention strategies. However, scaling up evidence-informed interventions requires robust implementation research to ensure practical and affordable solutions that are suitable to the context (9).

Resource limitations, however, often constitute a challenge to conducting research with the most potential to make impacts on population health outcomes. Although this is a global problem, LMICs face a greater challenge: the disease burdens are highest and resources for provision of basic health care, facilities, services and infrastructure are limited (65, 66). There is also often a paucity of primary research in LMIC settings that aims to address local contextual issues, improves population health and drives health equity, due to limited resources and capacity (65-67). This discrepancy between the disease burden and health research investment has been referred to as the "10/90 gap" by the Commission of Health Research and Development in their report in 1990 titled "Health Research - Essential Link to Equity" (65, 68). The so called 10/90 gap indicates that less than 10% of resources available worldwide for health research are spent on health conditions that affect 90% of the global disease burden (65, 68, 69).

In order to determine which research is most crucial in these resource-limited settings, an exercise of prioritisation is thus increasingly being considered to be essential (67, 70, 71). It is argued that without appropriate research priority setting, research conducted in low-resource settings may follow topics

preferred by funders in high resource settings, resulting in inefficiency in health services to address to the national health needs and policy goals (67, 72). Sridhar (2009) mentions that research priority setting in LMICs is affected by 'multi-bi financing', a practice where donors route non-core funding allocated for specific themes, countries, or regions through multilateral agencies and multi-stakeholder initiatives, thus imposing the priorities of powerful nations or institutions on resource poor countries (72). Examples include the Global Fund to Fight AIDS, Tuberculosis and Malaria (72). Similarly, Chalmers et al (2009) argues that a substantial proportion (85%) of research investment is "wasted" as it fails to address the health problems or does not take into account interventions and outcomes that are relevant to the addressed population (73). Four ways in which funders can reduce this waste resulting from research choices made include (i) investigating ways to improve the utilisation of basic research; (ii) increasing the transparency of the research prioritisation process; (iii) systematically assessing existing evidence before making funding decisions; and (iv) strengthening the source and use of information from research (74). In addition, researchers also highlight ethical considerations of research priority setting with the discussion revolving around the scope, i.e., whether global health priorities should impact national priorities or the other way around; the values and relevant substantive requirements involved in global health research priority-setting; and the methods necessary to guarantee fair and equitable decision-making regarding research priorities across various levels (75). Pratt et al (2018) and other researchers further argue that health research priority-setting must involve a wide range of stakeholders—from national and subnational actors, experts, policymakers, and healthcare providers to beneficiaries, citizens and independent voices—to ensure decisions are fair and inclusive (75-77). This means not only involving research producers, users, and beneficiaries but also actively engaging disadvantaged and vulnerable groups (78). Using various participation modes, such as lay control, partnership, and consultation, with early engagement is essential for achieving meaningful inclusion and ensuring that priorities of all groups are reflected (78, 79). Moreover, robust community engagement can help identify local evidence of need, ensuring that research priorities truly address the health issues affecting the most vulnerable populations (75, 80). Tomlinson et al (2011) also argues that a well-managed research priority setting exercise not only guides the appropriate allocation of public and private resources but can also unite global and/or national stakeholders (funders, donors, researchers, governments, civil society etc.) and strengthen their role as stewards of research agenda (71, 81).

Although there is growing acceptance of the need for priority setting in health research, there is no "one-fits-all" approach and research priority setting is being carried out in various forms at different levels (individual, community, national, or global) with the effectiveness of different approaches becoming difficult to evaluate. However, there is general consensus that priority setting is a "value-driven and political activity" that has to be conducted in a "fair and legitimate" way using flexible method(s)

tailored to benefit a community within the limitations posed by given policy, context, time, and financial resources (66, 75, 82).

1.5   Rationale and aim, and objectives of the research

Achieving the SDG targets for maternal and newborn mortality, particularly in LMICs, requires significant investments in research in addressing key contributors such as PTB and PE/E—the latter being both a major cause of medically indicated PTB and a significant contributor to maternal mortality. Despite increased attention to maternal and newborn health research, resources and funding in research in LMICs remain limited. A recent analysis of research funding for newborn health and stillbirths indicates that, although funding for LMIC organisations increased from 2011 to 2020, it still represents only 7% of global research funding annually (83). Moreover, implementation research—crucial for scaling up evidence-based interventions—has consistently received insufficient funding, with proper resource allocation being essential to hasten local progress in newborn survival and meet the SDGs by 2030 (83). Despite the increasing focus on maternal and newborn health research, only a few studies have prioritised research on specific contributors to adverse maternal and perinatal outcomes in low- and middle-income countries (LMICs) in the SDG era, such as prematurity (84-88). There is, therefore, an urgent need to guide governments, and other key stakeholders in developing a contextually relevant and impactful research agenda to address the burden of PTB and PE/E in the SDG era.

The overall aim of this study is, therefore, to identify and prioritise research areas for PTB and PE/E in LMICs using a systematic approach, while integrating community-level insights to ensure contextually relevant and impactful recommendations. By combining research prioritisation with an exploration of the lived experiences of high-risk groups, particularly adolescents in low-resource settings, this study seeks to bridge the gap between identified research needs and real-world challenges. Ultimately, the goal is to inform policy, practice, and future research agendas that effectively address PTB and maternal health disparities in LMICs.

The specific objectives are:

- To adapt and apply a systematic approach to identify research priorities for both prematurity (for LMICs and Bangladesh) and PE/E (for LMICs), while deriving lessons from the prioritisation process on delineating national versus international priorities, focusing on broad versus specific topics, and addressing other methodological variations.

- Undertake community level exploration of gaps and opportunities for improved care for preterm newborns among high-risk groups (adolescents as exemplars) in a low resource community in Bangladesh, to inform policy and practice.

- Use the data from community level exploration in Bangladesh to explore similarities and differences in the lived experience of those with premature babies and the research priorities

identified using a systematic approach and reflect on how communities should be meaningfully engaged when setting research priorities.

1.6   Summary of the research design and methods

To achieve these objectives, a mix of quantitative and qualitative research methods was employed. Research prioritisation was conducted using the Child Health and Nutrition Research Initiative (CHNRI) method, a systematic and transparent framework that engages experts and stakeholders in ranking research priorities based on predefined criteria. While a variety of structured and unstructured priority-setting methods have been used in health research over the past three decades, structured approaches have gained prominence to ensure fairness and legitimacy in the process. Among these, the CHNRI method has recently gained popularity, with over 100 applications. In this study, the CHNRI method was applied to establish research priorities for preterm birth (PTB) and pre-eclampsia/eclampsia (PE/E), involving collaborations with partners in four countries: Sheffield (UK), Cape Town and Pretoria (South Africa), Dhaka (Bangladesh), and Ilishan-Benin-Kano (Nigeria). Although the CHNRI method produces quantitative outcomes, it relies on simple qualitative inputs (Yes/No responses), eliminating the need for complex statistical computations. Further methodological details are provided in the relevant sections.

In addition to the CHNRI exercise, a qualitative exploratory study was conducted in a low-resource community in Bangladesh to examine the lived experiences of mothers and families with premature babies, with a particular focus on high-risk groups such as adolescent mothers. Data collection methods included in-depth interviews, focus group discussions, and key informant interviews with mothers, families, community members, and healthcare providers. The findings offer valuable insights into gaps and opportunities for improving preterm newborn care and will be compared with the CHNRI research priorities to explore how community perspectives can be meaningfully integrated into research agenda-setting.

This study was a part of a National Institute for Health and Care Research (NIHR) funded research project on prevention and management of preterm birth (PRIME) and carried out across a partnership that included four countries – Sheffield (UK), Cape Town and Pretoria (South Africa), Dhaka (Bangladesh), and Ilishan-Benin-Kano (Nigeria).

1.7   Format of the thesis

This thesis constitutes an alternative, publication format, thesis. It includes three primary studies conducted to address the research objectives. In each of the three studies I am the primary contributor. The methodologies used to carry out each of the studies have been elaborated within each chapter under their respective study headings, eliminating the need for a separate chapter.

The overall structure of the thesis consists of six chapters, beginning with an introduction. This is followed by a literature review on research priority setting, and two chapters detailing two research priority-setting exercises—one of which includes a published manuscript, while the other is prepared in the format of a publication (study 1 and 2). This is followed by a chapter on an in-depth exploratory study conducted in rural Bangladesh (study 3), which also includes a published manuscript. The thesis concludes with an overall discussion.

In Chapter 1, I present the background, aims, and rationale of the research.

In Chapter 2, I review various research priority-setting methods, highlighting their advantages, disadvantages, and lessons learned. The chapter focuses on the CHNRI approach, detailing its application, strengths, and limitations, as well as exploring its use in setting priorities for preterm birth research.

In Chapter 3, I describe the process and results of the research prioritization activity for the prevention and management of preterm birth (PTB) (study 1). I designed the study in collaboration with the corresponding and senior authors, conducted all statistical analyses, wrote the first draft of the paper, and following feedback from all co-authors, wrote the final version.

In Chapter 4, I describe the process and results of the research prioritization activity for the prevention and treatment of preeclampsia/eclampsia (PE/E) (study 2). I designed the study, led the data collection, conducted the statistical analysis, and wrote the first draft of the paper.

In Chapter 5, I present qualitative research undertaken to explore gaps and opportunities for improved care for preterm newborns at the community level among high-risk groups (adolescents) in rural Bangladesh (study 3). I designed the study in collaboration with the second and senior authors, led the data collection and analysis, wrote the first draft of the paper, and following feedback from all co-authors, wrote the final version.

In Chapter 6, the discussion and conclusion chapter, I summarise the key findings and explore the implications of national versus international priorities and methodological challenges. I also reflect on how community engagement can strengthen the prioritisation process. The chapter concludes by summarising the key insights and offering recommendations for future research and practice.

The papers included in the thesis are presented in the format in which they were submitted to the journals, apart from minor formatting changes to provide consistency throughout the thesis.

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2 Chapter 2: Health research priority setting: Methods, lessons learnt, CHNRI approach, and applications to PTB

This chapter provides a narrative review of various structured and unstructured research priority-setting methods used in health research, highlighting their advantages, disadvantages, and the overall lessons learned from their implementation. It then offers a detailed description of the CHNRI approach, including its application, strengths, and limitations, based on a summary of 102 research priority-setting exercises conducted using this method. Finally, the chapter explores the use of the CHNRI approach in setting research priorities for PTB, emphasising different priorities identified.

2.1 Methods used to set health research priorities.

The interest in and visibility of priority setting for health research at the national and global levels have increased over the last 3 decades (1). The 1990 report by the Commission on Health Research for Development has been recognised to be the first true attempt in creating this momentum (1, 2). It promoted the use of a systematic approach for health research prioritisation within each country's Essential National Health Research (ENHR) strategy (1990) (3). The Council on Health Research and Development (COHRED) was established in 1993 as a result of this report to assist LMIC countries in developing their own national strategies (1, 4). To complement the Commission's work and promote global health research priority setting, the Ad Hoc Committee on Health Research also published a landmark report "Investing in health research relating to future Intervention Options (1996)" that recommended a five-step process for priority setting in health research (1, 2). The Global Forum for Health Research was established in 1998 as a result of this report with a focus on correcting the 10/90 gap in research (1, 2). Other notable initiatives that followed were the development of the Combined Approach Matrix (CAM) tool by the Global Forum for Health Research (2004), The Grand Challenges in Global Health (2003) and the Child Health and Nutrition Research Initiative (CHNRI) (2007) (2). Figure 2-1 presents the key initiatives in research priority setting since 1990 summarised by Rudan el (2016).
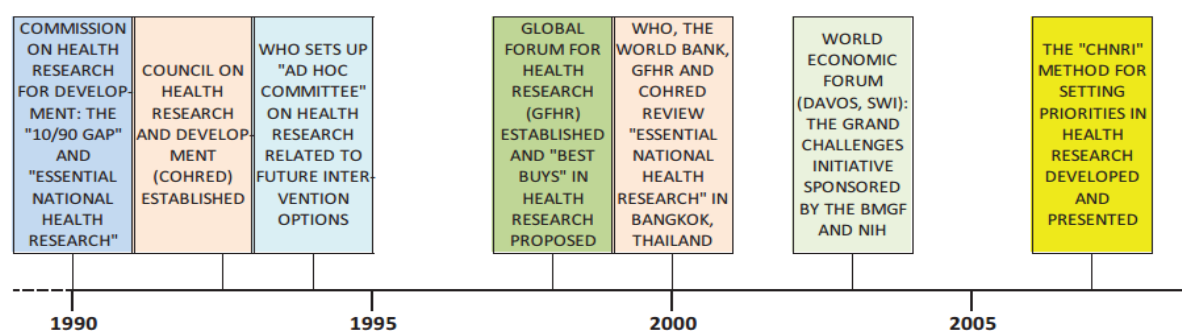
Figure 2-1 Key initiatives for health research priority setting at different level (5)

The following sections provides an overview of the different methods and approaches used in prioritising health research. These include very informal non-replicable methods (e.g., expert interview, national or regional conferences, stepwise approach); less structured methods (e.g., Delphi and Nominal Group technique); and more comprehensive structured approaches (e.g., 3-Dimensional Combined Approach Matrix (3D CAM), James Lind Alliance method, ENHR method, Child Health and Nutrition Research Initiative (CHNRI), and COHRED) (6-10). The advantages and disadvantages of the different methods have been summarised in Table 2-1.

2.1.1 Essential National Health Research (ENHR) strategy

The Commission on Health Research for Development developed the ENHR strategy to guide national health research priority setting and emphasised on equity and social justice (3, 4, 6, 11). The strategy builds on few characteristics and includes inclusiveness and stakeholders' involvement (researchers, decision makers, health service providers and community representatives); is multidisciplinary and involves a cross-sectoral approach; partnership development; participatory and transparent processes; and systematic analyses of health needs (3, 4, 6, 11). The process starts with stakeholders conducting a situation analysis and suggesting priority areas. Research ideas are then nominated by different stakeholders and collated. A list of criteria is prepared by brainstorming from a large list of possible criteria, removing duplicates, and including a clear definition. Different methods may then be used to determine research priorities such as consensus development, brainstorming, round table discussions or nominal group technique (6). At the national level ENHR has been applied widely for example in Philippines, Brazil, Nigeria, Cameroon, Iran and South Africa (6, 8, 12, 13). A few disadvantages of the method are that it may be biased by the decisions of the available experts, most cases need wider representation of stakeholders, and the process of criteria selection is also not well defined. Although the method emphasises in improving equity, this has not been applied in most exercises raising questions about the inherent value of the methodology (6, 10).

2.1.2 Council on Health Research and Development (COHRED)

COHRED uses an integrative approach for national level priority setting exercises (4, 6). Priority setting using this approach is a cyclic management process with six key steps- (i) Assessing the situation (ii) Setting the scene (iii) Choosing the best method (iv) Planning priority setting (v) Setting priorities (vi) Making priorities work (4). Priority issues are identified using the method best suited to local context (ENHR, CAM, Burden of Disease, Visioning, Delphi etc.) (6). COHRED also suggests the use of direct and indirect valuation techniques to rank the research priorities. COHRED has been applied to set priorities in Brazil, Cameroon, Peru, Philippines and Tanzania (8). Overall, this method is very unspecific, and priorities set using this approach is also based on the consensus of a panel of experts and may be biased by the research interest of the experts involved.

2.1.3 Combined Approach Matrix/ 3-Dimensional Combined Approach Matrix (CAM/3D CAM)

CAM/ 3D CAM is a tool developed by the Global Forum for Health Research to help stakeholders organize information for priority-setting processes and recognize gaps in health research (14-16). A matrix for priority setting is developed using the five steps (also known as public health dimensions) and the four groups of actors and factors (also known as institutional dimensions) determining the health status of a population. The five steps include measuring the burden of disease; analysing risk factors; assessing the status of knowledge; evaluating cost and effectiveness; and resource flows. The institutional actors include individual, household and community level actors; national health institutions such as the ministry of health; and other macroeconomic non-health sector actors (14, 16). The 3D CAM model adds another equity dimension (e.g., income and gender) to ensure that the process benefits those with greatest need (15). In the first step, relevant institutions, and stakeholders with expertise in the area populate the matrix via workshops and brainstorming sessions. The matrix reveals the amount of information available in the area making a case for future research needs. Each participant then determines the priority research topics based on the evidence available in the CAM and consolidating the ideas to establish the top priorities (6, 15). Between 2005 and 2007 Argentina used CAM as main method for classifying and organising the necessary knowledge and data (4) for their priority setting exercise. Other countries that have applied CAM include Pakistan and Malaysia (8). CAM/3D CAM is a tool for information gathering and does not present an algorithm for generating or ranking research priorities. The research questions are also not complied in a systematic way and consensus reached on priorities may be driven by the interests and biases of experts (2, 6, 10)

2.1.4 James Lind Alliance (JLA) Method

The JLA method, established in 2004, brings together patients, carers and service providers (e.g., clinicians) in Priority Setting Partnerships (PSPs) to identify and prioritise areas of treatment uncertainties that they agree are most important (17, 18). The JLA techniques have five key stages that results in ten research priorities for a particular condition or health care issue for consideration by funders. In the first step an area is chosen, the scope defined, partnerships identified, and a steering group formed. Recommendations by PSPs creates a list of uncertainties which is then verified through systematic reviews of databases (e.g., Cochrane, DARE, NICE, SIGN guidance) to identify research gaps. In the next step, an online survey and voting is conducted to reduce the list of uncertainties to a manageable number (<30). This is then reduced to ten in a final priority setting workshop through consensus building. Over 60 partnerships have been developed since 2004 to explore a wide range of treatment uncertainties including issues diabetes (19, 20), blood donation (21), mental health (22), dementia (23), psoriasis (24), stroke nursing (24), spinal cord injury (25) etc.

2.1.5 Child Health and Nutrition Research Initiative (CHNRI)

The CHNRI method, including its advantages and disadvantages, has been described in detail in section 1.3. The advantages and disadvantages are summarised below in Table 2-1.

2.1.6 Delphi

The Delphi concept was developed in the 1950s and is viewed as one of spinoffs of defence research (26). The Delphi technique obtains consensus of a panel of experts on a complex problem using questionnaires. In the first round, participants answer a questionnaire, the results are then summarised and circulated to all participants. Participants examine the group response and are given the opportunity to reassess their initial judgements, allowing sharing of information and reasoning among participants. This iterative process is usually carried out for two or more rounds to reach a consensus. A minimal representative pool of eligible participants i.e., experts with relevant backgrounds and expertise is needed for this exercise. The Delphi technique is quite popular and has been used to develop priorities in diverse range of issues including mental health (27-30), health services (31-34), palliative care, care for elderly population (35-37), non-communicable disease (NCD) prevention and climate change (38) research among many others. The Delphi technique is however time consuming, requires long time commitments from individuals and may result in high attrition rates and hence biased results (9).

2.1.7 The Nominal Group Technique

In the nominal group technique, research ideas are generated and consensus on research priorities reached in a single meeting or workshop (39-42). In the first step a question is posed. Once responses are obtained, they are collated and disseminated again to the wider group. The group members prioritise the research ideas put forward by the wider group making sure to discuss and resolve major areas of disagreement. Although this technique allows individual rankings and equal participation of all members in a group, excessive structuring of process may reduce refinement and discussions of ideas (9).

2.1.8 Informal non-replicable methods

Workshops, roundtables, focus groups, surveys, key informant interviews (KII) have usually been used in combination to bring key stakeholders together for research prioritisation (9). The use of these methods depends on the context, lacks clear criteria, priorities are usually not ranked, and the process is non-replicable (9). For example, in Nigeria, the operational research agenda for Malaria was set following planning meetings, online and paper-based surveys, KIIs, desk review workshop, qualitative data analysis, and report writing workshops (43). Ranson and colleagues used three steps to determine research priorities on health systems financing: key-informant interviews with policy makers, researchers, civil society in twenty-four LMICs; a review of research to date; and inputs from 12 key informants (mainly researchers) at a consultative workshop (44).

Table 2-1 Advantages and disadvantages of different methods of research priority setting

Advantages	Disadvantages
ENHR (3, 4, 6, 10, 11)	
• Inclusiveness and participation of different experts and stakeholders • Multidisciplinary and cross–sectoral approach • Partnership development • Transparent • Systematic analyses of health needs and detailed list of priorities are made • Can choose methods best suited to local needs, available data and resources More than one method can be used to improve usefulness of results	• Lack of transparency in individual country level processes • Criteria are not well defined and no guidelines to develop or apply those. • Needs stronger representation from the private sector, parliamentarians, donors, international agencies • Methods for identifying participants not provided • In most examples data on inequity is not included raising questions about the value of the methodology • The situation analysis is usually biased towards the supply side of the health system • Research questions are not compiled in a systematic way • No ranking of priorities
COHRED (4, 6)	
• Overview approach providing steps • Discusses wide range of options • Flexible	• Too general and unspecific • Criteria selection process not transparent
James Lind Alliance (6)	
• Takes into account underrepresented groups • Applicable to small scale prioritisation (e.g., hospital) • Mixture of methods	• Time consuming • Criteria selection process not mentioned • Not suitable for prioritising at the global level • Not suitable for prioritising diseases • Very clinically orientated • Needs appropriate and proportionally equal mix of participants
Delphi (6, 9, 26)	
• Iterative and opportunities for providing feedback • Flexible • Can be anonymous • Not face-to-face and hence is free from dominance	• No specific method for identifying participants • Investigators may bias results by imposing their perceptions and over specifying the structure • No criteria • Multiple iterations result in low response rate • Demanding and time-consuming due to multiple iteration

Advantages	Disadvantages
	• Potential for artificial consensus if disagreements are not explored

Nominal Group Technique (9)	
• Equal participation of members • Reduces domination by a single person or group of people. • Prioritised solutions are agreed democratically •	Structured process may reduce discussion and refinement of ideas.

CAM/3D CAM (6, 10, 14-16)	
• Creates a matrix for evidence gathering and data presentation • Identifies gaps in knowledge • Facilitates comparisons between sectors • Includes broad actors and factors • 3D–CAM includes equity	• Highly time consuming involving multistage discussions • Requires intensive inputs from experts and may be biased by their opinions • Not systematic and hence cannot be repeated • No methods for identifying participants • Suitable for diseases and related risks • May not be applicable for policy research and crosscutting issues • Does not provide an algorithm for generating priorities

CHNRI (6, 45)	
• Systematic and transparent • Clear criteria • Independent scoring by experts • Involves diverse group of stakeholders • Less costly	• May represent collective opinion of limited number of experts • Stakeholder engagement is challenging • Scoring affected by currently on–going research • Potential for introducing bias during collation of research ideas

2.2 Lessons learnt from research priority setting in health

Since its start in the 90's, several reviews have been conducted to identify and assess research prioritisation processes carried out over the last three decades. The major issues emerging from the reviews and challenges that still need to be addressed include: (i) Inconsistent use of existing methods and approaches affecting repeatability and transparency; (ii) Limited participation of diverse group of key stakeholders leading to opinion bias; (iii) Lack of an implementation strategy to translate the result into implementation of research projects; (iv) Lack of follow-up or evaluation plan to assess the impact on policy and practice; (v) Lack of use of appropriate criteria to make the process more objective and transparent; (vi) Lack of evidence base for priority setting (1, 6-9, 46).

In 2010, Viergever et al. reviewed 230 research prioritisation exercises organized or coordinated by WHO since 2005 and concluded that a wide variety of approaches were used for health research prioritisation and many researchers choose to develop their own, unique methods suitable to the context and level (47). Terry and colleagues' also reviewed 116 research priority documents completed by WHO technical units from 2002 to 2017 and found a mix of informal and systematic methods of research priority setting (26% Report, 22% WHO Guideline, 26% Research Prioritisation publication and 11% Meeting Notes) (46). McGregor et al (2014) conducted a systematic review of health research prioritisation activities over the period from 1966 to 2014 in LMICs. Authors found 91 initiatives and most used process for determining priorities was a conference or workshop (24%) and the CHNRI method (18%) followed by Delphi, Stepwise technique and ENHR. Similarly, Yoshida's methodical landscape review of the PubMed database (2001–2014) identified 165 relevant studies on research prioritisation. The CHNRI method (26%) was mostly used, followed by the Delphi (24%), JLA (8%), CAM (2%), and ENHR (<1%) (6). These exercises were conducted at a variety of levels (global, regional, national and individual hospital), explored a wide range of health, health systems and disease issues (6). Yoshida, however, concluded that the number of priority setting exercises in health research has increased since 2010 and the more structured transparent and replicable methods (such as the CHNRI, JLA and CAM) may replace the non–replicable Delphi, NGT or consultation processes (6).

Given the heterogeneity in the use of methods for research prioritisation exercises Viergever, Olifson et al (2010) proposed a generic framework that included 9 common themes to guide the prioritisation process. Authors argued that these steps could be used either with a defined comprehensive approach or without the use of an existing approach (10). The themes were divided into three phases and included defining context, use of comprehensive approach, ensure inclusiveness of participants, information gathering, planning for implementation during the preparatory phase; defining the criteria and choosing methods for deciding on priorities during the prioritisation phase; and planning the evaluation and writing a clear and transparent report of the methodology during the post-prioritisation phase (10). Mador et al used this checklist as the conceptual framework to evaluate the research priority setting process developed for the Locally Driven Collaborative Projects in Ontario, Canada in 2016 (48). The authors found that despite limited guidance on indicators or measurement tools or appropriate evaluation methods, it could be used for the assessment of the design and delivery of research priority setting processes (48).

Engaging a diverse group of stakeholders has been found to improve the legitimacy, credibility, inclusiveness, contextual relevance, ownership of the prioritised research leading to greater investment opportunities (10, 49, 50). The importance of involving a diverse range of stakeholders representing different disciplines, expertise, gender and has been mentioned in almost all of the priority setting methods mentioned in section 2 including CHNRI, CAM, ENHR and JLA (49). However, most exercises have reported stakeholder involvement to be challenging. In 2011, Tomlinson et al. reviewed

national research priority setting processes in Malaysia, Cameroon, South Africa, Peru, Brazil, and Argentina that employed one of the three methods: CAM, COHRED and CHNRI. One of the criteria used for the evaluation was stakeholder involvement. Their findings show that across the countries there was a relative lack of genuine stakeholder engagement. McGregor and colleagues review of 91 priority setting exercises in LMICs found researchers and government to be the most frequently represented stakeholders and engaging with key stakeholders such as affected populations (patients and civil society) and donors (only 16% in reviewed initiatives) to be minimal (7). Kapiriri explored the barriers to meaningful stakeholder engagement and concluded that this could be due to limited technical understanding of the priority setting processes, lack of resources to facilitate public involvement and limited skills to meaningfully engage the public (49). Similarly, Rikkers et al explored methods for engaging with the community in child health research priority setting and concluded that neither methods gained input that was representative of the entire community (51).

To promote social justice and equity Prat et al (2016-2021) proposed that global health research should meaningfully engage citizens and communities including those that are marginalized and lack power throughout the research agenda development process. They proposed "deep inclusion" or "inclusion" as a crucial procedural element that considers not only who is invited but also how they are involved and when non-elite stakeholders participate. The authors propose models and toolkits to guide the process and highlight that despite implementation challenges, these should guide more inclusive national health research priority-setting processes (52-55).

A common limitation identified in most of the reviews were that priority setting exercises were considered to be one-off events without any systematic revision, follow up or implementation plan involving the key stakeholders (7-9). According to Kapiriri and colleagues there are four major conditions of fair priority setting - relevance, publicity, revisions and enforcement (50) and revision and enforcement were absent in majority of the exercises. In addition, the authors noted that none of the models conducted a systematic assessment of the outcomes of the priority setting processes or assessed the impact of the generated priorities on policy or practice (7, 9). Bryant et al (2014) mentions several ways that could be used to evaluate the impact or outcome of a priority setting exercise: identifying the acceptability and usefulness of individuals involved; assessing the number and type of research initiated or funded as a result of the activity; and identifying the key process and outcomes indicators associated with the research initiatives (capacity development, publications, policy, programme or health service delivery design revised) (9). Improving the documentation of priority setting process can also help in assessment of outcomes (7, 8). In 2018, Terry and colleagues et al recorded the findings of 116 WHO research priority documents in a database and mapped to a five-category research cycle framework that was used to generate analysis and compare research priorities, and the different methods applied. The authors recommended a standard reporting approach, linked to established good practice, as an area for

future development (46). COHRED has introduced a web-based platform that includes a section for sharing national health research priorities in LMICs (https://healthresearchweb.org).

Another significant concern is lack of use of proper criteria for prioritisation. Rudan et al (2007) argues that use of improper or poorly defined criteria in health research investment decisions results in under-achievement of disease burden reduction and further aggravates health inequity (2). In a qualitative interview study conducted by Khan et al. (2019), participants suggested that criteria for selecting research should prioritise studies likely to have the most significant public health impact in affected countries, rather than focusing solely on filling scientific knowledge gaps (56). Furthermore, some participants emphasized the necessity to make politically challenging decisions that may result in certain research areas being given lower priority for funding (56). Data gaps that are inherent in LMICs and limited capacity to identify and implement health research are also concerns that affect fair priority setting process (1, 10, 57, 58). In addition, identified priorities often describe broad disease categories and not specific research questions (8). Without the right level of detail or prioritisation, research options may fail to provide guidance and may result in selection of research questions that is easier to implement or complements current activities (7).

Another important issue in global health research priority setting is the consideration of ethics and concerns related to health justice. Pratt et al (2018) highlighted several ethical concerns including the circumstances and ways in which national research priorities influence, or be influenced by, global priorities; the values that are at stake in global health research priority setting (such as equity); and how a fair and just process can be carried out involving the participation of all relevant stakeholders (52, 53, 59, 60).

2.3   CHNRI method for research priority setting

2.3.1 Background

The Child Health and Nutrition Research Initiative (CNHRI) was founded in 1999 under the Global Forum for Heath Research with a vision to improve health and nutrition of children in LMIC through research that informs health policy and practice (61). CHNRI became a Swiss foundation in 2006 and worked for 15 years playing an active role in Global Forum annual conferences, creating a knowledge network, funding research through global competitive processes and publishing research papers and policy briefs before being dissolved in 2015. In addition to expanding global knowledge on childhood disease burden and cost-effectiveness of interventions, one of its major objectives was to promote research agenda setting in LMICs by promoting research priority setting, developing research capacity and encouraging donors and countries to increase resources for research in LMICs (2, 61).

In 2005, the World Bank funded CHNRI to develop a systematic method to help priority setting in global child health and nutrition research investments. This effort was motivated by a few factors. First, in their World Health Report for 2005, WHO highlighted the unacceptable and persisting high levels of

maternal and child deaths. According to estimates by the Child Health Epidemiology Reference Group (CHERG) about 30,000 children aged less than five years were still dying each day (10.6 million a year) (62). The six main causes of deaths (73%) in children aged less than 5 years between 2000-2003 were pneumonia (19%), diarrhoea (18%), malaria (8%), neonatal pneumonia or sepsis (10%), preterm delivery (10%), and birth asphyxia (8%) (62). Second, despite the availability of low-cost, effective and feasible interventions and sufficient funds that would avert a substantially high proportions (63%) of child deaths each year if made available universally, there was lack of knowledge and interest in how to deliver and sustain these interventions at scale especially in resource poor settings (63, 64). It was understood that lack of systematic prioritisation of child research funding resulted in low interest in implementation research needed to address the persisting high levels of mortality in children (65). The development of effective interventions or technology were seen as endpoints of research and methodologically challenging and long-term implementation research needed to scale up the interventions or technology to the poor were not ranked highly or considered attractive by the scientific community (2, 66). As such, research funding for global child health favoured research on discovering new interventions such as vaccines for AIDS, TB and Malaria over implementation and delivery research needed to realise the full public health impact past novel interventions (2, 66). For example, although pneumonia and diarrhoea accounted for about 40% of global child deaths, there was a decline in interest in research as well as funding on how to implement and scale up antibiotics and oral rehydration therapy in resource poor countries (2).

Considering the above imbalances in investments and challenges in determining whether prioritised research fits in the process of knowledge translation or not, CHNRI conducted meetings with several global child health experts. The aim was to review existing priority setting processes, identify universally observed challenges as well as solutions that could help in developing a systematic method for research priority setting (67, 68). A range of challenges were identified which included problems in clarifying the process (person involved; defining criteria; risk preference; defining research, its boundaries and depth; systematic listing and scoring process; overcoming expert bias, ensuring replicability; systematic ranking process; stakeholder engagement and evaluation) (67, 69). Based on the discussion of these challenges, several key concepts were proposed and defined which formed the basis for the CHNRI method of research prioritisation. The CHNRI conceptual framework and method is described in the following sections.

2.3.2 The CHNRI process

The CHNRI methodology was developed between 2005-2007 through several consultative meetings with a panel of experts led by Professor Igor Rudan (69, 70). The standard CHNRI process consists of five major steps (Figure 2-2) which starts with the formation of a small team of process managers who defines the context and criteria for the prioritisation activity. This team then reaches out to a large number of experts who contribute a broad spectrum of research questions and later score the

consolidated research questions against the defined criteria (70-72). This "crowd-sourcing" process measures "collective optimism" and results in consensus development and agreement on the priorities (73, 74). In the next step, the inputs of the wider society who are not necessarily technical experts are obtained. These external stakeholders are invited to set thresholds and weights for each of the priority setting criteria (50, 75). The final step of the CHNRI process is developing a ranked list of research questions by their weighted or unweighted scores against several criteria (70). This section briefly highlights the key steps in the CHNRI process of research prioritisation with implementation examples provided from a scoping review of 102 published priority setting processes where the CHNRI method was used between 2007 to 2024 (Annex 1).

Step 1: Defining context and critera	• Identifying the process manager team • Defining the context • Defining the priority setting criteria and sub-critera
Step 2: Systematic listing and scoring of research ideas	• Identification of technical experts • Systematic listing of research ideas • Scoring of consolidated research ideas
Step 3: Addressing values of stakeholders	• Identification of stakeholders • Obtaining input from stakeholders
Step 4: Data analysis and evaluation	• Calculation research priority scores • Calculation of average expert agreement • Feedback, revision and evaluation

Figure 2-2 The CHNRI steps for research priority setting (66, 70)

2.3.2.1 Step 1: Defining the context and criteria

Process management team:

The process of prioritisation is managed by a small group of experts with considerable interest in the topic and able to represent the interest of the investors. This team of process managers will be responsible for carrying the prioritisation process forward.

Defining the context:

The first task of the process managers is to define the context for prioritising research ideas from a large pool. According to CHNRI's framework, "health research" is defined as "a process that begins with a research question and undertaken to generate new knowledge that will eventually be translated and/or

implemented to reduce the existing disease burden (or other health–related problem) in the population". CHNRI proposes 5 standard elements or components of the context which can guide the priority setting exercise based on this definition: population of interest, the disease burden of interest, geographic limits, time scale and the preferred style of investing with respect to risk (Table **2-2**). Since there will be variations in defining the different elements of context depending on the type of investors (government, private sector, or philanthropic foundations etc.) Rudan et al (2008) argues that these should defined before the start of the process and transparently communicated to scorers.

Table 2-2 Components of the context in which research priorities will be determined (69, 70)

Elements	Definition
Population of interest	The population whose health problems will be addressed
Disease, disability, and death burden	The burden of disease, disability, and death addressed by health research question
Time scale	The time (in years) by which the result of the proposed research is expected
Geographic limits	Geographical boundaries - global, regional, national, sub–national
Preferred style of investing	The risk preferences for investment; Will the funding support expensive high–risk research ideas (e.g., vaccine development), or diverse ideas with different risk and feasibility (delivery and implementation research)?

The use of CHNRI method has extended substantially from its initial focus to address the burden of child mortality. It has gradually been used to address questions on childhood morbidity and development (76-78), infectious diseases (79-82), maternal and perinatal health (83-85) and reproductive and sexual health (85, 86). In recent years, it is being applied to address the burden of mental health (87-89), disability (90), education (91, 92), quality of care (93) in the context of humanitarian emergencies as well (94-96), nutrition (77, 97, 98). Although majority were global or LMIC focused in scope, a lot of exercises were conducted nationally or regional e.g., in Brazil (88), Chile (99), Africa (100), India (101). The choice of time scale for majority of exercises was five to 10 years and influenced by the achievement of either the Millennium Development Goals (MDGs) or Sustainable Development Goals (SDGs). However, there were studies where the choice of time scale was considered urgent or two-five years, for example to respond to the COVID-19 pandemic (102, 103).

Identification of criteria and sub-criteria:

Each research question in the CHNRI process will be scored to determine which research questions are more appropriate in addressing the disease burden or health issue. Table 2-3 lists many possible criteria proposed by Rudan et al. Although there are no limitations to the number of criteria that can be used, inclusion of more criteria will produce overlaps, and the usefulness as independent criteria will decrease. Thus, CHNRI recommends five criteria to be used in almost all contexts: Answerability, deliverability, effectiveness, maximum potential reduction in disease burden and equity. For each criterion, a set of three simple and informative questions answerable as "yes" or "no" should be determined. These questions assess the likelihood that proposed research options satisfy the selected criteria. Table 2-4 provides examples of questions or sub-criteria that Rudan et al has used for the two of the five recommended criteria -answerability and effectiveness (70).

Table 2-3 Examples of possible criteria for setting health research priorities. (69, 70)

Criteria	Explanation
Answerability	The research question can be ethically answered
Attractiveness	The research question will result in publications in high-impact journals
Novelty	The research question will generate novel and non-existing knowledge
Potential for translation	The research question will generate knowledge that can be translated into health intervention
Effectiveness	The research question will generate/improve truly effective health interventions
Affordability	The translation or implementation of intervention generated through the research question will be affordable
Deliverability	The intervention resulting from the research question will be deliverable
Sustainability	The intervention resulting from the research will be sustainable
Public opinion	The research questions will be justifiable and acceptable to general public
Ethical aspects	The research will be ethical
Maximum impact on burden	The research question has greater potential to reduce disease burden

Equity	The intervention resulting from the research will be accessible to vulnerable groups thus decreasing equity
Community involvement	The research options will have more potential to involve community
Cost and feasibility	The intervention resulting from the research will be feasible and cost-effective
Generating patents/ lucrative products	Some research options will generate patents or potentially lucrative regardless of their impact on disease burden

The emphasis on the flexibility of the context and criteria is very evident when we review the 102 examples. Similar results were found by Yoshida in her analysis (6). Majority of the exercises deviated from using the original five criteria. These included either changing the number of criteria used or used different criteria altogether. The number of criteria used ranged from 3-13, with 53% using five criteria whilst 24% reduced to four, three or two and 25% expanded the number to more than five. The most frequently added criteria were feasibility, acceptability, low cost, sustainability, and relevance. Variations were also seen in the use of sub-criteria. For example, in order to avoid scorer fatigue and ensure maximum participation Arora et al (2017) decided to forego sub–criteria and score research questions against the criteria only ('Yes'/No/Not sufficiently informed) (97) whilst Tomlinson et al (2017) decided to reduce the number of sub-criteria for each criteria (76). Bermudez et al (2018) and Abu-Rmeileh (2018) also omitted the use of sub-criteria and used a full Likert scale for each criteria to reflect strong agreement (5 points) to strong disagreement (1 point); and insufficiently informed (considered non-applicable/no response) to allow for greater granularity when analysing scores (94, 104). Bermudez et al (2018), however, recommends that while Likert scales have been used in other crowd-sourcing methods there is a need to assess its benefits and drawbacks within the CHNRI framework (94).

Table 2-4 Example of possible sub-criteria for setting health research prioritisation (69, 70)

Criteria	Sub-criteria
Answerability	Is the research question well framed and endpoints well defined?
	Based on: (i) existing research capacity and (ii) the knowledge gap can a study be designed to answer the research question?
	Can ethical approval be obtained for the study needed to answer the research question?

Effectiveness	Based on the existing evidence and knowledge, would the intervention developed through the research be efficacious?
	Based on the existing evidence and knowledge, would the intervention developed through proposed research be effective?
	If the developed intervention is effective and efficacious, is the evidence for this decision of high quality?

2.3.2.2 Step 2: Systematic listing of research options/questions

Identification of technical experts

In this phase of the prioritisation process a group of technical experts preferably researchers are invited. These experts work closely with the management team (i) to provide a broad spectrum of research ideas; and (ii) use their judgment to decide whether the research ideas meet the defined criteria or not (71).

Consensus in research priorities in the CHNRI method is obtained through crowd-sourcing and assessing the collective opinion (in this case, optimism) and has been found to result in accurate predictions compared to any individual's expert judgment or biases (73, 74). However, Rudan et al (2016) mentions that, for collective opinion to be useful there must be diversity of opinion, independence of participants, participants should be able to draw on any local knowledge and a method available for analysing the collective opinion (69).

The choice of researchers as technical experts and not any other group is because researchers not only have better understanding and knowledge of the potential and novel research ideas but also are aware of the practicalities of the research field. Thus, restricting participation to researchers is expected to improve the distinction between the research ideas by using the collective knowledge and opinion of a small group of experts (71). However, based on the context of the research prioritisation exercise the choice of technical experts can vary and several exercises have also included health service providers, programme managers, policy makers, funders, representatives of international organisations etc. along with researchers. (78, 86, 97, 104-107). For example, Wazny et al (2014) conducted a CHNRI exercise to identify research gaps and resource priorities for a delivery strategy (Integrated Community Case Management -iCCM) and included experts who represented academics, international organizations, non-governmental organisations and Ministries of Health within countries that were involved and knowledgeable in implementing iCCM (78).

The number of technical experts approached in earlier exercises has varied from 6 to over thousands (Annex 1). An analysis conducted by Yoshida et al, however, found that the collective opinion of an expert group in ranking research question using categorical variables (Yes/No/Not Sure/Do not know),

stabilises quickly (73). According to their analysis, a high degree of reproducibility of the top 15/20 ranked research questions was achieved with only 45–55 experts and the suggestion was that a minimum sample size of 50 would result in a replicable CHNRI exercise (73). However, given high non-response rates especially during the scoring process (45), a large pool of technical experts should be approached and measures (such as repeated reminders) taken so that there is no self-selection bias (69, 89, 108, 109). Over-representation of technical experts with certain expertise or from a specific context may also result in bias in generation of specific domains of research questions (94, 110, 111). Different approaches have therefore been used to identify and select global or national technical experts ranging from personal contact and consultation to snowballing, using bibliographic metrics and searching databases such as Biomed Experts, Web of Science, Scopus, WHO, UN etc. (87, 104, 106, 111-113) to ensure that a diverse and knowledgeable pool of experts are identified.

Systematic listing of research ideas

Since the number of health research options is endless, CHNRI proposed a framework for assembling the large number of feasible research options. CHINRI proposed to use the "4D framework" as "instruments" (Discovery, Description, Development and Delivery research) within which research questions of different "depths" could be proposed. For example, very broad "research avenues" would represent broad research fields, more specific "research options" would represent a short term research programme (3-5 years) and very specific "research questions" would represent the title of a very specific research (

Table **2-5**) (70).

Review of CHNRI applications reveal that prioritisation of research ideas by the instruments (4D framework) depended on the focus of the exercise and the time horizons the grant agencies adopt (45). In most cases where the health problem was due to problems in implementation of available, low-cost interventions, especially in LMICs and due to relatively short timeframe for impact (<10 years), delivery research was favoured (45, 114). However, priorities in terms of discovery (fundamental) and development (translational) were also focused in several of the exercises (77, 80, 98, 115). Development research questions scored high when existing available interventions needed to be modified to enable their scale–up in LMICs (e.g., community–based initiation of Kangaroo Mother Care to reduce neonatal mortality of clinically stable preterm and low birth weight babies; or identifying mechanisms by which provision of regular and emergency contraceptives to adolescents be financed or subsidized) (45, 85, 116). On the other hand, discovery research was prioritised when there was absence of effective interventions and where the time scale needed to achieve desired reduction in the burden of disease was longer than 10 years (e.g., the effect of physical activity, nutrition, cognitive activity on dementia and Alzheimer disease) (87).

Table 2-5 CHNRI framework for systematic listing of research ideas (69, 70)

Research Instrument/domain	Research avenue	Research option	Research question
Description: Research to determine the burden of health problem and its risk factors	• Measuring the burden • Understanding risk factors • Measuring prevalence of exposure to risk factors • Evaluating efficacy and effectiveness of interventions • Measuring coverage of interventions	Research options within each avenue may refer to 3–5-year research programmes	Specific research questions within each of the research avenues (title of individual research paper)
Delivery: Research to improve population health status using interventions that are already available	• Health policy analysis • Health system structure analysis • Financing/costs analysis • Human resources • Provision/infrastructure • Operations research • Responsiveness/recipient		
Development: Research to improve already available health interventions	Improving existing interventions (affordability, deliverability, sustainability, acceptability etc.)		
Discovery: Research leading to discovery of new interventions or innovations	Basic, clinical, public health research to: • advance existing knowledge to develop new capacities • explore entirely novel ideas to develop new capacities		

Scoring of all research questions

Once the research questions have been consolidated, the technical experts will systematically and individually score all the finalized research questions against the criteria and sub-criteria selected in step1. The following scores will be assigned: "I agree" (1 point); "I neither agree nor disagree" (0.5 point); "I disagree" (0 points); "Not well informed" (blank). This is later transformed into un-weighted scores for each research idea ranging from 0% (absolutely no optimism) to 100% (where everyone is optimistic).

2.3.2.3 Step 3: Addressing stakeholder values

According to the CHNRI method, involving stakeholders when setting health research priorities is essential and increasingly being acknowledged to ensure that the views and values of investors, beneficiaries or wider community i.e., those who are interested in the process but lack the technical expertise, are reflected (50, 70). This not only ensures legitimacy of the process but also increases acceptability of the set priorities (49). A large, diverse and heterogeneous group of stakeholders is needed to "weigh" and set "thresholds" for minimum acceptable scores for each predefined criteria (50, 70). Examples of stakeholders include funders, representatives of international and regional organizations, researchers, policy makers, service users, or others benefiting from the exercise (advocacy groups, journalists, lawyers, economists, experts in ethics etc.) (70)

One of the shortcomings of the CHNRI process is that stakeholder involvement as envisaged originally has been quite difficult to implement. Among the 102 reviewed exercises, 28 has been able to involve stakeholders out of which 7 exercises included results from Kapiriri (2007) (107, 108, 114, 117-120) (Annex 1). Among the remaining 21 exercises, 15 were carried out at the national level indicating that involving stakeholders were considerably easier at this level (65, 97, 100, 106, 121). However, the sample and diversity of stakeholders has been quite limited (20-79) in all the exercises and cannot be considered as representative (75). In most exercises, the concept of threshold was not used and among those that applied the weights, the procedure didn't have sufficient impact on the rankings of the research ideas (75). Yoshida et al (2017) also suggested that for national level exercises, a sample of 500–1000 stakeholders may be sufficient and representative. A study to understand stakeholder involvement in research priority setting in Zambia found that although the process included research users, researchers, funders and the community, funders had more influence in the process whereas community, patients, people from rural areas, women and young professionals were not effectively involved (49). Mansoori et al (2018) used a popular instant messaging service in Iran called Telegram app to engage 68 stakeholders from different background (patients, caregivers, health professional, social and environmental activities, and pharmacist). Although their input also did not result in major changes it improved the ranks of several community participation related research questions (106). To strengthen the involvement of stakeholders in CHNRI exercises, Wazny et al (2019) asked a public stakeholder group of 1051 people to weigh the 15 CHNRI criteria using an online crowd-sourcing platform called Amazon Mechanical Turk (AMT). Their study revealed differences in weights by

individual and socio-demographic characteristics of respondents, by level (global/regional) and suggested ensuring adequate representation and transparent reporting to avoid undue bias of CHNRI results (122, 123).

2.3.2.4 Step 4: Data analysis and evaluation

According to Rudan et al (2008) the scores and expert agreement are calculated to determine the final list of priorities (70).

Calculation of research priority scores and ranking

Once all the scores from experts are obtained, intermediate and research priority scores (RPS) and average expert agreements are calculated for each research idea.

Intermediate scores

The intermediate score for each criterion informs process managers on the likelihood that the research option would satisfy a specific criterion. It ranges from 0-100% and is the sum of all the informed answers ("1," "0," or "0.5") divided by the number of informed answers. Blanks are left out of the calculation in both the numerator and denominator.

Unweighted Research Priority Score (RPS)

An overall unweighted research priority score (RPS) for a research option is simply a mean of all intermediate scores.

Weighted RPS

However, if inputs from stakeholders in the form of threshold and weights are obtained for each criteria the weighted overall RPS can be calculated. Initially, a check is done to ensure that all research ideas pass the threshold. Next, a weighted RPS for each research idea is calculated. This is the mean of all the weighted intermediate scores calculated using the average weights received for each criterion.

Average Expert Agreement (AEA)

The intention of calculating AEA is to inform the investors about how agreement was reached for research questions and the areas of greatest disagreements. The level of agreement among the scorers is measured using Kappa statistics.

Once the research ideas are prioritised, investors can use the information to fund based on their risk preference, cost and profit associated with the research. The informative quantitative outputs including areas of agreement and disagreement are one of the advantages of this method (69).

Feedback, revision, and evaluation

Rudan et al (2008) mentions that CHNRI methodology does not end with priority setting and allocation of research investments but must achieve a reduction in the burden of disease or health problem

addressed in an equitable way (70). It is thus considered to be a "feedback loop" where changes in context over time must be revisited and the priority setting process carried out again (69). In addition to that, no analysis or evaluation has been done to determine the impact CHNRI exercises may have had on research funders and research communities. Although difficult to attribute, CHNRI recommends a review of research conducted pre and post the prioritisation activity and discussion with key funding institutions and stakeholders to understand the uptake and implementation of the research agenda (45, 84). Odone et al tried to assess the impact of global priority research agenda to address HIV associated tuberculosis by measuring the number of publications since the prioritisation exercise. Despite their comprehensive review they could not clearly attribute the outcomes to the priorities set (124). A recent review assessing uptake of the 2014 WHO established global research priorities for newborn health until 2025 found that 40% of these priorities had seen high research uptake, while 55% had moderate uptake (125).

2.3.3 Application of the CHNRI method in relation to maternal, perinatal, and newborn health and PTB

The CHNRI method of research prioritisation was initially used to prioritising research to reduce child mortality. This was gradually extended to cover child morbidity and development and then to maternal and perinatal health. Annex 1 provides us with an idea of the extent of research topics prioritised by the CHNRI method till date.

Since 2014, i.e., after the endorsement of the Every Newborn Action Plan (ENAP) and Ending Preventable Maternal Mortality (EPMM) aimed to achieve the maternal and newborn mortality targets set out in the Sustainable goals (SDGs), several CHNRI exercises were carried out related to maternal, perinatal, and newborn health (Annex 1). These included studies to identify global priorities on maternal, perinatal or newborn health (112, 116, 126), or local or regional priorities on maternal, newborn, child health in India (101, 127), Ethiopia (128), Africa (129), Uganda (130), LMIC (131). Other exercises focused on child nutrition including wasting (77, 132, 133), child development (76, 90, 134, 135), child health in crisis setting (94, 95), private sector delivery (136), paediatric HIV (84, 113), prevention of mother-to-child transmission (PMTCT) (Africa) (100), integrated community case management (iCCM) (78).

Among the priority research questions identified in the exercises, thirteen questions were specifically focused on addressing issues related to PTB (

Table **2-6**). Other research questions on referral, quality of care, skilled attendance etc. were also identified in the exercises for improving maternal and newborn health, which would also improve prevention and management of PTB were not included in this table. Two prior CHNRI exercises were however conducted to identify research priorities related to prevention and management of preterm

birth (118, 137) that was aimed to help improve the progress in reducing global neonatal mortality as set out in the Millennium Development Goals.

Table 2-6 Research priority areas related to prevention and management of PTB

Reference	Questions	Research domain
(131)	How can we overcome the barriers to implementing kangaroo care in low-resource settings?	Delivery
(93)	Evaluate the effectiveness and cost of a package of community level interventions for preterm babies (e.g. implementing and providing guidelines for kangaroo mother care, home visits by community health workers (CHWs), and infection prevention strategies)	Delivery
(112)	Evaluate the effectiveness of midwife-led care when compared to other models of care across various settings, particularly on rates of foetal and infant death, preterm birth, and low birth weight	Descriptive
(116)	Can community–based initiation of KMC reduce neonatal mortality of clinically stable preterm and low birth weight babies?	Delivery
	How can facility-based initiation of KMC or continuous skin–to–skin contact be scaled up?	Delivery
	Can community based "extra care" for preterm/LBW babies delivered by CHWs reduce neonatal morbidity and mortality in settings with poor accessibility to facility care?	Delivery
(129)	Develop and evaluate strategies for improved utilisation of Kangaroo Mother Care (KMC) at community level. Assess uptake of best practices in hospital care of the preterm infants, evaluate coverage of KMC and determine the barriers and facilitators for its uptake.	Delivery
(128)	Describing the level of effective coverage of KMC in facilities and communities.	Delivery

Reference	Questions	Research domain
	Identifying effective strategies for improving health facility documentation of MNCH outcomes such as gestational age, preterm birth, facility births, hypertension and (pre)eclampsia.	Delivery
	Investigating a community specific, reliable gestational age measuring tool	Development
(127, 138)	Early identification, referral and management of high-risk pregnancies (having maternofoetal morbidities including IUGR, stillbirths, and preterm) at all levels of health care.	Delivery
	Low cost, feasible, portable technological innovations in equipment to improve capacity (diagnosis, identification, and management) and outreach for foetal and neonatal care (especially, LBW, preterm, CPAP, surfactant therapy, etc.,) at various levels of health system and their impact evaluation.	Development
	Determining optimal growth trajectory of LBW (preterm, SGA) babies; nutrient and calorie requirements; strategies to minimize, mitigate development of chronic disease	Descriptive
(95)	Develop and validate strategies to identify preterm babies at community level by CHWs and family members	Delivery
	Evaluate ways to provide thermal care and feeding for the very preterm baby at or close to home	Delivery

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3 Chapter 3: Research prioritisation on prevention and management of preterm birth in LMICs

In this chapter, I describe the process and results of the research prioritisation activity undertaken for the prevention and management of PTB. The chapter presents a detailed overview of the methodology used, the subsequent identification of key research priorities for PTB in LMICs and Bangladesh and explores how these findings can be used to inform future research and policy directions aimed at improving PTB prevention and management. Additionally, the chapter also highlights the limitations and challenges of the exercise. I designed the study in collaboration with the corresponding and senior authors, conducted all statistical analysis, and wrote the first draft of the paper. This chapter is presented as a manuscript published in the *Journal of Global Health*.

Authors' accepted copy of the paper is included in this thesis, pages 62-94.

Research prioritisation on prevention and management of preterm birth in low and middle-income countries (LMICs) with a special focus on Bangladesh using the Child Health and Nutrition Research Initiative (CHNRI) method

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3.1 Abstract

Background: Fifteen million babies are born preterm globally each year, with 81% occurring in low- and middle-income countries (LMICs). Preterm birth complications are the leading cause of newborn deaths and significantly impact health, quality of life, and costs of health services. Improving outcomes for newborns and their families requires prioritising research for developing practical, scalable solutions, especially in low-resource settings such as Bangladesh. We aimed to identify research priorities related to preventing and managing preterm birth in LMICs for 2021-2030, with a special focus on Bangladesh.

Methods: We adopted the Child Health and Nutrition Research Initiative (CHNRI) method to set research priorities for preventing and managing preterm birth. Seventy-six experts submitted 490 research questions online, which we collated into 95 unique questions and sent for scoring to all experts. A hundred and nine experts scored the questions using five pre-selected criteria: answerability, effectiveness, deliverability, maximum potential for burden reduction, and effect on equity. We calculated weighted and unweighted research priority scores and average expert agreement to generate a list of top-ranked research questions for LMICs and Bangladesh.

Results: Health systems and policy research dominated the top 20 identified priorities for LMICs, such as understanding and improving uptake of the facility and community-based Kangaroo Mother Care (KMC), promoting breastfeeding, improving referral and transport networks, evaluating the impact of the use of skilled attendants, quality improvement activities, and exploring barriers to antenatal steroid use. Several of the top 20 questions also focused on screening high-risk women or the general population of women, understanding the causes of preterm birth, or managing preterm babies with illnesses (jaundice, sepsis and retinopathy of prematurity). There was a high overlap between research priorities in LMICs and Bangladesh.

Conclusions: This exercise, aimed at identifying priorities for preterm birth prevention and management research in LMICs, especially in Bangladesh, found research on improving the care of preterm babies to be more important in reducing the burden of preterm birth and accelerating the attainment of Sustainable Development Goal 3 target of newborn deaths, by 2030.

3.2 Background

An estimated 11% of live births or 14.8 million babies are born preterm globally every year [1]. Preterm birth complications are the leading cause of death among newborns (n = 0.88 million (36.1%)) and under-five children (n = 0.94 million, (7.7%)), particularly in South Asia and East Asia and the Pacific region [2-4]. Additionally, the increasing rate of preterm birth in most countries and the insufficient rate of decline in preterm-related deaths (~ 1%) resulted in an increasing proportion of preterm-related deaths in newborns and under-five children [1,5], with proportionate mortality due to preterm birth complications increasing from 14.5% to 17.6% in the latter group between 2000 and 2019 [4]. If this trend continues, preterm birth complications will remain the leading cause of neonatal and under-five deaths even in 2030, at the end of the Sustainable Development Goals (SDGs) era [4,5].

Although high- and lower-resource countries do not differ drastically in rates of preterm birth, they do not share the resulting burden equally due to a large survival gap in preterm newborns between them and a substantially higher impact of preterm birth low- and middle-income countries (LMICs) [1,2,6]. In addition, there are daunting challenges in coverage, quality and equity of essential reproductive, maternal, newborn and child health (RMNCH) interventions needed for the prevention and management of preterm births in LMICs [7,8,9]. Simultaneously, other factors such as exposure to air pollution [10-12], low or advanced maternal age [13], poor maternal nutrition [14,15], and infections [16, 17] are either higher or increasing among women in these settings. The problem has been exacerbated by the coronavirus 2019 (COVID-19) pandemic, which adversely affected patients, health care workers, and health systems in LMICs that had already struggled with various health challenges before the pandemic. Recent reviews indicated that COVID-19 may not only be associated with increased risks of preterm birth, pre-eclampsia (an indirect cause of preterm birth), and other adverse pregnancy outcomes [18], but the indirect effect of disruption in routine health care, including those for preterm birth and access to food, would result in between 253 500 (least severe) to 1 157 000 (most severe) additional child deaths [19].

Bangladesh, a LMIC in South Asia, witnessed high neonatal and child mortality declines during a two-decade period starting in the early 1990s. However, this progress has stalled since 2010, requiring a re-evaluation of the current strategic focus and interventions to avert deaths due to preventable causes such as birth asphyxia, pneumonia, and prematurity [20,21]. Bangladesh is one of the top five contributors to the global burden of preterm births and low birth weight (LBW) complications, which are estimated to be responsible for 15 000 deaths yearly [1,20]. Preterm and LBW complications account for approximately 13% of all child deaths and 19% of deaths among newborns in the country, making them the third and second leading causes of death in children and newborns, respectively [20,21]. Between 2014 and 2017, the proportion of deaths due to prematurity increased higher than for any other cause, by 1.7 times in newborns and 1.9 times in under-five children [20,22].

Advancing a research agenda for the prevention and management of preterm neonates across the continuum of care is critical to addressing the burden of preterm births in LMICs, and specifically, in Bangladesh [23,24]. Research to understand the causes, mechanisms, and risks before, during, and between pregnancies will help with the development and implementation of innovative strategies for preterm birth prevention [9,23-25]. However, implementation research is critical in increasing the uptake and scaling up of evidence-informed preterm birth prevention and care interventions, including those outlined in the Every Newborn Action Plan (ENAP) (e.g. kangaroo mother care (KMC), antenatal corticosteroid, special care newborn units, etc.) in ways that are practical and affordable [8,25]. In the context of increasing funding constraints, there is a need to prioritise and guide research efforts to achieve maximum impact on mitigating preterm births to attain the SDG target of reducing newborn and under-five child mortality by 2030.

Given that preterm birth complications will continue to be the leading cause of newborn and child mortality, stagnation in efforts to address this issue may hinder progress towards achieving the SDG-3 targets in Bangladesh and many low-resource settings. The NIHR Global Health Research Group on Preterm Birth Prevention and Management (PRIME) , therefore, undertook a research priority-setting exercise using the Child Health and Nutrition Research Initiative (CHNRI) method [26]. Since the recognition of the "10/90 gap" in health research investments [27,28], several approaches have been employed over the past two decades to prioritise global health research needs across various settings, ranging from informal non-replicable consultation methods to the more comprehensive structured approaches [29,30]. Among the structured approaches that offer more transparency and replicability, the CHNRI method has been used repeatedly with over 100 applications and has become an often-applied approach for research priority setting [29,31]. This method, developed between 2005 and 2007, relies on the collective opinion of experts to systematically list and transparently score many competing research questions using predefined criteria [26]. Past research priority-setting exercises related to preterm birth, conducted by Bahl et al. [32] and George et al. [33] using the CHNRI method, offered important insight, but focused on the global level and improving progress towards attaining the Millennium Development Goal (MDG) 4. Here we report the research priorities needed for preventing and managing preterm birth for LMICs and Bangladesh in the post-MDG era and highlight considerations for successful implementation.

3.3 Methods

Study design

We adopted the CHNRI method [26] to set research priorities for preventing and managing preterm birth LMICs. The exercise involved four main steps to establish a list of priority research questions (Figure 1).
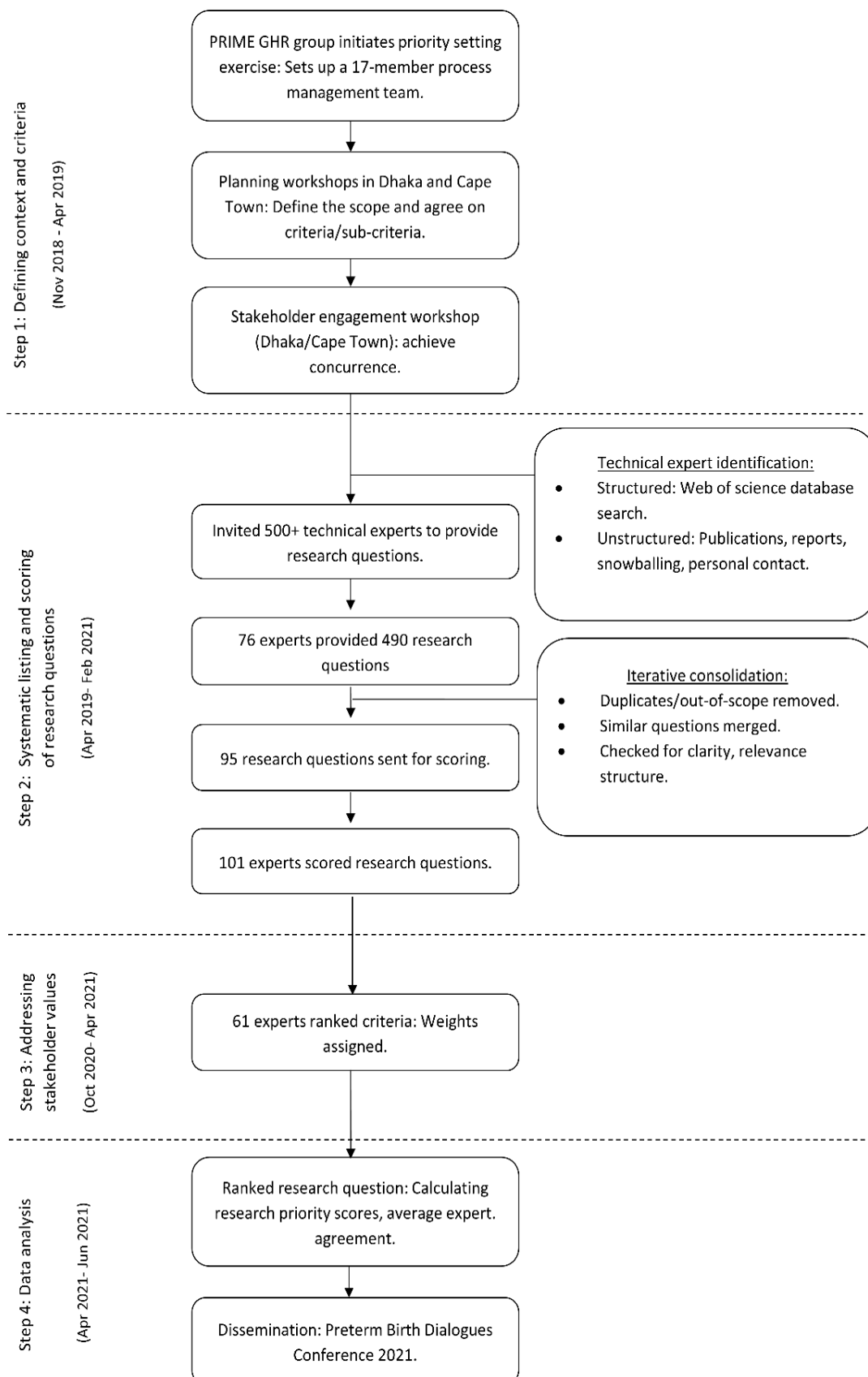
Figure 1. Steps in the CHNRI research priority setting process

Step 1: Defining the context and criteria

We identified and established a process management team of 17 members from the PRIME collaborating institutions in Bangladesh, South Africa and the UK, entrusting them to coordinate the research priority-setting exercise. All team members were experienced in conducting maternal and newborn health research and included biomedical and laboratory scientists, health systems and public health researchers, clinicians, and social scientists. The team conducted planning workshops in Bangladesh and South Africa to define the scope and scoring criteria for the priority-setting exercise. Online workshops were later held to iteratively review and consolidate research questions and discuss the research prioritisation activity results.

The process management team discussed and specified the context of this research priority exercise in terms of space, population, and time; disease, disability, and death burden; and research domains. The goal of this phase was to identify research questions that have the potential to reduce the burden of premature birth and accelerate the progress towards achieving SDG Target 3 in LMICs, with a particular focus on Bangladesh as a high-burden country (Table 1). Following the CHNRI methodology, the team decided to encourage longer-term (up to 10 years) investments and included research questions from all four broad research domains (epidemiological research to describe the burden and determinants, health systems and policy research to improve the delivery of current interventions, research to improve existing interventions, and research to develop new interventions).

Table 1. Context for the research priority setting exercise

Geographical area	In LMICs and Bangladesh
Time period	SDG period (2021-2030)
Target population	Women of reproductive age (15-49 y); pregnant women; preterm/ LBW / SGA babies.
Targeted disease burden	PROM, premature birth, LBW, SGA, short- and long-term morbidity in preterm babies.
Research domain	Health policy and system research; research to improve existing interventions; development of new interventions; epidemiological research to understand burden and risk factors.

LMICs – low and middle-income countries, SDG – Sustainable Development Goals, LBW – low birthweight, SGA – small for gestational age, PROM – premature rupture of membrane, y – year

The process management team carried out a ranking exercise followed by a detailed discussion to identify four to five criteria for the priority-setting exercise. The team reviewed all the criteria identified by Rudan et al. [26] and scored them based on their relative importance in scoring research questions (range = 1-10). Table 2 presents the top five criteria selected for the exercise. Since the agreed criteria were the same as the standard CHNRI criteria, the process management team also decided to retain the standard sub-criteria used to score research questions [26].

Table 2. List of selected criteria used to score research questions

Criteria	Explanation	Weights
Answerability	The research question can be ethically answered	1.01
Effectiveness	The research question will generate/improve truly effective health interventions	1.08
Deliverability	The intervention resulting from the research question will be deliverable	0.93
Maximum impact on burden	The research question has greater potential to reduce disease burden	1.08
Equity	The intervention resulting from the research will be accessible to vulnerable groups thus decreasing equity	0.90

Step 2: Systematic listing of research questions

We combined structured and unstructured approaches to identify global or international and local (Bangladesh) technical experts in the field of preterm birth research (Box 1). This included a bibliometric search of the Web of Science Core Collection database to identify the most scientifically productive researchers (with available contact details) in this field in the last 10 years, including those based in LMICs. Additionally, we enlisted experts from prior CHNRI priority-setting exercises related to preterm birth, authors from reviews on preterm birth, keynote speakers at preterm birth-related conferences and other related researchers based on personal communication. We also encouraged the invited experts to share the survey links within their network. The local (Bangladesh) experts included members from the national newborn technical working committee, the ministry of health, obstetric, gynaecological, newborn, and paediatric professional bodies, development partners, service providers, and researchers working in maternal and newborn health with interest in preterm birth. We made efforts to invite experts from diverse disciplines (e.g. researchers, clinicians, policymakers, programme implementers) and countries (including LMICs) to participate in the survey.

Box 1: Identification of technical experts in the field of preterm birth research

- Listing from previous CHNRI exercises
    - GAPPS, et al. (2011). "Setting implementation research priorities to reduce preterm births and stillbirths at the community level." PLoS Med 8(1): e1000380
    - Bahl, R., et al. (2012). "Setting research priorities to reduce global mortality from preterm birth and low birth weight by 2015." J Glob Health 2(1): 010403
    - Yoshida, S., et al. (2016). "Setting research priorities to improve global newborn health and prevent stillbirths by 2025." J Glob Health 6(1): 010508
- Listing other publications
    - Born too Soon report
    - PRIME mapping review
    - Separation and Closeness Experiences in the Neonatal Environment (SCENE)
- Keynote speakers in Preterm Birth Dialogues Conference (South Africa)
- Author list of articles published on PTB published in the last 10 years found in Web of Science™ Core Collection database
- Personal Communication
- Snowballing

An online platform was developed, and email invitations were sent to over 500 global technical experts to participate in the research priority-setting exercise. In the first online survey, we asked the technical experts to systematically list research questions on preventing and managing preterm birth across the four research domains according to the predefined context. The exercise was open to all research methodologies and study designs (e.g. observational, randomised trials, modelling, etc.). Participants could submit up to 10 priority research questions for each research domain based on their knowledge and expertise. Seventy-six technical experts (60 global and 16 from Bangladesh) submitted 490 research questions (an average of 6.4 research questions per person) between July and December 2019. Around two-thirds of the experts were public health and health systems researchers, while a half were involved in clinical services. Around 90% of the technical experts were experienced in working in LMICs (Table 3).

A few members of the process management team reviewed the research questions and collated them to a manageable number by research domains (Table 1) by removing questions outside of the scope of the exercise (e.g. not related to preterm birth), categorising and merging similar questions, and removing duplicates. We shared the ensuing list with the wider process management group, who reviewed the questions for relevance, clarity, and structure and reduced the list further to 95 unique questions through consultation. Most questions were from the epidemiological research domain (n = 38 (40%)) and health

systems and policy research field (n = 33 (35%)), while a smaller number were on research to improve existing interventions (n = 15 (16%)) or to develop new interventions (n = 9 (9%)).

The technical experts who were invited to provide the research questions were invited again to score the final list of 95 research questions using a separate online platform (Table 3). In the second online survey, the technical experts were asked to score the final list of research questions against the criteria and sub-criteria selected in the first step. The following scores were assigned: "I agree" (1 point), "I neither agree nor disagree" (0.5 points), "I disagree" (0 points), and "Not well informed" (blank). We also randomly presented the research questions to technical experts to overcome bias due to scoring fatigue. We considered the responses valid if experts had scored at least one whole research question. One hundred and nine technical experts (55 international and 54 from Bangladesh) scored the questions based on five pre-selected criteria: answerability, effectiveness, deliverability, maximum potential for burden reduction, and effect on equity between October 2020 and April 2021.

Step 3: Addressing stakeholder values

During the PRIME project, we carried out extensive stakeholder engagement activities/workshops with policymakers, programme implementers, public health professionals, researchers, and health care service providers in Bangladesh. By introducing and ensuring their concurrence for the research priority-setting exercise, we wanted to increase the contextual relevance, acceptability, and eventual uptake of identified priorities. We also asked all experts to rank each predefined criterion based on their perceived relative importance using a five-point Likert scale (1 = least important, 5 = most important) (step four), which we then used to calculate weighted research priority scores. Seventy-six experts ranked the criteria; those for effectiveness (3.25) and potential for burden reduction (3.25) received the highest ranks, followed by answerability (3.02), deliverability (2.79), and equity (2.70).

Table 3. Characteristics of technical experts participated in first and second online survey*

Characteristics	First online survey: Listing research questions (n = 76)	Second online survey: Scoring research questions (n = 109)	*P*-value†
Area of expertise			
Laboratory science research	9 (12)	8 (7)	0.244
Clinical science research	36 (47)	39 (36)	0.134
Public health and health systems research	49 (64)	69 (63)	0.889
Policy and programme implementation	30 (39)	45 (41)	0.785
Clinical services (direct health care)	38 (50)	45 (41)	0.226
Experienced in working in LMIC			
Yes	66 (87)	104 (95)	0.052
No	10 (13)	5 (5)	0.052
Experienced in working in South Asia			
Yes	41 (54)	78 (72)	0.012
No	35 (46)	31 (28)	0.012
Experienced in working in Africa			
Yes	44 (58)	35 (32)	0.000
No	32 (42)	74 (68)	0.000
Location (international/local (Bangladesh)			
Local (Bangladesh)	16 (21)	54 (50)	0.000
International	60 (79)	55 (50)	0.000
Years of experience in working in LMIC, mean (SD)	16 (12)	25 (10)	0.000
Years of experience in working in MNH, mean (SD)	23 (12)	26 (10)	0.066

SD – standard deviation, LMIC – low and middle-income country, MNH – Maternal and Newborn Health

*Values presented as n (%) unless otherwise specified.

†We used proportion test for frequencies and two sample independent *t* test for mean. $P < 0.05$ indicates statistical significance.

Step 4: Data analysis and evaluation

We used a password-protected Microsoft Structured Query Language (SQL) Server 2008 R2 as the central database for maintaining the quality and safety of data. We set up validation rules (such as

consistency checks, logical checks, and skip rules) to prevent inconsistencies and other errors during data entry.

We calculated intermediate, unweighted, and weighted research priority scores (RPS) for each of the five scoring criteria used to discriminate the 95 research questions for this exercise [26]. For each of the research questions, experts provided the following answers: 1 (agree), 0 (disagree), 0.5 (unsure) and blank (if experts were not informed enough to judge a research question). We calculated intermediate RPS by summing all the informed answers ("1", "0", or "0.5") and dividing this sum by the number of informed answers. We left the blanks out of the calculation in both the numerator and denominator. Ranging from zero to 100%, the intermediate RPS measured the collective optimism of the scorers and informed experts on the likelihood that the research question would satisfy a specific criterion. This method of dealing with missing answers/blanks increases the accuracy of collective prediction by allowing experts who do not necessarily know to adequately score a research question against each criterion to withdraw from answering [33]. We calculated the unweighted RPS as the mean of all five intermediate priority scores.

In the next step, we calculated weights by dividing the observed average rank for each criterion by the expected average rank where all five criteria are equally important (which should be 3.00) [34]. In our exercise, for each scored research question, the intermediate score for effectiveness and impact on burden criteria were increased by 8%, there was almost no change in score for the answerability criteria, and the score decreased by 7% and 10% for deliverability and equity criteria, respectively (Table 2). We multiplied the weights with the intermediate scores of each criterion to calculate weighted intermediate scores and computed the weighted RPS as the mean of all the weighted intermediate scores.

We also calculated the average expert agreement (AEA) for each of the 95 research questions using the formula below [26]. The AEA informed us about the proportion of scorers who gave the same most frequent response for all the informed answers ("1", "0", or "0.5") [35,36]. It is a measure of concurrence/disagreement in the scorers' opinion around the RPS and is unaffected by the varying number and composition of scorers per criterion [37].

Ethics

We obtained ethical approval for the study from the research and ethics review committees of International Centre for Diarrhoeal Disease Research Bangladesh (icddr,b) (PR-18055). Experts provided informed consent during the start of both online surveys, and participants were aware that they could exit the surveys at any time without any penalty. We maintained the participants' privacy and confidentiality during data collection, management, and analysis, and used contact information only to send survey invitations and reminders. We removed personal identifiers (i.e. names) before analysis and kept the data in secure and password-protected devices.

3.4 Results

3.4.1 Research priorities for LMICs

The overall weighted RPS for the 95 research questions ranged from 0.903 (highest) to 0.638 (lowest). The AEA ranged from 0.85 to 0.66, and we observed a positive association between AEA and RPS (Table S1 in the Online Supplementary Document).

The top-ranked research priority was identifying barriers and challenges to implementing facility-based KMC in LMICs (#1). Among the top 20 research priorities for LMICs (Table 4), six were focused on various aspects of KMC, including assessing the effectiveness of community-based KMC (#6), increasing acceptability and compliance of KMC (#8), determining clinical outcomes of preterm newborns discharged to continue KMC at home (#10), and assessing the impact of quality improvement initiatives in improving KMC counselling (#14). The remainder of the top 20 research priorities focused on promoting early and exclusive breastfeeding (#4), health systems-related research such as assessing the impact of the availability of skilled birth and neonatal care attendants on survival outcomes of babies (#2), strengthening referral systems for women and preterm/LBW newborns (#3 and #5), evaluating quality improvement activities (#17), exploring barriers and facilitators to using antenatal steroid use in health facilities (#19) and post-discharge follow-up of preterm newborns (#12 and #20). Several of the top 20 questions also focused on screening of high-risk or general population women (#11), understanding the cause or managing preterm babies with illnesses including jaundice, sepsis and retinopathy of prematurity (#7, #13, #15, and #16).

Eleven (55%) of the top 20 research priorities were categorised as health systems and policy research, four as research to develop existing interventions (20%), three as epidemiological research, and two as the development of new interventions.

Table 4. Top 20 research questions for LMICs (n = 109) with scores for each criterion, overall weighted RPS, and AEA

Rank	Research questions	Domain	Answerability intermediate RPS	Effectiveness intermediate RPS	Deliverability intermediate RPS	Burden intermediate RPS	Equity intermediate RPS	Weighted RPS	AEA
1	What are the barriers and challenges of implementing facility-based KMC in LMICs?	HPSR	0.984	0.952	0.945	0.747	0.895	0.903	0.847
2	How does the presence of skilled birth and neonatal care attendants influence survival outcomes for babies?	HPSR	0.928	0.944	0.923	0.737	0.918	0.888	0.823
3	How can referral network and systems be strengthened for timely referral of women experiencing obstetric emergencies (including preterm labour) from rural/primary care to higher care level facilities in LMICs?	HPSR	0.923	0.934	0.884	0.712	0.959	0.880	0.809
4	How to promote early initiation and exclusive breast feeding of preterm, LBW and SGA infants in LMICs?	RIEI	0.916	0.943	0.929	0.706	0.871	0.871	0.800
5	How can transport and referral systems for preterm, LBW, SGA newborns be improved or maximised in LMICs?	HPSR	0.936	0.912	0.877	0.721	0.920	0.871	0.813
6	Assess the effectiveness of community-based KMC in reducing neonatal mortality of clinically stable preterm and LBW infants?	HPSR	0.944	0.929	0.907	0.698	0.879	0.870	0.810
7	What is the prevalence and cause of neonatal sepsis in preterm, LBW and SGA infants in LMICs?	EPI	0.952	0.897	0.895	0.720	0.876	0.866	0.787
8	How can acceptability and compliance of KMC be increased in LMICs?	RIEI	0.911	0.926	0.921	0.720	0.851	0.865	0.789
9	What are barriers and challenges to improving existing skin-to-skin practice in LMICs?	HPSR	0.961	0.928	0.938	0.662	0.819	0.860	0.807
10	What are the clinical outcomes of preterm newborns discharged to continue KMC at home?	EPI	0.950	0.897	0.920	0.653	0.880	0.857	0.798
11	Evaluate interventions to screen women at risk of PTB during ANC (e.g. anaemia, pre-eclampsia, NCDs, malnutrition) and improve maternal and newborn outcomes in LMICs.	HPSR	0.927	0.893	0.894	0.660	0.877	0.847	0.769
12	Develop effective strategies to improve post discharge follow-up of preterm, LBW and SGA infants in LMICs.	RDNI	0.910	0.885	0.865	0.677	0.878	0.841	0.756
13	What are barriers of doing ROP screening for all eligible preterm babies in LMICs?	HPSR	0.966	0.907	0.838	0.686	0.803	0.840	0.761
14	Assess the impact of quality improvement initiatives in improving KMC counselling.	HPSR	0.905	0.912	0.920	0.634	0.839	0.839	0.779

1 5	How can we provide safe and effective phototherapy for premature neonates in LMICs?	RIEI	0.922	0.912	0.861	0.655	0.855	0.839	0.777
1 6	What intervention packages can be developed to manage premature and small infants with neonatal jaundice in LMICs?	RDNI	0.894	0.898	0.889	0.701	0.809	0.837	0.771
1 7	Evaluate the effectiveness and cost-effectiveness of QI activities in improving care of preterm babies at health facilities in LMICs.	HPSR	0.886	0.893	0.865	0.695	0.847	0.836	0.746
1 8	What is the effect of nutritional status (e.g. underweight, overweight and obesity, micronutrient deficiency etc.) on LBW, SGA and PTB in LMICs?	EPI	0.931	0.868	0.885	0.671	0.832	0.835	0.755
1 9	Explore barriers and facilitators to antenatal steroid use in public health facilities in LMICs.	HPSR	0.921	0.898	0.902	0.669	0.782	0.833	0.766
2 0	Evaluate the use of digital technologies (e.g. mobile phone etc.) to improve follow-up of preterm babies after discharge from health facilities.	RIEI	0.935	0.876	0.872	0.646	0.838	0.831	0.757

LMICs – low and middle-income countries, KMC - Kangaroo Mother Care, RPS – research priority scores, AEA – average expert agreement, HPSR – health policy and systems research, EPI – epidemiological research, ANC – antenatal care, RIEI – research to improve existing interventions, RDNI – research to develop new interventions, LBW – low birth weight, SGA – small for gestational age, PTB – preterm birth, ROP – retinopathy of prematurity, QI – quality improvement

3.4.2 Top-ranked priorities across research criteria in LMICs

The research question on identifying barriers and challenges of implementing facility-based KMC received the highest score for four criteria – the likelihood of burden reduction, answerability, effectiveness, and deliverability (Table S2 in the Online Supplementary Document). For the criteria reduction of the burden, the other two leading research questions that experts agreed on were determining the impact of skilled birth and neonatal care attendants on survival outcomes for babies and improving transport and referral systems for preterm, LBW, or small for gestational age (SGA) infants in LMICs. There was also high agreement that improving or strengthening referral and transport systems for women and newborns, followed by assessing the impact of the presence of skilled birth and neonatal care attendants on survival outcomes for babies, would improve equity (Table S2 in the Online Supplementary Document).

3.4.3 Subgroup analyses

We conducted subgroup analyses for Bangladesh-based (Table 5) and international scorers (Table 6) outside Bangladesh to search for any variations in priorities identified. We also compared the ranks for each research priority between these groups and the overall LMIC scores (Table 7). Ranks within the subgroups over a 10-point deviation compared to the LMIC ranks are marked with an asterisk(*) (Table 7).

Table 5. Top 20 research questions for Bangladesh (n = 54) with scores for each criterion, overall weighted RPS, and AEA

Rank	Research questions	Domain	Answerability intermediate RPS	Effectiveness intermediate RPS	Deliverability intermediate RPS	Burden intermediate RPS	Equity intermediate RPS	Weighted RPS	AEA
1	How does the presence of skilled birth and neonatal care attendants influence survival outcomes for babies?	HPSR	0.956	0.965	0.948	0.752	0.947	0.911	0.860
2	What are the barriers and challenges of implementing facility-based KMC in LMICs?	HPSR	0.982	0.960	0.942	0.752	0.919	0.909	0.859
3	What is the prevalence and cause of neonatal sepsis in preterm, LBW and SGA infants in LMICs?	EPI	0.969	0.940	0.927	0.773	0.897	0.900	0.844
4	How can referral network and systems be strengthened for timely referral of women experiencing obstetric emergencies (including preterm labour) from rural/primary care to higher care level facilities in LMICs?	HPSR	0.944	0.954	0.935	0.718	0.965	0.900	0.840
5	How can acceptability and compliance KMC be increased in LMICs?	RIEI	0.924	0.956	0.952	0.750	0.864	0.888	0.827
6	How to promote early initiation and exclusive breast feeding of preterm, LBW and SGA infants in LMICs?	RIEI	0.941	0.954	0.943	0.708	0.904	0.887	0.821
7	Assess the effectiveness of community-based KMC in reducing neonatal mortality of clinically stable preterm and LBW infants?	HPSR	0.972	0.937	0.919	0.711	0.901	0.886	0.834
8	What are the clinical outcomes of preterm newborns discharged to continue KMC at home?	EPI	0.954	0.938	0.938	0.681	0.900	0.880	0.825
9	Assess the impact of quality improvement initiatives in improving KMC counselling.	HPSR	0.946	0.963	0.955	0.663	0.884	0.879	0.830
10	What are barriers and challenges to improving existing skin-to-skin practice in LMICs?	HPSR	0.955	0.944	0.934	0.712	0.857	0.879	0.844
11	How can transport and referral systems for preterm LBW, SGA newborns be improved or maximised in LMICs?	HPSR	0.939	0.914	0.923	0.722	0.909	0.879	0.837
12	What is the effect of antepartum complications in the current pregnancy (e.g. multiple gestation, cervical incompetence, pre-eclampsia, eclampsia, hypertension, diabetes etc.) on LBW, SGA and PTB in LMICs?	EPI	0.972	0.950	0.912	0.735	0.792	0.873	0.803

13	What is the effect of nutritional status (e.g. underweight, overweight and obesity, micronutrient deficiency etc.) on LBW, SGA and PTB in LMICs?	EPI	0.945	0.927	0.951	0.719	0.827	0.873	0.817
14	Evaluate interventions to screen women at risk of PTB during ANC (e.g. anaemia, pre-eclampsia, NCDs, malnutrition) and improve maternal and newborn outcomes in LMICs.	HPSR	0.941	0.916	0.914	0.700	0.903	0.872	0.805
15	What are barriers of doing ROP screening for all eligible preterm babies in LMICs?	HPSR	0.965	0.915	0.896	0.729	0.841	0.868	0.808
16	How can care for preterm and LBW newborns in remote community settings be improved?	HPSR	0.917	0.935	0.905	0.687	0.901	0.866	0.794
17	What are the short- and long-term health and developmental outcomes of babies born preterm, LBW, or SGA in LMICs?	EPI	0.951	0.926	0.933	0.673	0.847	0.864	0.787
18	How can clinical support and supervision of community health workers in the management of small and sick newborns be improved in LMICs?	HPSR	0.945	0.891	0.913	0.692	0.884	0.862	0.787
19	What are the barriers and enablers of improved accuracy of gestational age assessment in LMICs?	HPSR	0.946	0.936	0.886	0.685	0.851	0.860	0.803
20	Evaluate the effectiveness and cost-effectiveness of nutritional interventions in improving nutritional status of preterm infants in LMICs.	EPI	0.937	0.893	0.892	0.692	0.899	0.860	0.807

LMICs – low and middle-income countries, KMC - Kangaroo Mother Care, RPS – research priority scores, AEA – average expert agreement, HPSR – health policy and systems research, EPI – epidemiological research, RIEI – research to improve existing interventions, RDNI – research to develop new interventions, LBW – low birth weight, SGA – small for gestational age, PTB – preterm birth, ROP – retinopathy of prematurity, NCD – non-communicable disease

Research priorities for Bangladesh

The RPS ranged from 0.911 to 0.719, and the AEA ranged from 0.82 to 0.58. There was considerable overlap between research priorities in LMICs and Bangladesh, with 16 questions of the top 20 questions in Bangladesh appearing in the overall LMIC list (Table 5 and Table S3 in the Online Supplementary Document). The top research priority was assessing the impact of the availability of skilled birth and neonatal care attendants on the survival outcomes of babies (Table 5). Like that of LMICs, six of the 20 Bangladesh-based research questions were on KMC (#2, #5, #7, #8, #9, and #10), while others included understanding the burden and cause of sepsis in preterm newborns (#3), strengthening referral systems (#4 and #11), promoting early and exclusive breastfeeding (#6), screening of high-risk women (#14), and exploring barriers of screening children with retinopathy of prematurity (#15). Experts also gave high scores to several epidemiological questions focusing on short and long-term developmental

outcomes in preterm newborns, the accuracy of gestational age estimation, and understanding the effects of antepartum complications, nutritional status, and nutritional interventions on preterm birth outcomes. Two questions also specifically focused on improving care at the remote community level (#16) and improving support and supervision of community health workers (#18).

Table 6. Top 20 research questions scored by international experts (n = 55) with scores for each criterion, overall weighted RPS, and AEA

Rank	Research questions	Domain	Answerability intermediate RPS	Effectiveness intermediate RPS	Deliverability intermediate RPS	Burden intermediate RPS	Equity intermediate RPS	Weighted RPS	AEA
1	What are the barriers and challenges of implementing facility-based KMC in LMICs?	HPSR	0.987	0.938	0.949	0.739	0.856	0.893	0.826
2	How can transport and referral systems for preterm, LBW, SGA newborns be improved or maximised in LMICs?	HPSR	0.931	0.908	0.787	0.719	0.938	0.855	0.771
3	Determine the effectiveness and cost-effectiveness of various strategies (e.g. CPAP, high flow oxygen, T-piece resuscitation etc.) for treating preterm infants with respiratory failure in health facilities in LMICs.	RIEI	0.867	0.955	0.845	0.682	0.893	0.847	0.777
4	How does the presence of skilled birth and neonatal care attendants influence survival outcomes for babies?	HPSR	0.872	0.903	0.873	0.711	0.867	0.844	0.751
5	How can referral network and systems be strengthened for timely referral of women experiencing obstetric emergencies (including preterm labour) from rural/primary care to higher care level facilities in LMICs?	HPSR	0.883	0.897	0.791	0.703	0.950	0.843	0.753
6	Assess the effectiveness of community-based KMC in reducing neonatal mortality of clinically stable preterm and LBW infants?	HPSR	0.889	0.913	0.882	0.669	0.833	0.836	0.759
7	How to promote early initiation and exclusive breast feeding of preterm, LBW and SGA infants in LMICs?	RIEI	0.862	0.918	0.897	0.700	0.802	0.835	0.757
8	Explore barriers and facilitators to antenatal steroid use in public health facilities in LMICs.	HPSR	0.928	0.878	0.921	0.683	0.731	0.828	0.741
9	What are barriers and challenges to improving existing skin-to-skin practice in LMICs?	HPSR	0.970	0.899	0.944	0.571	0.756	0.826	0.762
10	Develop effective strategies to improve post discharge follow-up of	RDNI	0.914	0.853	0.814	0.652	0.895	0.823	0.721

	preterm, LBW, and SGA infants in LMICs.								
11	How can acceptability and compliance of KMC be increased in LMICs?	RIEI	0.884	0.866	0.858	0.658	0.829	0.817	0.712
12	Understand the epidemiology of nosocomial infections in newborn nurseries or SCANU in LMICs.	EPI	0.915	0.873	0.902	0.658	0.692	0.808	0.731
13	What intervention packages can be developed to manage premature and small infants with neonatal jaundice in LMICs?	RDNI	0.891	0.892	0.850	0.660	0.742	0.807	0.713
14	What are the clinical outcomes of preterm newborns discharged to continue KMC at home?	EPI	0.942	0.806	0.881	0.589	0.838	0.807	0.739
15	Evaluate the use of digital technologies (e.g. mobile phone etc.) to improve follow-up of preterm babies after discharge from health facilities.	RIEI	0.932	0.810	0.854	0.617	0.819	0.803	0.720
16	Can providing proper training to community health workers ensure community continuation of KMC through domiciliary follow-up?	RIEI	0.941	0.879	0.843	0.519	0.851	0.802	0.759
17	What is the prevalence and cause of neonatal sepsis in preterm, LBW and small for gestational age SGA infants in LMICs?	EPI	0.922	0.818	0.838	0.611	0.840	0.802	0.705
18	Evaluate interventions to screen women at risk of PTB during ANC (e.g. anaemia, pre-eclampsia, NCDs, malnutrition) and improve maternal and newborn outcomes in LMICs.	HPSR	0.899	0.845	0.854	0.586	0.831	0.799	0.703
19	Assess the effect of ECD interventions (e.g. early infant stimulation/parenting interventions) on health and developmental outcomes of preterm newborn.	EPI	0.899	0.873	0.796	0.603	0.813	0.795	0.717
20	Evaluate the effectiveness and cost-effectiveness of QI activities in improving care of preterm babies at health facilities in LMICs.	HPSR	0.875	0.803	0.795	0.670	0.828	0.792	0.664

SCANU – specialised care newborn units, LMICs – low and middle-income countries, KMC - Kangaroo Mother Care, RPS – research priority scores, AEA – average expert agreement, HPSR – health policy and systems research, ANC – antenatal care, CPAP – continuous positive airway pressure, EPI – epidemiological research, RIEI – research to improve existing interventions, RDNI – research to develop new interventions, LBW – low birth weight, SGA – small for gestational age, PTB – preterm birth, ROP – retinopathy of prematurity, QI – quality improvement

Table 7. Comparison of ranks within subgroup analyses (geographical location)

Rank	Research questions	LMIC participants (n = 109)	Bangladesh participants (n = 54)	International participants (n = 55)	International HIC participants (n = 32)	International LMIC participants (n = 23)
1	What are the barriers and challenges of implementing facility-based KMC in LMICs?	1	2	1	1	1
2	How does the presence of skilled birth and neonatal care attendants influence survival outcomes for babies?	2	1	4	5	12*
3	How can referral network and systems be strengthened for timely referral of women experiencing obstetric emergencies (including preterm labour) from rural/primary care to higher care level facilities in LMICs?	3	4	5	6	11
4	How to promote early initiation and exclusive breast feeding of preterm, LBW and SGA infants in LMICs?	4	6	7	2	24*
5	How can transport and referral systems for preterm, LBW, SGA newborns be improved or maximised in LMICs?	5	11	2	3	7
6	Assess the effectiveness of community-based KMC in reducing neonatal mortality of clinically stable preterm and LBW infants?	6	7	6	13	3
7	What is the prevalence and cause of neonatal sepsis in preterm, LBW and SGA infants in LMICs?	7	3	17*	29*	6
8	How can acceptability and compliance of KMC be increased in LMICs?	8	5	11	10	17
9	What are barriers and challenges to improving existing skin-to-skin practice in LMICs?	9	10	9	9	8
10	What are the clinical outcomes of preterm newborns discharged to continue KMC at home?	10	8	14	12	20*
11	Evaluate interventions to screen women at risk of PTB during ANC (e.g. anaemia, pre-eclampsia, NCDs, malnutrition) and improve maternal and newborn outcomes in LMICs.	11	14	18	17	19
12	Develop effective strategies to improve post discharge follow-up of preterm, LBW, and SGA infants in LMICs.	12	26*	10	7	18
13	What are barriers of doing ROP screening for all eligible preterm babies in LMICs?	13	15	23*	15	36*
14	Assess the impact of quality improvement initiatives in improving KMC counselling.	14	9	29*	43*	27*
15	How can we provide safe and effective phototherapy for premature neonates in LMICs?	15	24	21	24	9
16	What intervention packages can be developed to manage premature and small infants with neonatal jaundice in LMICs?	16	27*	13	22	16

17	Evaluate the effectiveness and cost-effectiveness of QI activities in improving care of preterm babies at health facilities in LMICs.	17	22	20	28*	15
18	What is the effect of nutritional status (e.g. underweight, overweight and obesity, micronutrient deficiency etc.) on LBW, SGA, and PTB in LMICs?	18	13	25	14	37*
19	Explore barriers and facilitators to antenatal steroid use in public health facilities in LMICs.	19	36*	8*	8*	14
20	Evaluate the use of digital technologies (e.g. mobile phone etc.) to improve follow-up of preterm babies after discharge from health facilities.	20	29	15	36*	4*

LMICs – low and middle-income countries, KMC - Kangaroo Mother Care, RPS – research priority scores, LBW – low birth weight, SGA – small for gestational age, PTB – preterm birth, ROP – retinopathy of prematurity, QI – quality improvement, HIC – high-income country, ANC – antenatal care

*Cells with ranks over a 10-point deviation from the LMIC ranks.

Research priorities identified by global/international scorers

We also observed a high overlap (16 questions) between the top 20 questions identified by LMIC and international experts (Table 6 and Table 7). The top-ranked research priority proposed to identify barriers and challenges to implementing facility-based kangaroo mother care in LMICs (#1) (Table 6). International scorers also highlighted questions such as determining the effectiveness and cost-effectiveness of various strategies (e.g. continuous positive airway pressure (CPAP), high flow oxygen, T-piece resuscitation, etc.)) for treating preterm infants (#3), understanding the epidemiology of nosocomial infections in newborn units (#12), improving community continuation of KMC by proper training to community health workers (#16), and assessing the effect of early childhood development interventions in improving preterm newborn (#19) outcomes as important (Table 6). We further stratified the analysis by international scorers based on high-income countries (HICs) and LMICs (Table S5 and S6 in the Online Supplementary Document); 14 of the top 20 questions prioritised by researchers in HICs and 16 prioritised by those in LMICs appeared in the overall LMIC list (Table 7 and Table S7 in the Online Supplementary Document).

Research priorities segregated by the expertise of scorers

We also attempted to classify research priorities by the expertise of scorers listed in Table 3. Findings are presented in Tables S8-13 in the Online Supplementary Document. While we observed some differences among individuals with expertise in laboratory science research (LSR), we found an overlap in about 15-18 questions between the different groups and the overall LMIC list. We did observe a substantial difference among those experts in LSR and the overall LMIC list.

3.5 Discussion

Many children are still being born preterm and are suffering from short- and long-term consequences of preterm-related complications. With only a decade left to reach the SDGs, many countries will fail to achieve the targets related to child mortality and newborn mortality unless the challenges in the prevention and management of preterm birth are addressed urgently [2,4,5]. As such, this priority-setting exercise aimed to identify research questions that reflect the knowledge gaps that need to be addressed to accelerate progress in this area in LMICs and Bangladesh within the SDG era. Overall, participating experts have prioritised research questions primarily aimed at improving the survival of preterm infants rather than identifying long-term potential preventative solutions. The survey results have strongly prioritised health policy and systems research to understand barriers and improve effectiveness, deliverability, acceptance, and uptake of evidence-based interventions combined with other epidemiological research to address the critical gaps in knowledge in resource-poor settings. This is in line with the distribution in other CHNRI exercises, where health policy and systems-related research questions were more prioritised than other research types primarily for their ability to immediately address the disease burden in low-resource settings [31]. The positive association between expert agreement and research priority scores also indicates substantial agreement in the high ranked priorities among experts.

Of the top 20 research questions in LMICs or Bangladesh, six were related to identifying gaps or challenges or improving the implementation of either facility-based or community-based KMC. Although KMC has been identified and epitomised as a critical intervention in reducing mortality and morbidity in preterm infants (including ENAP), as recommended by the World Health Organization (WHO), its application and scale-up, especially in LMIC settings, have been challenging due to health systems bottlenecks and demand side barriers such as poor quality, lack of awareness, acceptability, and access [38-40]. For example, the Government of Bangladesh adopted KMC as the primary approach for averting preterm-related deaths through the Promise Renewed Declaration in 2013 [41]. Despite this, to date, KMC has been scaled to only around 400 facilities in Bangladesh, and only 12896 of the estimated 573 000 preterms and 192 000 low-birth-weight babies (<10% coverage) received KMC services at health facilities in 2022 [42]. Consequently, this exercise has identified relevant research priorities that aim to identify gaps in the implementation/scale-up of facility-based KMC, improve the quality of KMC counselling, and improve acceptability and compliance with KMC. Although a few studies have been launched recently [43-47], there is still limited evidence on the benefits of community KMC (cKMC) or community continuation of facility-based KMC, and area that has also been prioritised in this exercise. Research priority-setting exercises during [32,33] and after the MDG era [37,48,49] have also highlighted similar research questions confirming that stark evidence gaps in implementing KMC services remain. For example, Yoshida et al. [37], Alobo et al. [48], and Souza et al. [49] conducted CHNRI exercises to determine research priorities for maternal and newborn health

the post-MDG area in the global and African contexts. Research on KMC was featured in the top 10 priorities in those exercises and included evaluation of the impact of cKMC on neonatal mortality, improving utilisation of KMC at the community level, evaluating coverage, identifying facilitators and barriers, and scaling up of facility based KMC [37,48,49].

Despite increases in access to institutional care, about one-third of women in LMICs still deliver at home without adequately skilled staff or cannot timely access care due to poor referral and transport mechanisms linking women and newborns to care [42,50,51]. Similarly, a substantial proportion of newborn deaths in LMICs still occur at home, with delays and challenges in accessing care. There is, therefore, a need to implement interventions across the continuum of care and in the community, improving maternal and newborn survival by helping families to adopt sound health practices, identifying high-risk women, encouraging facility delivery, appropriate care-seeking and ensuring timeous referral for mothers at risk of preterm birth and sick preterm newborns. To date, there is little implementation research on establishing a responsive and equitable referral mechanism to facilitate the transfer of women and newborns from home to facilities or between facilities during the small and often fatal window of time around delivery [51-54]. Additionally, due to the insufficient availability and distribution of neonatal intensive care or specialised newborn units in low-resource settings, reliable and well-equipped transportation is often a challenging and neglected missing link to timely emergency care, with systematic reviews indicating scarcity of high-level evidence relating to effective implementation of neonatal transport in developing countries [55-57]. Also of concern is the gap in the quality of inpatient services provided to women and newborns, both in terms of actual facility capability or readiness and provider's knowledge and competencies, with many studies indicating services that are delayed, inadequate, unnecessary, harmful, and disrespectful, and that result in easily avoidable deaths [58-65]. It is, therefore, fitting that the top research priorities identified in this study relate to understanding the impact of skilled birth and neonatal care attendance on newborn outcomes, strengthening referral and transport linkages for critically sick mothers and preterm newborns, evaluating approaches to identifying pregnancies at most significant risk of preterm birth, and improving quality of care for sick preterm newborns at health facilities. The participating experts also emphasised the need for studies to improve the care of preterm newborns at the community level and follow-up of preterm newborns once discharged from facilities. Other global or regional CHNRI priority-setting exercises on maternal and newborn health have also highlighted similar research questions related to breastfeeding [37,66], referral and transport [48,49], improvement in the quality of maternal and newborn care at facilities [37,48], and community-based care [37,49,66].

This priority-setting exercise has also highlighted several epidemiological studies, mainly from experts from Bangladesh, such as determining the prevalence and cause of sepsis in preterm newborns, understanding the effect of antepartum complications, nutritional status or nutritional interventions, ECD interventions on birth outcomes or preterm babies. This indicates that, although there is evidence

from many HICs, there is still a lack of evidence regarding epidemiological studies from many LMICs including Bangladesh [67].

Although most participating experts had experience conducting research in LMICs, we attempted to stratify our analysis based on their geographical location and by expertise of scorers. While our findings indicate a high overlap in the top 20 research priorities, there is a 10%-30% divergence between groups. For example, while international experts have prioritised research related to the implementation of antenatal corticosteroids, determining the effectiveness and cost-effectiveness of various strategies (e.g. CPAP, high flow oxygen, T-piece resuscitation, etc.) for treating preterm infants, the effect of ECD interventions on preterm newborns, epidemiology of nosocomial infections in newborn nurseries or SCANU, experts from Bangladesh ranked them as #36, #49, #48, and #52, respectively; they also focused on questions related to improving care for newborns at the community level in the top 20, which were given lower scored by international participants. Similarly, differences were observed by scorer's expertise, especially those with expertise in LSR, possibly due to the low response in this category (n = 8). Previous exercises have highlighted similar discordance between regional, international, or high and LMIC contexts or by expertise [36,48,68,69]. Despite a general agreement among the key research priorities, this disagreement may be due to differences in the groups' characteristics and differential requirements in the different contexts [36,48,69]. A scoping review of systematic reviews found a lack of primary research evidence on developing and testing interventions for the prevention of spontaneous preterm birth from low-income country settings and emphasised that this may lead to a risk of inappropriate and unsafe recommendations for practice within those contexts [67]. It is, therefore, essential to highlight and consider this disagreement to ensure that funding allocation decisions and proposals for future work are in line with the contextual needs.

Analysis of research questions by criterion revealed how the criteria could be used to determine the strengths and weaknesses of specific research questions [68]. For example, strengthening referral and transport systems for mothers experiencing obstetric emergencies was ranked the #3 research priority in LMICs and received the highest scores in the "equity" criteria. However, it ranked #18 according to the "answerability" criteria, indicating a potential for difficulty in designing and implementing a study to appropriately address this issue.

One of this exercise's main strengths is adapting the CHNRI methodology. Apart from being transparent, structured, and flexible, other practical benefits are its low cost and the ease of conducting it online. However, we also faced some challenges. Our survey response rates were low during the elicitation of research questions and the scoring process. This is not uncommon with this method [31,70] and may result in a self-selection bias. Yoshida et al. [71], however, found that the collective opinion of an expert group in ranking research questions using categorical variables (yes/no/not sure/do not know) stabilises quickly, resulting in a high degree of reproducibility of the top 15-20 ranked research questions with only 45-55 experts [71]. To improve response rates and ensure that a diverse group of

experts participated, we used structured and unstructured methods to list a large pool of experts and sent them regular requests and reminders to participate in the study. We also invited the larger pool of experts (and not only those who submitted research questions) to participate in the scoring process [31], which increased the number of people participating and allowed individuals who were hesitant to provide research questions or may not have had to do so another opportunity to contribute [70]. About half of the experts who participated in the scoring process were from Bangladesh, which enabled us to conduct a country-level analysis and present the findings to key stakeholders at the national level in Bangladesh.

The list of research questions to be scored was also long and time-consuming to collect, resulting in scorer fatigue. For the set of 95 research questions, each respondent had to provide a total of 1425 (95×15) scores, which took over an hour to complete. About 61% of the scorers had completed the scoring process in full, and about 69% scored at least half of the questions. To reduce preferential bias due to scoring fatigue, we randomly presented research questions to each scorer, ensuring that all questions had an equal chance of being scored [48,72] and allowing us to include responses from experts who had scored at least one full question.

Other potential biases inherent in this methodology include the possibility of excluding valuable research ideas during the research question elicitation phase or consolidation phase [31]. While the range of research ideas is infinite, through this process, we obtained a good coverage of ideas related to preventing and managing preterm birth across the four research domains. Additionally, more than 90% of the experts participating in the surveys had experience working in an LMIC setting or Bangladesh, which enhanced the chances of receiving contextually relevant ideas. George et al. [33] suggest that scores for missing research questions could be estimated by relating them to a similar question or having it scored by one or a group of experts and then comparing the scores.

Engaging a diverse group of stakeholders has improved the legitimacy, credibility, inclusiveness, contextual relevance, and ownership of the prioritised research, leading to greater investment opportunities [34,73-75]. However, identifying and engaging stakeholders per the original CHNRI method has been challenging [75]. Following previous exercises [35,76], we asked our technical experts to rank the five pre-selected criteria and participate in the idea generation and scoring processes. They assigned higher scores to "answerability", and "effectiveness" and lowest scores to the "burden reduction" criterion, yet they allocated a greater weight to "effectiveness" and "burden reduction" compared to "answerability" or "delivery". Consequently, we observed changes in ranks between weighted and unweighted scores. However, the top 20 questions remained almost identical [75]. Assignment of domains to research priorities was also prone to subjective variation in the interpretation of domains [36]. To reduce bias, the two primary authors independently assigned domains to the research priorities, and a senior researcher resolved any disagreements.

This exercise drew on the expertise of a diverse group of participants who contributed to and scored questions to develop a set of research priorities that reflect the needs in Bangladesh and other LMICs on prevention and management of preterm birth going forward. The findings provide guidance to national level and LMICs stakeholders on future research investments in the area. Prior reviews of research priority setting exercises have continually stressed the importance of having a dissemination strategy with key stakeholders for optimal uptake of the identified priorities [77]. As such, dissemination will be done with relevant experts and stakeholders including policy makers and programme implementers from the Ministry of Health and Family Welfare, researchers, development partners and donors in Bangladesh. This should be coupled with regular and continuous monitoring of research investments and progress in key standardised outcome indicators related to prevention and management of preterm birth.

3.6   Conclusion

Preterm birth is the leading cause of newborn deaths in LMICs. Achieving the highly ambitious SDG target of reducing neonatal mortality rate (NMR) to ≤12 per 1000 live births will require accelerated efforts to prevent and manage preterm birth and its complications. The findings from this study offer a set of prioritised research questions related to improving the prevention of preterm birth and care and management of the preterm baby, which, we hope, will help bring further attention and more secure funding from donors, researchers and policymakers globally, in LMICs and Bangladesh.

3.7   Declarations

Disclosure of interest: The authors completed the ICMJE Disclosure of Interest Form (available upon request from the corresponding author) and disclose no relevant interests.

Additional material: Online Supplementary Document.

3.8   References

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4   Chapter 4: Research priority setting on prevention and management of pre-eclampsia and eclampsia in LMICs.

In this chapter, I describe the process and results of the research prioritisation activity undertaken for the prevention and treatment of PE/E in LMIC setting. The chapter presents a detailed overview of the CHNRI methodology used, the subsequent identification of key research priorities, implications of the findings and limitations and challenges of the exercise. I designed the study in collaboration, undertook all activities to collect data, conducted all statistical analysis, and wrote the first draft of the paper. This chapter is written in a manuscript format.

4.1   Abstract

Background: Pre-eclampsia and related hypertensive disorders (HDP) affect 5-10% of all pregnancies and are one of the leading causes of maternal and perinatal morbidity and mortality worldwide. Although a threat to both low- and high-income countries, the impact is inequitably distributed and felt severely in countries with limited resources. The "NIHR Global Health Research Group on PReterm bIrth prevention and manageMEnt (PRIME)" therefore, aimed to carry out a globally representative exercise to set research priorities related to the prevention and treatment of pre-eclampsia and eclampsia (PE/E) for low-and middle-income countries (LMICs). The goal was to prioritise research to facilitate the attainment of the 2030 SDG target of maternal and child health and wellbeing.

Methods: The Child Health and Nutrition Research Initiative (CHNRI) method was adapted to set research priorities for prevention and management of PE/E. Forty-nine experts submitted 254 research questions online, which was collated into 76 unique questions and sent for scoring to all experts. Sixty-nine experts scored the questions using five pre-selected criteria: answerability, potential for translation, deliverability, maximum potential for burden reduction, and effect on equity. Weighted and unweighted research priority scores and average expert agreement was calculated and a list of top-ranked research questions for LMICs, Sub-Saharan Africa and South Asia was generated.

Results: The experts prioritised health systems and delivery research uncertainties aimed at enhancing the detection, transfer, and management of women with PE/E. These priorities included reducing delays in care, improving the availability and quality of supplies in facilities, assessing the readiness of service providers and facilities, implementing guidelines, utilizing Magnesium Sulphate, addressing knowledge and skill gaps among service providers, and improving referral systems. Five questions focused on enhancing early identification, screening, diagnosis, and follow-up of women at risk of or with PE/E. Only one discovery research question concerning the development and testing of LMIC specific prediction model ranked among the top 20 priorities. A high overlap was observed between the top 20 research priorities in LMICs and Sub-Saharan Africa, with 16 questions of the top 20 questions in Sub-Saharan Africa appearing in the overall LMIC list.

Conclusions: This exercise has identified key research priorities for preventing and treating pre-eclampsia/eclampsia (PE/E) in LMICs. Addressing these priorities can significantly improve outcomes for mothers and babies in resource-poor settings and contribute to achieving SDG targets in maternal and newborn health. These priorities serve as a valuable resource for health funders, researchers, policymakers, and other stakeholders, informing future research decisions in this area.

4.2 Background

Worldwide, hypertensive disorders of pregnancy (HDPs) including chronic hypertension, gestational hypertension, and pre-eclampsia–eclampsia continue to be one of the leading causes of maternal mortality accounting for 14% of maternal deaths (1-3). About 18 million women suffered from HDPs in 2019 with approximately 27,000 dying (4). There are wide disparities in rates and age-standardized incidence, or prevalence and mortality rates are higher in Sub-Saharan Africa and South Asia and in countries with lower socio-demographic and human development indices (2-5). Among the different HDPs, pre-eclampsia and eclampsia (PE/E) are the most prominent and feared complications, sometimes requiring emergency response (including early caesarean delivery). These conditions significantly increase the risk of maternal and perinatal mortality and morbidity (5, 6). Globally, PE/E affects 3-5% of all pregnancies with wide variations across countries and regions (7-9). A systematic review from 40 countries estimated that 4.6% and 1.4% of all deliveries were complicated by PE/E, respectively (8), whilst other population-based studies reported that 5.7%, 4.3%, 4.7% and 3% of Indian, Pakistani, Mozambican and Nigerian pregnancies were complicated by PE/E (10). PE can lead to various acute maternal complications including severe hypertension, acute renal failure, liver failure, Haemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome, stroke, progression to eclampsia and death. The deleterious impact on the foetus includes intra-uterine foetal growth restriction (IUGR); preterm delivery and its associated complications; and perinatal death (6, 11). In addition, growing evidence indicates increased risks of future cardiovascular, metabolic and renal diseases in both mother and child as well as psychological, neurological and/or behavioural problems in the child (12-17).

Despite being keenly sought, there is no cure for PE/E and the focus of medical interventions revolves around prevention, early identification and diagnosis, stratification of care and timely delivery in foetal and maternal interests. However, the impact of these interventions in reducing adverse pregnancy outcomes over the last few decades has been substantially higher for high -income countries compared to low-income countries. Widespread use of prenatal care with blood pressure and urine protein measurement, increased access to hospital care for timely induction of labour or caesarean delivery for women with severe pre-eclampsia or seizures have led to 90% reduction in the incidence of eclampsia and a 90% reduction in the case fatality rate in women in high income countries (18, 19). In contrast, several challenges in LMICs impede timely and appropriate management of the condition across the pregnancy care continuum including, delays in identification of mothers at risk; delays in seeking care

by women and their families; and poor quality of care during labour, birth and post-partum period due to lack of implementation of management protocols and shortage of drugs, equipment and trained personnel among many others (20-25). The problem is further exacerbated by the uncertainty in its aetiopathogenesis and its largely unpredictable course. Addressing the problem in resource poor settings not only requires large scale implementation of cost-effective integrated maternal and newborn health interventions but also further targeted research to (i) understand gaps in knowledge of causes and pathogenesis of the disease and discover new predictive, preventative and therapeutic strategies; (ii) generate evidence on how best to deliver at scale and increase coverage of cost-effective and comprehensive package of evidenced based interventions; and (ii) improve data for understanding the burden and measuring changes.

Achieving the SDG target for maternal and newborn mortality, particularly in LMICs, will require investments in key contributors one of which is PE/E. However, despite increased attention to maternal and newborn health research, resources and funding in LMICs are still limited and there is a need to guide government, funders and research organisations on how best to develop a contextually relevant and impactful research agenda to address the burden of PE/E in the SDG era. Although Souza et al (2014) used the CHNRI method to identify key research priorities to accelerate improvement in maternal and perinatal health for the next decade (2015-2025), the broad scope of their exercise limited prioritisation of research specific to prevention and treatment of pre-eclampsia and eclampsia (26). Recognising the limitations in research for the prevention and treatment of PE/E in LMICs and being aware of the importance of targeting and prioritising research in resource limited settings the Global Health Research Group on prevention and management of preterm birth (PRIME) in partnership with Universities in Nigeria conducted a research priority setting exercise in 2020-2021 using the Child Health and Nutrition Research Initiative (CHNRI) method. The aim was to determine research priorities specific to management and treatment of PE/E in LMICs. Given the high burden of PE/E in several Sub-Saharan countries including Nigeria (4, 8, 10, 27, 28), and its contribution to indicated as well as spontaneous preterm birth we partnered with Universities in Nigeria to implement this research prioritisation activity.

4.3   Methods

An adapted CHNRI method (29) was used to set research priorities related to prevention and treatment of pre-eclampsia and eclampsia in LMICs. Figure 4-1 describes the four key steps of the CHNRI method adapted for the PE/E research prioritisation exercise.
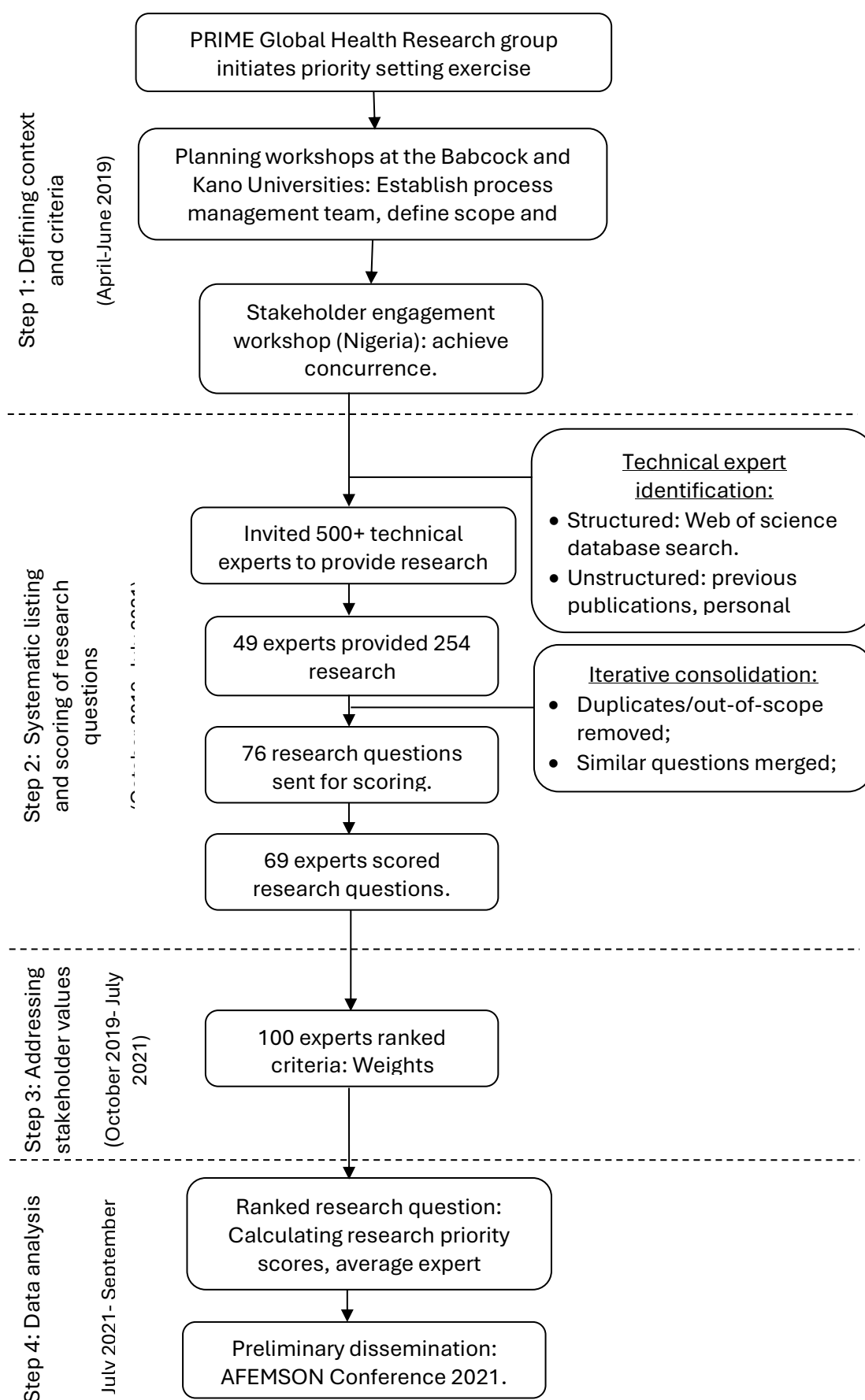
Figure 4-1. Steps in the CHNRI research priority setting process

4.3.1 Step 1: Establishing the process management team, defining the scope and criteria

Two planning workshops were conducted by the PRIME global health research group in Nigeria in April and June 2019 to initiate the research priority setting exercise. A process management team comprising of researchers from The University of Sheffield, and the Universities of Benin, Babcock and Kano in Nigeria was formed who carried out the priority setting exercise. The team included biomedical scientists, public health researchers, social scientists with experience in conducting maternal, perinatal and newborn health research, as well as clinicians.

The aim of this exercise was to identify research questions that would help reduce the burden of maternal, foetal and newborn mortality and morbidity due to PE/E in LMICs by 2030 in line with global SDG targets. (Table 4-1). It was agreed that the 4D-framework proposed by Rudan et al (2008) would be used to systematically list the research questions into the four themes across the development continuum (30):

- description (epidemiologic research to identify burden and risk factors);
- discovery (research to discover new innovative interventions or strategies);
- development (research to develop/improve existing interventions or strategies); and
- delivery (health policy or systems research to optimise health status of the population of interest).

The team also reviewed the criteria to be used for discriminating the potential research questions, identified by Rudan et al (2008), and from previous exercises. The team agreed on the following criteria and sub-criteria to score research questions: answerability; deliverability; maximum potential to reduce disease burden; equity; and maximum potential for translation (Table 4-1 List of selected criteria and sub-criteria used to score research questions and weights).

Table 4-1 List of selected criteria and sub-criteria used to score research questions and weights

Criteria	Explanation/sub-criteria	Weights
Answerability: The research question can be ethically answered	Based on clarity of research question, required research capacity, current knowledge and ethical considerations: Would you say that the question can be answered in ethical way?	0.88
Potential for translation: The research question will generate knowledge that can	Would you say that the research question will generate knowledge that can be translated into health intervention or will lead to improvement in health interventions?	1.08

Criteria	Explanation/sub-criteria	Weights
be translated into health intervention		
Deliverability: The intervention resulting from the research question will be deliverable	Considering the infrastructure, resources required and users, would you say that the proposed research will lead interventions/strategies that would be deliverable and scalable within the context of interest?	0.99
Maximum impact on burden: The research question has greater potential to reduce disease burden	Would you say that the result of the research is likely to reduce maternal and/or newborn mortality due to pre-eclampsia or eclampsia?	0.97
	Would you say that the result of the research is likely to reduce maternal and/or newborn morbidity due to pre-eclampsia or eclampsia?	
Equity: The intervention resulting from the research will be accessible to vulnerable groups thus decreasing equity	Would you say that the underprivileged and vulnerable would be the most likely to benefit from the results of the proposed research after its implementation?	1.08
	Would you say that the proposed research has the potential to improve equity in the population by 2030?	

4.3.2 Step 2: Systematic listing and scoring of research questions

A combination of structured and unstructured approaches was used to identify over 500 experts in the field of pre-eclampsia and eclampsia research. The structured process included a bibliometrics search of the Web of Science Core Collection database with keywords *pre-eclampsia* or *eclampsia* to identify the most scientifically productive researchers. These were authors with 15 or more publications as first, second or senior author of 50 most cited papers. In order to ensure representation from LMICs, authors with 5 or more relevant publications from LMIC countries were also included. The unstructured processes included identifying experts from relevant reports e.g., WHO guideline on pre-eclampsia and eclampsia and prior CHNRI exercises (26) and personal communication. Experts invited to participate in the exercise were also asked to share the invitation with other experts.

An online survey was created using SurveyMonkey Inc (San Mateo, California, USA) and identified experts were invited via email to participate and provide 1-3 research questions for each research

domain in the 4D framework. Forty-nine (49) experts provided 254 research questions (Figure 1). Experts with a wide range of skills provided research questions, but those involved in clinical services (n=31, 63%), clinical science research (n=28, 57%) and public health and health systems research (n=15, 31%) were the main providers (Table 2). About 78% of the experts had experience in working in a LMIC context and there was representation from all regions, including Sub-Saharan Africa (n = 31, 63%), South Asia (n=10, 20%) and Europe and Central Asia (n=16, 33%) (

Table 4-2).

The original research questions were iteratively reviewed by the process management team to consolidate them into a smaller list of 76 research questions. During this process, duplicates or overlapping questions and those beyond the scope of the exercise were eliminated, similar ideas were merged, and wordings refined to ensure clarity of the questions included. In May 2021, we emailed the larger pool of over 500 experts and requested them to participate in another online survey developed using Qualtrics to evaluate the 76 research questions. For each research question, experts were asked to answer, "I agree" (1 point); "I neither agree nor disagree" (0.5 point); "I disagree" (0 points); "Not well informed" (blank) to the 7 sub-criteria set for this exercise. Research questions were randomly presented to experts to mitigate bias due to scorer fatigue and responses were considered valid if at least one question was fully scored. Sixty-nine respondents participated in the scoring process with 48 participants (70%) completing the entire scoring process and 54 (78%) completing over 50%. The basic characteristics of participants were similar to that of the first **survey (**

Table 4-2). Clinicians (n=41, 66%), followed by clinical science (n=34, 55%) and public health (n=20, 32%) researchers were more likely to participate in the scoring process. Also, majority of those who participated in the scoring process were from Sub-Saharan Africa (n= 35, 57%) or South Asia (n=19, 31%). Among those who completed the scoring process and provided background information, 20% (n=12) were involved only in research; 26%(n=16) were not researchers and involved in either providing direct health care or policy and programme implementation; and 54% (n=33) were involved in research as well as direct health care or policy and programme implementation. Non-responders in both the surveys were followed-up up to two times to increase response rates.

Table 4-2 Characteristics of technical experts participating in the first and second online surveys

	Survey 1: Listing research questions (n=49)	Survey 2: Scoring research questions (n=62*)	Survey 1& 2: Ranking Criteria (n=100)
Area of expertise, n (%)			
Laboratory science research	10(20.4)	6(9.7)	13(13)
Clinical science research	28(57.1)	34 (54.8)	57(57)
Public health and health systems research	15 (30.6)	20 (32.3)	31(31)
Policy and programme implementation	5 (10.2)	15 (24.2)	21(21)
Clinical services (Direct health care)	31(63.3)	41 (66.1)	62(62)
Others	8 (16.3)	8 (12.9)	11(11)
Region of work			

South Asia	10 (20.4)	19(30.7)	24(24)
Europe and Central Asia	16 (32.7)	13 (21)	28(28)
Middle East and North Africa	5 (10.2)	3 (4.8)	5(5)
East Asia and Pacific	3 (6.1)	4(6.5)	6(6)
Latin America and Caribbean	6 (12.2)	5(8.06)	9(9)
Sub-Saharan Africa	31 (63.3)	35(56.5)	59(59)
North America	6 (12.2)	3(4.8)	8(8)
Experienced in working in LMIC, n (%)	38(77.6)	53 (85.5)	82(82)
Years of experience in working in LMICs, mean (SD)/Median (range)	16.8 (10.8)/ 14.5(1-40)	16.8 (9.8)/ 15 (1-45)	15.7(9.2)/ 15 (1-45)
Years of experience in working in maternal, perinatal or newborn health, mean (SD)	20.1 (10.4)/ 20 (1-40)	18.4 (10.3)/ 15.5 (3- 45)	17.9(9.5)/ 19(1-45)

*Details of 7 experts not available; SD=Standard Deviation

4.3.3 Step 3: Addressing stakeholder values

Two workshops were conducted in Nigeria involving key stakeholders (policy makers and programme implementers, public health professionals, researchers, and health care service providers) to orient them to the research prioritisation process and ensure their concurrence and participation. In addition, experts participating during the process of listing and scoring of research questions were asked to rank the criteria used to score research questions using a five points Likert scale (1 = least important; 5 = most important). Among the experts reached out to during either of the surveys, 100 ranked the criteria. The criteria for potential for translation (3.25), Equity (3.24), deliverability (2.96) received the highest ranks followed by impact on burden (2.91) and answerability (2.64).

4.3.4 Step 4: Data analysis

Data analysis was conducted according to the methods outlined by Rudan et al (2008) (31) and intermediate, un-weighted and weighted and research priority scores (RPS) were calculated for each of the five scoring criteria used to prioritise the 76 research questions for this exercise. The intermediate RPS for each research question was calculated by summing all the informed answers ("1," "0," or "0.5") and dividing this sum by the number of informed answers. Experts who lacked the necessary knowledge to accurately score a research question against each criterion were permitted to withdraw from answering. They could indicate their lack of information or expertise by selecting the option 'not well informed (blank)' instead of providing a potentially inaccurate or biased score. These responses were

left out of the calculation, both in the numerator and denominator (28). The un-weighted RPS was then calculated as the mean of all five intermediate priority scores.

The ranks obtained for each criterion were then converted to weights. This was done by dividing the observed average rank for each criterion by the expected average rank (i.e., 3.00) assuming that all criteria are equally valued. The weights obtained were multiplied with the intermediate scores of each criterion to calculate weighted intermediate scores and the weighted RPS was computed as the mean of all the weighted intermediate scores. For each scored research question, the intermediate score for potential for translation and equity were increased by 8% whereas deliverability, impact on burden and equity were reduced by 1%, 3% and 12% respectively (Table 4-1).

Average expert agreement (AEA), measured as the proportion of scorers who gave the same most frequent response for all the informed answers ("1," "0," or "0.5"), was calculated for each research questions using the formula below (31).

$$AEA = \frac{1}{15}\sum_{q=1}^{15} \frac{N\left(Scorers\,who\,provided\,most\,frequent\,response\right)}{N\left(Scorers - those\,who\,scored\,\,"not\,well\,informed"\right)}$$

Sub-groups analysis was done to see variation in research priorities by the scorer's region of work (Sub-Saharan Africa and South Asia) and by their expertise (e.g., direct health care providers vs. health systems researchers).

4.4   Results

4.4.1 Research priorities for LMICs

Table 4-3 presents ranked research questions, the intermediate scores in each criterion, overall unweighted and weighed RPS and AEA. The overall weighted RPS for the 76 proposed research questions ranged from 55.0% (lowest ranked research priority) to 95.8% (highest ranked research priority). The level of agreement between the 69 experts ranged from 46% to 93%. In line with previous CHNRI exercises, higher agreement among experts was observed for research questions that also received high overall priority score.

The top-ranked research priority was to evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs (#1). Among the top 20 research priorities for LMICs (**Error! Reference source not found.**), five focused on improving care at health facilities including improving the availability of supplies (e.g., drugs, blood etc.) to manage PE/E (#2), understanding determinants of type-3 delay (#4), investigating availability, adherence and barriers to implementation of PE/E related guidelines (#6), assessing readiness of health facilities and providers (#7), and effectiveness of quality improvement initiatives (audit, death registration etc.) (#10). Several questions were related to early detection, diagnosis, screening or follow-up. These included broad questions on developing and evaluating strategies for early diagnosis/screening (#8), follow-up (#3), the use of

prediction models (#11), or to motivate early antenatal checkups (#5). Two questions were raised on the use of specific interventions, scaling up of midwifery services (#15) and using community health workers in monitoring BP (#13), to improve screening and management of women with PE/E in LMICs. Questions in the top 20 also focused on treatment using specific drugs. For example, two research questions focused on determining factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities (#9) or assessing the feasibility, safety, and efficacy of loading dose magnesium sulphate at the primary care level (#18). Similarly, two other questions on treatment using Aspirin aimed to know the best time to commence low dose Aspirin in women with previous history of PE/E (#12) and the effect of low dose Aspirin on minimization of PE or preventing recurrent PE in high-risk women (#16). Other questions in the top 20 were on assessing knowledge and skills of service providers (#14), on understanding challenges with the referral process of women with PE/E from one facility to another (#17) or developing strategies for improving referral of critically ill women and neonates (#20) and determining maternal, foetal or newborn outcomes for women with PE/E. Majority of the top 20 research questions (n=10, 50%) were categorised as delivery research, three as descriptive, one as discovery, whilst the others were categorised into multiple domains (n=6).

Table 4-3. Ranked research questions for LMICs (n = 69) with scores for each criterion, overall unweighted and weighted RPS, and AEA

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	3	4	7	2	1	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.980	0.970	0.939	0.965	0.939	0.959	0.958	0.931
2	2	2	2	5	5	6	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	0.981	0.981	0.944	0.948	0.906	0.952	0.951	0.909
3	4	19	6	2	1	5	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.940	0.960	0.959	0.969	0.911	0.948	0.948	0.897
4	3	4	7	9	3	3	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.978	0.956	0.933	0.951	0.922	0.948	0.947	0.918
5	5	7	12	11	11	2	Evaluate strategies to motivate and facilitate early and continual	Del	0.972	0.953	0.931	0.923	0.933	0.942	0.942	0.888

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
							antenatal care check-ups for women in LMICs.									
6	6	18	3	1	6	22	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.945	0.973	0.962	0.945	0.866	0.938	0.937	0.871
7	7	9	5	4	9	20	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.964	0.964	0.952	0.936	0.867	0.937	0.935	0.890
8	8	8	1	23	4	9	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del/Dis	0.965	0.982	0.882	0.949	0.891	0.934	0.933	0.886
9	9	11	14	16	8	7	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	0.964	0.945	0.917	0.940	0.898	0.933	0.932	0.889
10	10	22	11	3	12	12	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.936	0.954	0.953	0.917	0.887	0.929	0.929	0.869
11	11	23	17	8	7	14	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	0.936	0.929	0.936	0.945	0.881	0.925	0.924	0.872
12	12	14	10	6	16	26	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	0.954	0.954	0.941	0.909	0.854	0.922	0.921	0.864
13	13	24	9	15	17	10	Asses the effectiveness of community health workers in monitoring blood pressure to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.936	0.955	0.917	0.900	0.891	0.920	0.920	0.857
14	14	20	16	18	18	8	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	0.939	0.938	0.909	0.900	0.892	0.915	0.915	0.851
15	15	15	20	31	10	4	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	0.952	0.920	0.860	0.925	0.912	0.914	0.913	0.858
16	16	32	18	10	13	19	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.926	0.926	0.933	0.915	0.868	0.914	0.913	0.874
17	17	36	35	14	14	11	What are the challenges encountered in referring a pre-eclamptic/eclamptic	Del/Desc	0.922	0.882	0.920	0.915	0.890	0.906	0.905	0.841

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
							patient from one health facility to another?									
18	18	28	22	19	15	23	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	0.933	0.913	0.902	0.912	0.863	0.905	0.903	0.866
19	19	1	8	22	33	35	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	0.991	0.955	0.889	0.854	0.827	0.903	0.901	0.837
20	20	16	19	26	19	24	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.952	0.922	0.873	0.899	0.861	0.901	0.900	0.812
21	21	12	15	21	25	28	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	0.955	0.938	0.891	0.873	0.844	0.900	0.899	0.823
22	23	42	13	17	30	29	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	0.913	0.952	0.912	0.863	0.840	0.896	0.896	0.819
23	22	13	28	24	26	15	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.955	0.902	0.875	0.868	0.880	0.896	0.895	0.792
24	24	29	25	13	36	17	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.933	0.904	0.920	0.845	0.872	0.895	0.894	0.801
25	25	5	30	30	29	21	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.974	0.895	0.861	0.863	0.866	0.892	0.890	0.839
26	26	46	29	27	21	13	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.900	0.902	0.870	0.881	0.884	0.887	0.887	0.819
27	27	10	39	43	20	16	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	0.964	0.879	0.830	0.883	0.875	0.886	0.884	0.843
28	28	21	21	41	27	18	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	0.938	0.920	0.833	0.866	0.868	0.885	0.884	0.812
29	29	34	23	12	41	32	How can we standardise and improve data collection regarding maternal	Dev	0.925	0.912	0.922	0.824	0.830	0.882	0.881	0.786

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
							and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?									
30	30	17	32	25	35	33	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.946	0.893	0.873	0.849	0.829	0.878	0.876	0.799
31	31	31	26	20	44	34	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	0.930	0.904	0.898	0.819	0.827	0.876	0.874	0.781
32	32	30	27	45	24	30	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.931	0.902	0.823	0.875	0.838	0.874	0.873	0.790
33	33	53	40	34	22	25	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.886	0.878	0.852	0.881	0.856	0.871	0.870	0.788
34	34	47	38	37	40	27	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium Sulphate for pre-eclampsia/eclampsia in LMICs.	Del	0.898	0.880	0.843	0.838	0.852	0.862	0.861	0.831
35	35	48	41	28	34	37	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.898	0.870	0.867	0.852	0.820	0.861	0.860	0.769
36	36	25	37	33	38	43	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.934	0.880	0.853	0.840	0.786	0.859	0.856	0.776
37	37	26	43	42	39	36	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	0.934	0.860	0.833	0.838	0.820	0.857	0.855	0.776
38	38	40	45	32	42	31	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.915	0.852	0.858	0.821	0.830	0.855	0.854	0.817
39	40	59	31	35	23	42	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.854	0.894	0.851	0.875	0.787	0.852	0.852	0.799
40	39	6	24	44	45	50	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	0.972	0.907	0.827	0.810	0.752	0.854	0.850	0.770

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
41	41	58	42	38	28	41	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.866	0.866	0.843	0.864	0.795	0.847	0.846	0.772
42	42	63	34	46	31	38	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.816	0.892	0.823	0.857	0.816	0.841	0.842	0.770
43	44	60	36	29	37	47	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.833	0.880	0.867	0.845	0.773	0.840	0.839	0.772
44	43	54	44	40	32	44	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.873	0.855	0.836	0.856	0.782	0.840	0.839	0.757
45	45	38	51	36	53	45	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.921	0.830	0.848	0.772	0.777	0.830	0.827	0.692
46	46	39	48	48	46	48	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.918	0.840	0.816	0.801	0.768	0.829	0.826	0.726
47	47	41	49	39	56	49	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing PE and improving neonatal outcomes in LMICs?	Desc	0.915	0.840	0.837	0.755	0.764	0.822	0.820	0.740
48	48	45	52	47	57	40	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.909	0.827	0.817	0.748	0.804	0.821	0.819	0.731
49	49	33	46	67	43	46	Can (self) home-based blood pressure monitoring improves identification of women at risk of pre-eclampsia and eclampsia in LMICs?	Del/Desc	0.926	0.849	0.689	0.821	0.776	0.812	0.810	0.749
50	50	55	53	52	48	39	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.870	0.800	0.776	0.785	0.816	0.809	0.808	0.726
51	52	43	33	61	55	55	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.913	0.892	0.721	0.760	0.733	0.804	0.802	0.691
52	51	35	47	57	49	57	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.923	0.843	0.740	0.784	0.730	0.804	0.801	0.698

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
53	53	27	57	53	54	52	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.933	0.783	0.761	0.766	0.744	0.798	0.793	0.702
54	55	61	55	51	47	51	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	0.833	0.793	0.783	0.786	0.750	0.789	0.787	0.711
55	54	49	50	49	52	66	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.894	0.833	0.788	0.775	0.665	0.791	0.787	0.694
56	56	52	61	60	51	54	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.888	0.770	0.724	0.777	0.737	0.779	0.776	0.640
57	57	66	56	50	50	58	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.811	0.784	0.786	0.779	0.725	0.777	0.776	0.663
58	58	56	67	54	59	60	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.870	0.745	0.760	0.733	0.712	0.764	0.760	0.636
59	59	69	54	55	61	61	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.794	0.800	0.755	0.729	0.701	0.756	0.755	0.652
60	61	65	66	58	64	59	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.814	0.745	0.735	0.702	0.725	0.744	0.743	0.642
61	60	44	70	66	60	63	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	0.913	0.722	0.693	0.730	0.678	0.747	0.742	0.649
62	62	50	60	73	58	65	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.892	0.774	0.615	0.743	0.672	0.739	0.735	0.627
63	63	62	64	68	66	53	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.830	0.750	0.677	0.687	0.738	0.736	0.735	0.608
64	65	70	62	56	69	67	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.792	0.760	0.740	0.673	0.663	0.726	0.724	0.616
65	66	67	73	62	65	56	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.808	0.690	0.710	0.689	0.731	0.726	0.723	0.584

Rank (weighted)	Rank (unweighted)	Rank (answerability)	Rank (Translation)	Rank (Deliverability)	Rank (Burden)	Rank (Equity)	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
66	64	57	71	69	62	62	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.869	0.713	0.659	0.718	0.679	0.727	0.723	0.603
67	67	51	63	59	71	70	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.889	0.755	0.725	0.605	0.624	0.720	0.715	0.560
68	68	72	59	64	63	69	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.731	0.774	0.702	0.715	0.649	0.714	0.714	0.618
69	69	68	68	63	73	68	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.808	0.740	0.706	0.596	0.660	0.702	0.700	0.580
70	70	74	65	65	68	64	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.695	0.750	0.700	0.676	0.675	0.699	0.700	0.562
71	71	37	72	70	70	72	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.922	0.708	0.653	0.613	0.586	0.696	0.690	0.562
72	72	71	58	71	72	71	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.780	0.776	0.650	0.605	0.602	0.683	0.681	0.540
73	73	64	69	74	67	74	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.816	0.724	0.583	0.682	0.547	0.671	0.666	0.561
74	74	73	74	76	74	75	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.724	0.684	0.462	0.588	0.500	0.591	0.589	0.506
75	75	76	76	72	76	73	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.602	0.592	0.625	0.495	0.569	0.577	0.576	0.442
76	76	75	75	75	75	76	How can MRI aid in the diagnosis of foetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.674	0.616	0.477	0.551	0.448	0.553	0.550	0.458

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

4.4.2 Top ranked priorities across research criteria in LMICs

We also ranked research ideas by specific criteria.

Table 4-4 presents the top three ranked research questions by the criteria whilst **Error! Reference source not found.** also presents the criteria-based rankings for all 76 research questions. When research ideas were considered by the answerability criterion, questions that received maximum score were determining maternal, foetal and newborn outcomes among women with PE/E, followed by evaluating innovative strategies to improve the availability of supplies and reducing delays across the care pathway for women with PE/E. According to scorers, the greatest impact on burden was associated with ideas that aimed to evaluate strategies to improve follow-up and management and reduce delays for women with PE/E. There was high agreement among scorers that research questions focusing on evaluating strategies to reduce delays, motivating and facilitating early antenatal checkups, and determining determinants of type three delay would enhance equity. Research questions on developing and evaluating strategies for early diagnosis and screening, improving supplies, and investigating availability, adherence, and barriers to implementation of relevant guidelines scored high for the criteria potential for translation. Based on deliverability, assessing effectiveness of quality improvement initiatives in improving management of PE/E in health facilities received was ranked as one of the most deliverable questions.

Table 4-4 Top three (3) research ideas by criteria

Rank	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
Answerability										
1	What are the maternal, foetal and newborn outcomes in	Desc	0.991	0.955	0.889	0.854	0.827	0.903	0.901	0.837

Rank	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation [...] RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
	women with pre-eclampsia/eclampsia in LMICs?									
2	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	0.981	0.981	0.944	0.948	0.906	0.952	0.951	0.909
3	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.980	0.970	0.939	0.965	0.939	0.959	0.958	0.931
Potential for translation										
1	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	0.965	0.982	0.882	0.949	0.891	0.934	0.933	0.886
2	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	0.981	0.981	0.944	0.948	0.906	0.952	0.951	0.909
3	Investigate availability, adherence, and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.945	0.973	0.962	0.945	0.866	0.938	0.937	0.871
Deliverability										
1	Investigate availability, adherence, and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.945	0.973	0.962	0.945	0.866	0.938	0.937	0.871
2	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/ Dev	0.940	0.960	0.959	0.969	0.911	0.948	0.948	0.897

Rank	Research question	Domain[1]	Answerability intermediate RPS	Potential for translation RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
3	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.936	0.954	0.953	0.917	0.887	0.929	0.929	0.869
Impact on burden										
1	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/ Dev	0.940	0.960	0.959	0.969	0.911	0.948	0.948	0.897
2	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.980	0.970	0.939	0.965	0.939	0.959	0.958	0.931
3	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del /Desc	0.978	0.956	0.933	0.951	0.922	0.948	0.947	0.918
Equity										
1	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.980	0.970	0.939	0.965	0.939	0.959	0.958	0.931
2	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	0.972	0.953	0.931	0.923	0.933	0.942	0.942	0.888
3	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del /Desc	0.978	0.956	0.933	0.951	0.922	0.948	0.947	0.918

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score;

AEA= Average Expert Agreement

4.4.3 Research priorities identified by experts who had experience in working in Sub-Saharan Africa and South Asia.

Subgroup analyses was conducted by scorers who had experience in working in Sub-Saharan Africa (n=35) (Annex 2) and South Asia (n=19) (Annex 3). Analysis was not done for other locations due to the small number of scores from each region. Ranks for each research priority between these groups were also compared with the overall LMIC scores (Annex 4). Ranks within the subgroups that deviate by more than 10 points compared to the ranks in LMICs are marked with an asterisk (*) (Annex 4).

For Sub-Saharan Africa, the RPS ranged from 0.975 to 0.502, and the AEA ranged from 0.945 to 0.460 (Annex 2). The top ranked priorities were determining the determinants of type-3 delay in the treatment of PE/E (#1), determining the factors that influence the use of Magnesium Sulphate at different tiers of health facilities (#2) and evaluating strategies to reduce delays across the care continuum (#3). A high overlap was observed between the top 20 research priorities in LMICs and Sub-Saharan Africa, with 16 questions of the top 20 questions in Sub-Saharan Africa appearing in the overall LMIC list (Table 3C in Annex). Other priorities identified for Sub-Sahara Africa included improving screening, detection and management of hypertension and pre-eclampsia postpartum; exploring barriers and challenges to early identification of high-risk women; evaluating the use of digital technologies in improving diagnosis and monitoring of PE/E and assessing the effectiveness of anti-hypertensive medications for the treatment of PE/E.

For South Asia, the RPS ranged from 0.988 to 0.548, and the AEA ranged from 0.978 to 0.511 (Annex 3). The top ranked priorities were assessing the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium Sulphate (#1), exploring barriers and challenges to early identification women at high risk of PE/E (#2), and developing and evaluating strategies for early diagnosis/screening of women at risk of PE/E (#3). A considerable difference was seen between the top 20 research priorities in LMICs and South Asia, with only 12 questions of the top 20 in South Asia appearing in the overall LMIC list (Appendix table 3c). Several other questions not appearing in the overall LMIC and Sub-Saharan Africa list were prioritised including establishing PE registry, evaluating the impact of education and awareness on PE/E outcomes, exploring knowledge, awareness and practice of communities and families on PE/E, and evaluating the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of PE.

4.4.4 Research priorities segregated by expertise of scorers

Research priorities were also analysed according to the expertise of the scorers (Annex 5-9). Ranks for each research priority between these groups were also compared with the overall LMIC scores (Table 3I in Annex). Again, ranks within the subgroups over a 10-point deviation from the LMIC ranks are marked with an asterisk (*) (Annex 10). Differences were seen between the top 20 LMIC rank and the sub-groups, with the highest overlap being with those involved in direct clinical services (80%, 16

questions overlapped), followed by those involved in clinical science (75%, 15 questions overlapped) or public health and health systems research (75%, 15 questions overlapped). Least overlap was seen with those involved in policy or programme implementation and laboratory science research.

4.5 Discussion

4.5.1 Main findings

This priority setting exercise represents the consensus of a large number of global experts in identifying research priorities to reduce the burden of PE/E in LMICs by 2030. The participating experts prioritised health systems and delivery research uncertainties that would help improve detection, transfer and management of women with PE/E. This pattern mirrors other CHNRI exercises, where implementation, health policy and systems research questions tend to receive higher prioritisation compared to other research types. This is primarily due to their potential to address disease burden more rapidly and be more impactful, particularly in resource-poor settings. (26, 32, 33). Health systems questions to improve transfer and management focused on reducing delays to care, improving availability of supplies and quality of care in facilities, assessing readiness of service providers and facilities, implementing guidelines in facilities, utilising Magnesium Sulphate, assessing gaps in knowledge and skills of service providers and improving referrals to optimal facilities and care providers. Further five questions were related to improving early identification and screening, diagnosis, and follow-up of women at risk of or with PE/E. Only one question related to the discovery of new intervention (developing and testing prediction models suitable for use in LMICs) was proposed in the top 20. The positive association seen between expert agreement and research priority scores indicate substantial agreement in the high ranked priorities among experts

4.5.2 Findings in the context of the literature

To our knowledge this is the first research prioritisation exercise to focus on PE/E, a major cause of maternal mortality and morbidity in LMICs, as well as a cause of perinatal morbidity and mortality from preterm birth, and fetal growth restriction. This priority setting exercise is one of few that specifically focuses on the burden of PE/E in low resource settings. Its implementation will contribute to addressing the SDG targets for maternal and newborn health in resource poor settings. A few other priority setting exercises have identified research priorities related to hypertensive disorders of pregnancy or PE/E (26, 33-35). However, the context of these studies were either global or a HIC or the focus was on overall maternal health which limited the ability of the exercises to prioritise uncertainties related to PE/E in low resource settings (26). For example, Souza et al (2014), in their CHNRI exercise to determine maternal and perinatal health research priorities beyond 2015, identified several research questions to address the global burden of hypertensive disorders of pregnancy (26). None of the questions featured in the top 20 but comprised 14% of the questions in the upper quartile (top 56). These included questions on evaluating the effectiveness/cost-effectiveness of different

strategies such as screening, increasing access to Magnesium Sulphate use, primary care management, minimum dose of calcium for prevention, implementation of guidelines and training of community health workers in screening and detection (26, 33). Similarly, only one research idea on pregnancy induced hypertension was prioritised by Alobo et al (2021) in their CHNRI exercise for identifying maternal and newborn health priories in Africa and was on developing strategies to improve detection of pregnancy-induced hypertension at the primary care level (33). Other priority setting exercises focusing on maternal, newborn and child health in India and Ethiopia identified priorities related to antenatal care adherence, health facility documentation of MNCH outcomes, identification of main causes of intrapartum mortality, development of algorithms for severe acute maternal morbidity (SAMM), and improving referral of high risk pregnancies, maternal death audits and emergency obstetric care services, which may have positive affect on outcomes related to PE/E in addition to other indicators on maternal health (36, 37). Ho et al (2019) used the James Lind Alliance approach to identify research priorities for pregnancy hypertension in the UK, which gives a good indication of how priorities may vary or be similar between high and low resource settings (34). Identifying the best screening test, identifying the causes of pregnancy hypertension, appropriate management, prevention of hypertension in future pregnancies, predicting and preventing short-term and preventing long-term complications, identifying long-term physical and mental health consequences, provision of support for women and their families were some of the uncertainties highly prioritised for UK throughout the process (34).

Experience from high-income countries and recent evidence from low resource settings have highlighted that a well-functioning health care system capable of detecting and diagnosing PE/E at the community or primary care level together with appropriate care at higher level facilities (e.g., competent well-trained providers, adequate equipment, and medications) is crucial for reducing morbidity and mortality associated with PE/E in LMICs (18, 19, 38-42). The research agenda generated by the experts in this priority setting exercise has mostly aimed to address these gaps in the health systems in LMICs. The identified research questions have attended to key phases in the care continuum with a focus on improving detection, ensuring transfer to higher levels of care and appropriate care at the health facility in LMICs. It is important to note that, although research and publication on PE/E has doubled since 2012, majority are conducted in developed countries with only 10 countries accounting for about 70% of the global total research (3).

Identifying women at risk of or with pre-eclampsia is the first step necessary to provide adequate care and requires access to early and regular antenatal care, as rightfully identified by experts in this priority setting exercise (#5 and #8 in LMIC and Sub-Saharan Africa ranking). World Health Organization (WHO) has increased the minimal number of visits from four (4) to eight (8) mostly to increase the possibility of identifying and treating more women for PE/E (43). However, the coverage and quality of ANC varies in LMICs with multifaceted barriers to access and implementation including health

systems, geographic, economic, cultural and societal, psychosocial and gender related (44-53) that needs to be addressed. Strategies to screen and predict PE in LMICs has also been highlighted by the experts in this exercise. Current screening strategies use either clinical risk factors, maternal plasma or serum biomarkers, imaging modalities or a combination of approaches (54-56). Systematic reviews have identified over 40-60 prediction models (57, 58). However, most models are developed with data and assumptions from developed countries and are rarely validated internally, externally or for use in LMICs (55-59). Improving screening and prediction in LMICs will require strategies that are cost-effective and feasible to implement in low resource and low literate settings (20, 58, 59).

Experts in this exercise have also prioritised ideas on developing strategies to reduce delays and improve referral. Other related questions were on scaling of midwifery services, administration of Magnesium Sulphate at the primary care level, use of BP machines by community health workers, or digital technologies to improve identification, diagnosis and management of PE/E. Task sharing particularly at the community and primary health care level using health workers has been advocated as one of the strategies to improve detection, reduce delays, and triage women at risk (20, 40, 60, 61). Recent evidence highlights challenges in using community health workers (CHWs) and emphasises that CHWs can be effective in detection, triage and referral provided that they are appropriately selected, trained, supervised and have adequate supplies, medicines, and equipment (20-22, 59-66). Use of digital technologies has been found to be promising with systematic reviews suggesting the need for further prospective experimental and longitudinal studies prior to recommending the use of digital health interventions for PE/E (67). Recent evidence also stresses that, community level interventions without health systems strengthening and improvement at the facility level is not effective in reducing outcomes related to PE/E (38, 40). As such, research questions identified in this exercise focus on improving gaps in services that are related to availability of supplies, implementation of guidelines, readiness of health facilities and service providers, knowledge and skills of service providers, quality improvement, third delay in management and referral as indicated by findings in some LMICs (20, 21, 23, 25, 62, 63).

The analysis was segregated based on the expert's region of work (Sub-Saharan Africa, South Asia) and by their expertise. The findings indicate a 60-80% overlap between the overall LMIC priority and the different regions and a 30-80% overlap by expertise. The disagreement has been highlighted by prior exercises and may be due to differences in the groups' characteristics and differential requirements in the different contexts (26, 33, 68-70). However, the overlap in research questions increased with the increasing number of experts in the sub-group and should be carefully considered while making decisions on research investments.

Research questions were analysed by criterion and revealed how the criteria could be used to determine the strengths and weaknesses of specific research questions (69). For example, determining maternal, foetal and newborn outcomes in women with PE/E in LMICs was ranked #1 in 'answerability' but ranked #33 and #35 in the 'burden' and 'equity' criteria, respectively. This indicates that while this

question is answerable, addressing these questions may not result in sufficient reduction in burden or address equity. Similarly, the research question on evaluating strategies to reduce delays across the care pathway for women with PE/E in LMICs was ranked highly in all the criteria but was #7 for 'deliverability' indicating a potential difficulty in implementing a deliverable and scalable intervention to address the issue.

4.5.3 Research and policy implications

This exercise drew on the expertise of a diverse group of experts who contributed to the development of a list of ranked research priorities for the prevention and management of PE/E in LMICs in the SDG era. The top 10 research questions, as summarised in Table 4-5, primarily concentrate on research aimed at different stages of care to not only pinpoint obstacles and implement strategies for streamlining the care pathway for high-risk women but will also facilitate the implementation of WHO recommendations on PE management (71). These questions are tailored to address the burden of PE/E in LMICs in the short term rather than focusing on discovery and basic science research. The findings should guide researchers, funders, programme and policy implementors in LMICs on future research investments in this area. Previous reviews of research priority-setting exercises have consistently highlighted the significance of implementing a dissemination strategy involving key stakeholders to ensure the effective uptake of identified priorities (72). As such, we carried out dissemination of the findings in several local and global scientific conferences in 2021 including AFEMSON (Nigeria), RCOG (UK), PRIME virtual global health conference (UK) and 3rd international conference on Maternal, Newborn and Child Health (MNCH) (India). Furthermore, regular and continuous monitoring of research investments and progress using key standardised outcome indicators related to prevention and treatment of PE/E will aid in understanding progress.

Table 4-5 Top 10 research questions

Rank	Research questions
1	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.
2	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.
3	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.

4	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?
5	Evaluate strategies to motivate and facilitate early and continual antenatal care check-ups for women in LMICs.
6	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.
7	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia in health facilities in LMICs?
8	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.
9	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?
10	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.

4.5.4 Strengths and limitations

The CHNRI method, which has been applied in over 100 research priority setting exercises in health, was used to set research priorities in PE/E. It has the benefits of being structured, flexible and can be conducted online making it low cost. Challenges encountered were related to low response rates, scorer fatigue, question consolidation and engaging stakeholders.

The list of research questions to be scored (n = 76 research questions) was also long and resulted in scorer fatigue. To reduce scorer fatigue and improve efficiency, the process management team reduced the number of sub-criteria to be scored from 15 originally identified by Rudan et al (2008) to seven (07) for this exercise. About 70% (n=48) of the scorers completed the scoring process in full, and about 78% (n=54) scored at least half of the questions. Research questions were randomly presented to each scorer (33, 73, 74) which eliminated preferential bias in scoring and allowed responses from experts who had scored at least one full question to be included in the analysis.

Structured and unstructured methods were used to list a large and diverse pool of experts for the study. Regular requests and reminders were also sent to experts and the larger pool of experts, not only those who submitted research questions, were invited to participate in the scoring process. This method guaranteed that individuals who might have been reluctant or unable to submit research questions in the first phase still had a chance to participate in the study (32, 75). Despite this, the survey response rates were low and out of the 500+ experts reached out to, only 49 and 69 experts participated during research question elicitation and scoring processes, respectively. Although, the method produces reliable results with only 45-55 experts (76), the participation of a select few individuals may have resulted in self-selection bias (32, 75). Regardless of this, a large number of experts participating in the surveys had expertise in carrying out research in LMICs (86%, n=53) or Sub-Saharan Africa (56%, n=35) which enabled us to prioritise contextually relevant ideas for LMICs and segregate priorities by region especially for Sub-Saharan Africa.

Other potential biases embedded in this methodology include the possibility of excluding valuable research ideas during the research idea generation and compilations phases (32). Despite this, we believe that this process has effectively captured a comprehensive range of contextually relevant ideas related to prevention and treatment of PE/E in LMICs across the four research domains. Assigning domains to research priorities was occasionally challenging and relied on subjective interpretation of the domains (74). This was resolved by discussion between the primary and the senior researcher.

Rudan et al (2008) recommended involving a wide range of stakeholders (i.e., those who have a stake in the prioritisation process e.g., funding agencies, researchers, policy makers, general population, advocacy groups and many others) to ensure legitimacy and fairness of priority setting decisions in health research (29, 77). However, the original CHNRI method's approach of identifying stakeholders proved challenging. Instead, during the research question elicitation or scoring processes, we requested the involved experts to rank the five pre-selected criteria (73, 78). They assigned higher scores to "answerability", and "potential for translation" criteria and lowest scores to the "equity" criterion, yet they allocated a greater weight to "potential for translation" and "equity" compared to "answerability" or "delivery" or "impact on burden". Consequently, we observed some changes in ranks between weighted and unweighted scores, but they were minimal and the top 20 questions remained almost identical. Further research or innovative strategies may need to be devised to involve stakeholders in this process.

4.6 Conclusion

This exercise has identified a key list of ranked research priorities related to prevention and treatment of PE/E in LMICs. These priorities encompass multiple stages of the care pathway, including detection, transfer, and management, ultimately aiding in streamlining care for high-risk women. Addressing the research priorities will help make significant improvements in the lives of mothers and babies in

resource poor settings and attain the SDG targets in maternal and newborn health. The identified priorities should act as a valuable resource for health research funders and donors, researchers, policy and programme implementors and other relevant stakeholders and help inform choice of future research in this area.

4.7 References

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5 Chapter 5: Perception and experiences of adolescent mothers and community in caring for their preterm babies: An in-depth study in rural Bangladesh

This chapter presents a qualitative study aimed at exploring gaps and opportunities for improving care for preterm newborns in rural Bangladesh, focusing on high-risk groups, particularly adolescents. The findings of the study were published in BMC Pregnancy and Childbirth on February 17, 2024, and can be accessed through the following link: doi: 10.1186/s12884-024-06345-x.

This chapter is an extended version of the published manuscript, with particular emphasis on an expanded analysis of the background issues influencing adolescent motherhood in Bangladesh and how the government is addressing these critical challenges. Additionally, the description of the methodology has been broadened to include a discussion of the philosophical and methodological underpinnings of this qualitative study, as well as a reflection on my position as a native female researcher and how this positionality may have influenced data collection and the study's findings. These discussions could not be included in the published manuscript due to the journal's word limit restrictions. However, my examiners, supervisors, and I agreed that readers would benefit from the inclusion of these reflections and analyses in the thesis.

Authors' accepted copy of the paper is included in this <u>Annex 11</u>.

5.1 Background

Adolescent pregnancy and motherhood continue to be considered a priority public health and human rights issue because of its profound consequences and long-term negative effects on young individuals, their families, and entire communities. Globally, 16 million adolescent mothers aged 15–19 years and 2 million below the age of 15 experience the physically and emotionally demanding journey of pregnancy and childbirth every year (1, 2). More than 90% of these births occur in low- and middle-income countries (LMICs) and within marginalized communities – commonly driven by poverty, lack of education and employment opportunities in these areas (3-5). Adolescent childbearing is generally associated with negative health consequences for both the mother and baby including increased risks of maternal and neonatal deaths, stillbirths, preterm births (PTB), small-for gestational-age (SGA) babies, severe neonatal complications, pregnancy and childbirth complications, and maternal undernutrition, as compared to childbearing for those older than 19 years (6-10). In addition, adolescent mothers must simultaneously adapt to the demanding role of being a mother and nurturing a baby while they are still going through their own biological, physical, emotional, and psychological development as an adolescent (11-13). Without the necessary knowledge, skills, and resources to deal with early parenthood, they face several social, economic, personal and relational challenges (11-13).

5.1.1 Adolescent marriage, fertility and motherhood in Bangladesh: Trends and determinants

Bangladesh has a notably large adolescent population. According to the most recent data, adolescents-defined by the World Health Organization (WHO) as individuals aged 10 to 19 years (14) -make up 19.9% of the total population, approximately 32.8 million individuals (15). This is an increase from 2011, when 30.68 million individuals were classified as adolescents (16). As the largest population cohort, adolescents require urgent attention to their health needs. Nearly half (16.3 million) are girls, highlighting the importance of gender-responsive interventions (15).

Despite improvements in health indicators, Bangladesh continues to face a high prevalence of teenage marriages and consequent pregnancies. Historically, the country has had one of the highest rates of teenage marriage in South Asia, with the 2022 Bangladesh Demographic and Health Survey (BDHS) indicating that about half of women aged 20-24 marrying before the legal age of 18 (17). Although the proportion of women aged 20-24 marrying before 18 has declined from 65% to 51% between 2011 and 2022, and those marrying before 16 has dropped from 43% to 27%, early marriage remains a major issue, with these numbers still alarmingly high (17, 18). Teenage pregnancy in Bangladesh primarily occurs within the context of marriage, with the high prevalence of child marriages driving the high pregnancy rates among adolescent girls (19). In Bangladesh, although a decrease from 31% in 2014, about one-fourth (24%) of teenage girls aged 15–19 have begun childbearing, with 18% having had a live birth and 6% currently pregnant (17). The median age at first birth varies by education level, with those who completed secondary education or higher having a median age of 22.2 years, compared to 18.3 years for those with no education. Teenage pregnancy is also more common in rural areas (25%) than urban areas (20%) and is more prevalent in the lowest wealth quintile (29%) compared to the highest (14%). Additionally, 3% of young women have experienced a pregnancy loss (17).

Early marriage and childbirth in Bangladesh are influenced by a combination of demographic, socioeconomic, cultural, and health system factors. A major driver of early marriage and childbearing is low education levels, with both women and their husbands often lacking formal schooling, limiting their awareness and access to resources that could delay marriage and childbirth (20-22). Poverty also plays a significant role, as girls from lower wealth quintiles are more likely to marry and bear children at an early age (20, 22). Dowry payments remain a major factor in early marriage in Bangladesh. Although prohibited under the Dowry Prohibition Act of 2018, the practice persists, with dowry amounts rising with girls age and as potential grooms attain higher education. This financial burden pressures families to marry off their daughters early before the legal age of 18, reinforcing child marriage as a widespread practice (23). Educational policies, such as the Female Secondary School Stipend Project, have been more effective in delaying marriage and childbearing by increasing school enrolment for girls, but challenges remain with early marriage being strongly linked to early high school dropout among girls in Bangladesh (19, 23, 24).

Additionally, patriarchal norms and gender inequality significantly restrict young girls' ability to make decisions regarding their reproductive health (25). Studies in rural Bangladesh indicate that many adolescent brides have little or no decision-making or financial autonomy, with choices about marriage, childbirth, and contraception often made by their own families, husbands or in-laws (25-27). Qualitative studies indicate that in many rural communities, families- especially mothers-in-law - pressure young brides to prove their fertility through early childbirth (26, 27). Bearing a child strengthens a young wife's position, offering her respect and security, whereas remaining childless may expose her to mistreatment or abandonment. In such contexts, young brides have limited agency to negotiate family planning, leading to early pregnancies. Other studies on family planning, indicate that, a lack of knowledge, misconceptions and religious views about contraceptives, including fear and social stigma around infertility, further prevent young women from using contraceptives (26, 28). Moreover, limited knowledge about and access to quality reproductive health services, particularly in rural and marginalised areas, makes it difficult for young girls to delay childbirth (26, 29). These cultural, economic, and healthcare barriers, combined with weak enforcement of laws against child marriage, create a cycle that perpetuates early marriage and pregnancy among adolescent girls in Bangladesh.

5.1.2 Health challenges of adolescent pregnancy and motherhood in Bangladesh

Adolescent childbearing has also been found to associated with negative health consequences for both the mother and baby in Bangladesh. Several observational hospital- and population-based studies in the country found that adolescent pregnancy poses significant obstetric risks, including anaemia, preeclampsia, eclampsia, severe infections, jaundice, and urinary complications (30-34). Delivery-related risks include excessive bleeding, placental abruption, and a higher likelihood of caesarean section, primarily due to foetal distress, eclampsia, and obstructed labour (30, 32-34). Adolescent mothers also experience prolonged and more challenging postpartum recovery compared to adults. The 2022 BDHS highlights that eclampsia, followed by haemorrhage, is the leading cause of death among adolescent mothers in Bangladesh, further underscoring the severe health risks associated with adolescent pregnancies. Their newborns face increased risks of adverse birth outcomes, such as PTB, low birth weight, birth asphyxia, and jaundice, along with poorer growth indicators, including lower height-for-age and weight-for-age scores. Bangladesh has one of the highest incidences of PTB in the world world. An estimated 603,698 babies were born prematurely in 2014 i.e., 19% of the total number of births that year (35). The 2017-18 BDHS estimated that about 19% of all neonatal deaths are directly attributed to PTB (36). In addition to this, several studies report significant barriers to healthcare utilisation for adolescent mothers across different levels. These include limited knowledge, fear of C-sections, and shyness about male doctors affecting care-seeking at the individual level (25, 37-40); family traditions favouring home delivery, with decisions strongly influenced by husbands and mothers-in-law, as well as financial constraints, cultural beliefs, and reliance on traditional healers at the family

and community levels; and the availability, accessibility, and quality of health services at the health systems level (25, 37-39).

5.1.3 National response to adolescent health in Bangladesh

In Bangladesh, both the government and various multilateral and bilateral partners, including UN agencies, work together to strengthen adolescent health initiatives. Bangladesh, as a signatory to the Child Rights Convention and a supporter of the International Conference on Population and Development (ICPD), the Beijing Platform for Action, and the SDGs, has made significant pledges to enhance adolescent health in the country (19, 41). The Ministry of Health and Family Welfare (MOHFW) of Bangladesh has developed the National Strategy for Adolescent Health (2017–2030) to ensure all adolescents lead healthy, productive lives (41). The strategy focuses on sexual and reproductive health, violence, nutrition, and mental health, with crosscutting themes of behaviour change communication and health system strengthening (41). Supporting this strategy, the 4th Health, Population, and Nutrition Sector Program (HPNSP) (2017–2022) includes two operational plans Maternal, Neonatal, Child, and Adolescent Health and Maternal, Child, Reproductive, and Adolescent Health. The Directorate General of Family Planning and Directorate General of Health Services are providing health care services to adolescents through establishing adolescent-friendly health services (AFHSs) at some existing public health facilities, namely district hospitals, maternal and child welfare centres (MCWCs), upazila health complexes, and upazila health and family welfare centres (42, 43) (Figure 5-1). However, implementation of AFHS struggles with gaps in implementation including lack of awareness, resource shortages, inadequate training, coordination issues, weak referrals, concerns of privacy and confidentiality, and cultural barriers, limiting effective service delivery (42, 43).
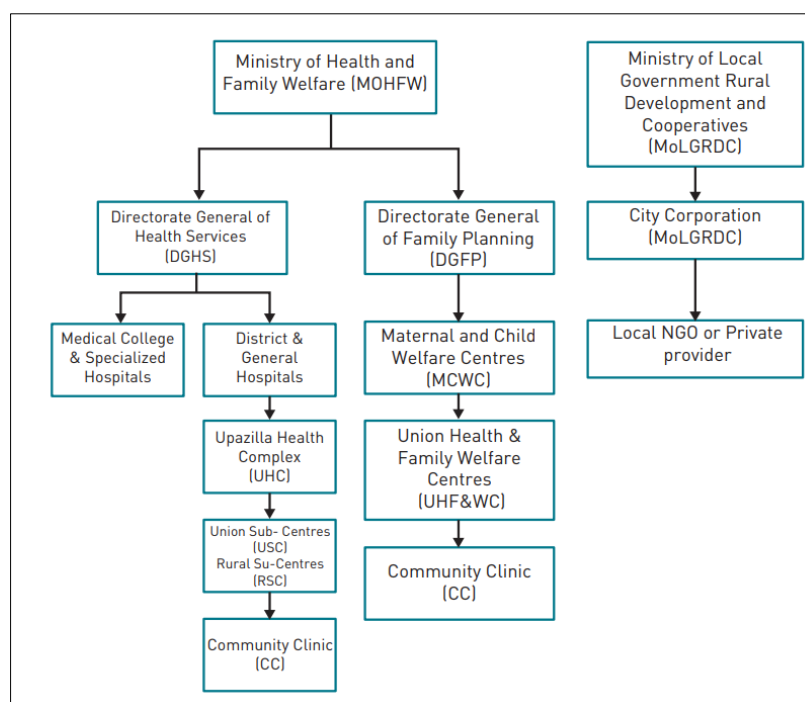
Figure 5-1 Health service delivery organizational structure in Bangladesh (44)

5.2   Rationale and aims of this study

Despite the high rate of adolescent pregnancies and preterm births in Bangladesh, there is a dearth of evidence documenting the understanding and experiences of adolescent mothers in caring for their preterm babies. Equally, little is known about the interventions needed to prepare and assist them in caring for their premature babies. Exploratory studies in African settings, including Malawi, Uganda and Ghana, indicate that inadequate care of preterm babies is commonly driven by a (i) lack or inadequate knowledge about the causes of preterm birth, diseases severity and how to care for preterm babies; poverty which prevented families from buying warm materials, living in properly build warm houses or paying transport costs and costs of health facilities; and (iii) poor quality of care at health facilities due to lack of protocols, skilled service providers and basic equipment, drugs and other supplies (45-48). In addition, findings from these studies as well as in Bangladesh reveal low rates of care-seeking or using traditional medicines and care-seeking from unqualified providers for complications and illnesses in preterm babies (45-49). However, whether these factors are important barriers in other settings specially among adolescent mothers in rural Bangladesh is unknown

This was also echoed by stakeholders during initial stakeholder engagement workshops conducted for the CHNRI research priority setting process in Bangladesh. During that workshop, stakeholders expressed keen interest in investigating evidence gaps related to PTB among adolescents, given the high rates of adolescent motherhood and PTB in Bangladesh. In response, this study was designed with their consultation, focusing on exploring the perceptions and experiences of adolescents in caring for their preterm babies. Additionally, other groups such as adult mothers with PTB experience, family,

and community members were included in the study to provide a comprehensive community-level perspective. The aim of this research was to contribute to improved support for adolescent mothers in caring for preterm babies (any live birth before 37 completed weeks of gestation) in rural Bangladesh, by providing in-depth qualitative evidence from the perspective of mothers, communities and the health service providers involved. The primary objectives were to:

- Explore perceptions and understanding of adolescent mothers, mothers >19 years and communities regarding PTB;

- Explore current care and health-care-seeking practices for preterm babies who are born to women of different ages including adolescent girls;

- Explore opportunities and challenges for improving post-natal support and infant care for adolescent mothers at community level with attention to preterm babies.

5.3 Methodology

This section outlines the methods selected to carry out this research, including the underlying philosophical approach, research design, and ethical considerations.

5.3.1 Research paradigm

The chosen research paradigm for this study is interpretivism, with phenomenology employed as a methodological approach. Interpretivism acknowledges that reality is socially constructed and context-dependent, shaped by cultural, social, and historical factors (50, 51). This interpretivist stance focuses on understanding the subjective experiences and meanings that adolescent mothers and their communities attach to caring for preterm babies. By using phenomenology as a method, we aimed to explore the lived experiences of participants, providing a deeper, more empathetic understanding of their perceptions, challenges, care practices, and support systems surrounding preterm birth in rural Bangladesh (52). Though this approach we wanted to gather a rich understanding of the individual, social, and cultural dynamics of preterm birth while keeping the voices and perspectives of participants central to the research findings.

5.3.2 Study design

We adopted a qualitative approach, grounded in phenomenology, involving in-depth interviews (IDI), focus group discussions (FGD), and key informant interviews (KII) to gain a deeper understanding of mothers' and the community's experiences in caring for preterm babies. This approach allowed us to generate detailed insights into the lived experiences of mothers, focusing on the individual, social, and cultural factors surrounding preterm birth (PTB). Quantitative methods would not have captured the personal and contextual nuances needed to understand these deeply subjective experiences. By using qualitative methods, we were able to build rapport and explore this sensitive topic in depth, engaging

participants at individual, family, and community levels—crucial for understanding the broader implications of PTB in rural Bangladesh.

5.3.3 Study setting

The study was conducted in rural villages of Baliakandi sub-district in Rajbari District, central Bangladesh (Figure 5-2). The sub-district was chosen as International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) operates a demographic and health surveillance system among a population of approximately 200,000 in 261 villages in the sub-district. The surveillance system collects information on key demographic and reproductive events every four months including age, births, deaths, date of last menstrual period (LMP) etc. This facilitated identification of participants with recent births including preterm births.
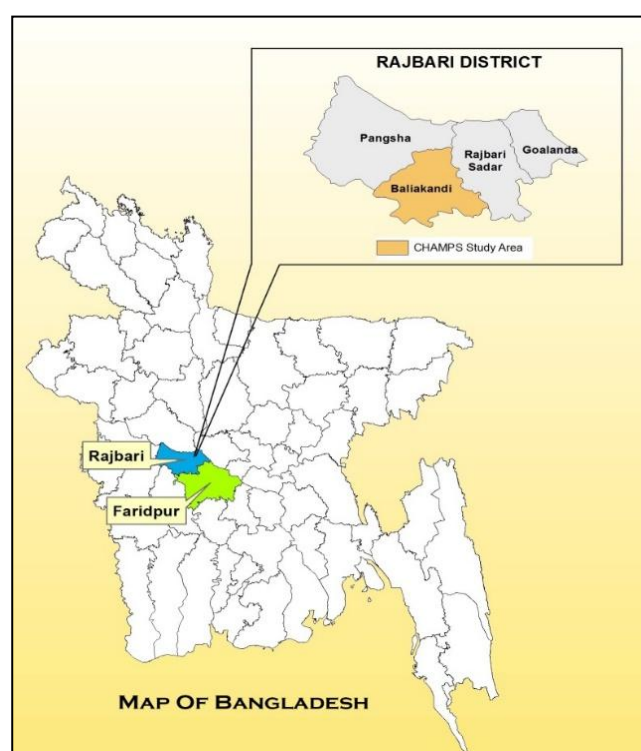
Figure 5-2 Map of study area

Birth and death registries in Bangladesh are not consistently implemented, and vital statistics on maternal health—such as prenatal care, delivery, maternal and newborn mortality, and pregnancy complications—are largely gathered through surveys (e.g., Bangladesh Maternal Mortality and Health Care Survey (BMMS), Bangladesh Demographic and Health Surveys) and a few surveillance systems implemented in the country (53, 54). Due to these limitations, we relied on icddr,b's surveillance system to obtain available data on recent births including preterm births to young mothers.

5.3.4 Participants:

The primary participants for this study were adolescent mothers aged 15–19 years who had given birth to preterm babies (any live birth before 37 completed weeks of gestation) in the 6 months prior to the start of data collection. However, we also aimed to explore whether perception, experiences and care-practices varied by age of mother and gestation of baby i.e., whether perception or experiences of adolescent mothers with a PTB differ or is similar to adolescent mothers with term birth or adult mothers with PTB. As such, data was also collected from adolescent mothers (15–19 years) who gave birth to a term baby and older mothers (> 19 years of age) who gave birth to a preterm baby in the six months prior to the start of data collection. Mothers who had given birth in the past six months were selected to ensure recent and relevant information while minimising recall bias. To obtain maximum variation in experiences of caring for premature babies, we tried to include mothers with different characteristics, such as those who had lost a premature child, as well as those with home or facility births, and those living in nuclear or joint families. We aimed to explore how these factors influenced care practices and coping strategies among women and families. Understanding the experiences of mothers who had lost a preterm baby was particularly crucial, as their stories provided deep insights into the challenges they faced.

The secondary participants of the study included immediate family members (e.g., fathers and grandmothers of the preterm baby), community members (other mothers, elderly women and fathers) and health care providers. Immediate family members were included to obtain detailed understandings of their experiences surrounding the birth and care of the baby as well as to triangulate the information obtained from the mothers. To understand and obtain more information about cultural norms and social practices regarding PTB in the community, FGDs were conducted with several homogenous groups including young mothers (with preterm or term births), elderly women and fathers. In addition, we conducted key-informant interviews (KIIs) with health care providers selected purposively from public and private health facilities providing newborn and childcare in the sub-district to understand the challenges faced in providing services to preterm babies.

5.3.5 Recruitment of participants and data collection

The data management personnel overseeing the surveillance system obtained information on births from the past six months, provided village-wise data during this period We obtained contact details, the mother's age, and the gestational age at birth, and the child's status (alive or deceased) to identify eligible participants. Gestational age at birth was calculated by the data management officer from the date of LMP. Instead of employing a systematic sampling approach, we began with a village that was logistically easier to access from our place of stay in the sub-district and then expanded to nearby villages to identify potential participants. Priority was given to villages with multiple eligible participants. Family members were selected opportunistically; however, they were not from the same

participant's household. When a husband was interviewed, we aimed to interview a different participant's mother or mother-in-law to capture diverse family perspectives on preterm birth and caregiving experiences. In total we visited 26 villages to collect our data. The identification of participants including those for focus groups was greatly facilitated by the local surveillance team, who had an in-depth understanding of the community and the geographical location. Their familiarity with the area and families helped us reach mothers who had recently given birth, including those who had a preterm baby or had lost a preterm child. This local support was not only essential in navigating remote or hard-to-reach areas but also helped in building trust and ensuring that participants felt comfortable sharing their experiences.

Data was collected by trained social science researchers and anthropologists between July 2019 and December 2019. Individual IDIs, FGDs and KIIs were conducted to add breadth to the data and triangulate the findings (Table 5-1). There was no overlap in participants data of IDIs, FGDs or KIIs. Data collection continued until saturation was reached, meaning that no new information, insights, were emerging from the data. Saturation was carefully monitored during regular debriefing sessions, where we discussed the emerging patterns and reviewed the data to ensure that no critical elements were being overlooked (55, 56).

In-depth interviews with mothers and family members: Interview guides were developed, translated into the local language Bangla. Topics covered in the interview guide included understanding of PTB, experiences with pregnancy and delivery, care practices of preterm babies, care-seeking for illnesses and the associated challenges. All questions were open-ended with prompts to elicit details and description from the participants.

The in-depth interview guide was pilot tested with two mothers and a family member who had recently given birth in a village near the capital city. We were unable to identify mothers with preterm babies during the pilot testing phase. During the pilot testing, we found that the guide was too long, leading to several changes in how we administered it. This included changing the order of questions to ensure that information on birth and care for preterm babies as well as perception are captured. After asking general questions, we therefore proceeded with questions about their experiences with the birth and delivery, newborn care, care-seeking for newborn illnesses, and their knowledge and perceptions of preterm babies. This was followed by questions aimed at gathering information on their pregnancy care, family planning, and future childbearing intentions.

Each interview or discussion was conducted in a private location at a time convenient for the participant. A two-person team consisting of female interviewers conducted the interviews with mothers and family members, with one person primarily leading the interview and the other taking notes. Additionally, the second interviewer also played a key role in minimising interruptions during the interviews by engaging with other family members, such as mothers, sisters, or anyone else present, to explain the research

objectives. This not only reassured curious family members and neighbours about the purpose of the discussion but also helped participants feel supported by their families. As a result, it ensured privacy and created a more comfortable, open environment for them especially the adolescents to share their experiences. Participants were also explained the research aims, process and assured that their responses will be anonymised and remain confidential. All these helped reduce social desirability bias and participants were able to share their experiences without fear of being judged. Written informed consent was obtained from study participants above 18 years of age prior to all interviews. For participants less than 18 years of age, assent from them and informed consent from their legal guardian was obtained. Each of the interviews lasted between 30 and 115 min and, with the permission of the participant or group, the entire interview was audio-recorded.

We conducted 36 IDIs, including adolescent mothers with preterm or term babies (n = 18), adult mothers with preterm babies (n = 10), family members (n = 8). This was conducted from 26 villages in the sub-district (Table 5-1). Immediately after each interview, a short summary was prepared, noting any important points or challenges to facilitate with data analysis.

Focus group discussions: Each FGD included six participants, and efforts were made to keep the groups as homogenous as possible to encourage open discussions and shared experiences. A topic guide was used to steer the discussions, although it was not pretested prior to the sessions. The discussions focused on key topics related to preterm birth, including their knowledge of preterm birth, its causes and risks, management and care practices, healthcare-seeking behaviours, and the availability and accessibility of healthcare services. Each session lasted about an hour, depending on the depth of the discussion. The FGDs were held in a quiet area, such as the yard of the participants' homes, at a time that was mutually agreed upon in advance. Informed consent was administered at the start of each session. With the participants' permission, all FGDs were audio-recorded, while a note-taker simultaneously took handwritten notes to ensure accurate documentation of key insights and non-verbal cues. A total of five FGDs were conducted: young mothers (n = 1), grandmothers (n = 1), fathers (n = 2), village doctors/community people (n = 1) (Table 1).

Key informant interviews: We conducted Key Informant Interviews (KIIs) with formal and informal healthcare providers (n = 12), including nurses in labour and neonatal wards (n = 3), obstetricians and gynaecologists (n = 2), a neonatal consultant (n = 1), a healthcare worker (n = 1), and traditional birth attendants (n = 3). The topics of the interviews focused on their experiences in managing preterm birth and the challenges they face in providing care. An interview guide was used, and informed consent was administered before each interview. All interviews were conducted in private locations and recorded with the participants' consent.

Table 5-1: Data collection methods

Interview type	Number of participants (n=82)
IDIs	
Adolescent women with PTBs	10
Adolescent women with term births	8
Adult women with PTBs	10
Grandmothers	3
Fathers	5
Sub-total	*36*
KIIs	
Birth attendant	3
Trained/Formal health care provider	9
Sub-total	*12*
FGDs	
Elderly women	2 groups (12)
Fathers	2 groups (16)
Young mothers	1 group (6)
Sub-total	*5 groups (34)*

5.3.6 Debriefing sessions

After each data collection day, we held debriefing sessions to reflect on our initial observations and evaluate how the data collection process could be improved (57). These sessions were vital in ensuring that we remained focused and aligned with the study's objectives. During these discussions, we were able to clarify our understanding of the emerging data, address any issues we encountered in recruiting participants, make immediate adjustments to our approach and plan for the next day. This ongoing dialogue also allowed us to triangulate the information we had gathered, cross-checking the data from different sources and methods to ensure its consistency and reliability.

It was also a space where we could talk about any biases we might have had, whether we unintentionally influenced the responses, or if there were any areas we needed to approach differently. And since the

topics we were discussing were sensitive and emotional, the debriefs also gave us the chance to support each other and make sure we were handling everything with care.

Furthermore, a few days into the interviews, we shared our preliminary findings, including the challenges encountered, with senior researchers in Bangladesh and Sheffield. This collaborative feedback process was crucial for refining our data collection strategies. Senior researchers offered valuable guidance on how to recruit participants, approach service providers from different health facilities, and improve our approach or techniques ensuring that the research remained on track and that our methods were ethically sound. This constant reflection and feedback loop was essential for producing high-quality, meaningful data and ensuring that we were responsive to both the needs of the participants and the goals of the study.

5.3.7 Data analysis

Preliminary data from this qualitative study were analysed using an inductive thematic approach, a process where both data collection and analysis occurred simultaneously (58). This approach allows for the development of themes based on the data rather than imposing preconceived notions or hypotheses. Audio recordings from focus group discussions (FGDs) and interviews were and transcribed verbatim in Bangla immediately following the interviews, ensuring minimal data loss. The transcriptions were enhanced by adding detailed field notes, which provided further context to the data collected. To ensure transcription quality and accuracy, random checks were done by comparing the transcripts with the audio recordings. All transcripts were anonymised before coding and analysis.

The data analysis process was iterative and involved continuous refinement. Initially, the transcripts were read and re-read to familiarise the researchers with the data, ensuring a deep understanding before proceeding. A coding structure was developed by the primary author based on this initial reading. Key themes and frequent patterns observed in the data were coded and applied to subsequent data. As new data was analysed, emerging patterns were identified, and new codes were integrated into the existing structure. Multiple authors (3) coded the data, and regular meetings were held to compare and discuss codes, helping to identify discrepancies and ensure consistency across researchers. This approach allowed us to remain flexible and responsive to the data, making necessary adjustments throughout the analysis.

Once the coding structure had evolved, the codes were grouped into broader categories. These categories were then analysed and collated into potential themes and sub-categories (59). Once the themes and sub-categories were identified, a matrix with themes/sub-categories and different participant types, i.e., adolescents with preterm and term babies, adults with preterm babies, and family members, was developed. This matrix was based on the framework method of qualitative data analysis, providing a structured approach to understand how each group contributed to the overall themes and facilitating comparison across different participant groups. These activities were done by the primary author but

discussions were held frequently with all involved in coding and collection to ensure correct reflection of the data. The initial analysis was conducted using NVivo v12, while the matrix was developed in Excel to visually organise, categorise, and compare the data based on participant types.

5.3.8 Ethical considerations

Ethical clearance for the study was obtained from the Institutional Review Boards (Research Review Committee and Ethics Review Committee) at icddr,b (PR-19024) and The University of Sheffield (alternative ethics application 000275).

Written informed consent was obtained from study participants above 18 years of age. For participants less than 18 years of age, assent from them and informed consent from their legal guardian was obtained. Before starting the interviews or focus groups, we made sure all participants had all their questions answered and fully understood the study. They were reassured that their responses would stay anonymous and confidential, and that they could stop at any time without any consequences. Given the sensitive nature of their experiences if any participant became distressed during the interview, we paused and allowed for breaks. The interview was resumed only when the participant agreed and were also reminded that answering any question was voluntary and that they had the right to withdraw from the study at any time without explanation. Permission to record was obtained from all participants.

All recordings were conducted using encrypted recorders. These were immediately downloaded and deleted once the transcriptions were complete. Participant identifiers were replaced with codes to ensure anonymity. These files were stored on a password-protected devices, accessible only to authorised research team members. Any paper-based documents, such as consents, were kept in a locked cabinet with the local data collection team. Data will be retained and deleted according to institutional guidelines. Personal information such as names, addresses, or any identifying details were not linked to any of the research findings or shared outside the research team.

5.4   Results

In this paper we have presented perceptions and experiences of adolescent mothers on PTB, comparing it with the views of adult mothers, family and community members. Information on challenges of caring for PTB at health facilities were obtained from heath care providers. We concentrate on the two major themes emerging from our data: firstly, perceptions and understanding of PTB (length of gestation, causes, appearances); secondly, care practices and care-seeking for preterm babies.

5.4.1 Background characteristics

We had a mix of participants by birthplace (facility or home birth), delivery mode (normal or c-section births), and family type (nuclear or extended) in both groups - adolescent (15–19 years) and adult (20–36 years) women with recent births and their family members (Table 5-2). However, a majority had six or more years of education, were housewives living with extended families, delivered at health facilities,

and had normal vaginal deliveries. The mean gestational age for PTBs was 31 weeks (28–36 weeks). The fathers who participated in the IDIs were between 19 and 35 years (mean 25.2 years old), grandmothers were between 41 and 50 years (mean 46.7) years, whereas the key informants were between 30 and 86 years (mean 51.6 years) old.

Table 5-2: Background characteristics of women with recent preterm/term births

	Adolescents with PTB	Adults with PTB	Adolescents with term birth
	n=10	n=10	n=8
Education			
No/Primary (1-5 y)	4	3	1
Secondary + (6+ y)	6	7	7
Religion			
Islam	9	9	7
Others (Hindu)	1	1	1
Child status			
Alive	8	7	8
Dead	2	3	-
Occupation			
Housewife	10	9	2
Student	-	1	-
Family type			
Nuclear	2	5	2
Extended	8	5	6
Delivery place			
Home	3	4	4
Facility	7	6	4
Delivery type			
NVD	8	5	5
C/S	2	5	3
Birth Order			
Primiparous	7	1	8
Multiparous	3	9	-
Mean gestational age at birth (weeks)	30.9	31.0	39.4

5.4.2 Perception and understanding of PTB

Length of gestation

The overall concept of babies born preterm was well understood among all mothers and community members in Baliakandi. Locally, PTBs were referred to as *"births that occur before time"* or "*shomoyer age"* and this appropriate time was mostly defined as the time needed for the baby in the womb to become *fully or well-nourished* or "*pushto.*" The length of gestation was always described in months

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rather than in weeks and we observed variations in participants' opinion as to what that appropriate time or length of gestation should be. The most common responses by adolescents with PTBs included, nine months, nine months 10 days, between nine to 10 months, 10 months, 10 months 10 days whereas other adolescent mothers with term births or adult mothers with PTBs mostly mentioned 10 months. Any births at the 8th or 7th month were considered by all to be early.

> *"Elders say that a baby is healthy if born at 10 months 10 days and doesn't have problems with being undernourished." (IDI03 Adolescent mother with a preterm baby).*

> *"When the baby is nourished… if the baby stays in the womb for nine months, then it is nourished." (IDI27 Adolescent mother with a preterm baby).*

The responses of family members and other community participants varied like those of adolescent mothers with premature births, with some mentioning that although 10 months is ideal, nine months is also good: *"Baby is nourished if 10 months… but nine months is also not bad, its medium…" (FGD01 Elderly women).*

All participants used or were aware of using the date of last menstrual period (LMP) to estimate the month of pregnancy and birth. However, participants also relied heavily on dates provided during ultrasonography (USG) to estimate their due dates. Often these USGs were done during the 2nd or 3rd trimester to know the status of the baby or to estimate the gestational age in cases where mothers were confused with their LMP date, for example those with irregular periods or spotting during pregnancy, as one participant mentioned:

> *"I couldn't remember clearly when I became pregnant. So, I went to do an ulta (USG) to determine the date…I have heard that you can even tell how many months old the baby is if you do an ulta (USG). I told them I forgot the date of my last menstruation. Accordingly, they gave me a date of delivery." (IDI11 Adult mother of a preterm baby).*

Appearance of PTB

When mothers and community members were asked to describe a preterm baby, they used several external physical features. The most common notion mentioned by all participants was that babies born before time are under-nourished (*opusto*), small (*choto*), weak (*kabu*), have less weight, frail (*finfina*), have long and thin hands, and legs *(haat pa. noli noli)*. The term *opusto*, which literally means being under-nourished, was mentioned by all participants to describe preterm babies and was often synonymously used to mean babies who are not fully grown. For babies born as early as seven months, a common way to identify them, as mentioned by adolescents as well adults, was that the baby's eyelids are fused together (*chokh fute na*). Other terminologies used by older participants and community members who had seen preterm babies included visible veins around the stomach (*pet-er rog dekha jai*), wrinkled skin, sunken forehead, and no hair.

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Problems preterm babies may face

Participants highlighted problems that preterm babies may suffer from, or their preterm babies had suffered. Adolescent and adult mothers with preterm babies, recollected problems mainly from their experience, whilst about half of the adolescent mothers with term babies mentioned that they were not aware. Participants of FGDs, family members and adult mothers, however, could promptly mention problems faced by preterm babies. Several participants including adolescent mothers emphasized that babies born at nine months or later are generally healthy whereas babies born at seven months rarely survive. A mother mentioned, *"babies who are born in the 7th or 8th months are not born with good health. Those who are well-nourished, survive and those who aren't, die" (IDI14 Adolescent mother of a preterm baby)*, whilst others highlighted the need to spend a lot of money to ensure survival, or shared recollections of incidents where babies born early were kept in *glass houses* (*Kacher ghor-* incubators), some of whom had survived:

> *"...babies born at seven months may not survive and those at 8 months have more possibility but need to spend a lot of money..." (IDI12 Adult mother of a preterm baby).*

> *"The baby was not nourished as much as he would have been if born after 10 months. His parents took him to hospital where the baby was kept in a glass house [incubator] so that his eyes develop. They returned after three months when the baby started feeding." (FGD04 A participant of FGD with fathers).*

Other problems mentioned include babies are undernourished; eyelids are fused, babies have difficulty breastfeeding; have breathing difficulties requiring hospitalization; baby turns blue or black; more prone to diseases (such as cough and cold, diarrhoea, pneumonia etc.) due to the babies being undernourished; physically and mentally disabled; ongoing poor nutritional state, and that their health doesn't fully recover when they grow up.

> *"Baby may suffer from heart problem or be weak or their eyes may not develop." (IDI27 Adolescent mother of a preterm baby).*

> *"Baby will either be less intelligent or disabled. Or he will have any other parts of his body damaged...he may have underdeveloped eyes, or hands or legs...he may not be talented. He did not complete his full growth." (FGD04 A participant of FGD with fathers).*

> *"After delivery, the two big problems are difficulty in breathing and cough. Makes wheezing sound inside the throat, noses are blocked, and baby cannot breathe. These happen more to babies born in the 7th or 8th month." (KII06 Untrained birth attendant).*

Causes of PTB

Findings revealed that awareness about the causes of PTB is limited in rural Bangladeshi settings and that many of the perceived causes are outside modern medicine. Over half of the adolescent mothers

(10 out of 18) and half of the adult mothers (five out of 10) could not explain why babies could be born prematurely or why her newborn was born premature. Other participants, either mothers or family and community members, mentioned several causes which have been grouped into (i) maternal health related, (ii) lifestyle or behavioural, and (iii) supernatural/spiritual causes (Table 5-3).

Table 5-3: Perceived causes for PTB

Maternal health

Less maternal age / less maternal age leading to c-section

Poor nutritional status

Use of medications (fever, deworming etc)

Inadequate sleep

Falls

Trauma to abdomen

Excessive vaginal discharge

Low-lying placenta

Convulsions, eclampsia

Urine infection

Indicated c-section

Sex during pregnancy

Lifestyle and behavioural

Heavy work, lifting heavy objects (using tube-well etc)

Inadequate eating

Not taking recommended vitamins, calcium, folic acid during pregnancy

Being beaten by husband

Stress due to familial issues e.g., disagreement with in-laws, husband's extra marital affairs

Attempted abortion

Elective c-section

Supernatural/spiritual

Evil spirits (being possessed by Jinn, *dosh, chut, upri, groher shomossa, bhoot)*

God's will

Poor nutritional status of the mother or inadequate eating was one of the most mentioned causes for premature birth. Because premature babies were born small and weak, many participants, including

mothers, opined that this was because the mother was weak, under-nourished, or because she did not eat enough food or vegetables or take the recommended vitamins, iron, or calcium medications:" My *baby was born early, as I didn't get enough to eat…" (IDI08 Adolescent mother of a preterm baby)*. On the contrary, one young mother mentioned that food or eating habits had no effect on premature birth, as her relative who had a similar outcome used to eat adequately, whilst another mother stated that in order to prevent PTB and unnecessary c-sections, pregnant women should eat smaller but frequent meals, so that the baby does not grow too big in the womb.

Trauma to the abdomen, accidents/falls, risky work, lifting heavy objects were also mentioned by a few participants across the different groups. According to a young man whose child was born premature: *"We are farmers, we go to the field. Then there is rice to look after in the house or five cows. I would ask her to put the rice away. There is always some work at home, she did a lot of risky work…she used to carry heavy items and that is why my child was like this (born preterm)" (FGD04 A participant of FGD with fathers)*.

Use of medicines during pregnancy such as for fever, pain or deworming was highlighted during FGDs. A participant of an FGD highlighted that, failed abortions using abortive medications may later result in early delivery or even still-births. Another mother whose twin preterm babies had died, expressed concern and confusion whether taking iron-folic acid and calcium medications had resulted in such an outcome or not.

Many mothers and community participants believed that supernatural or spiritual causes such as God's will or evil spirits (*dosh, chut, upri, groher shomossa, bhoot, Jinn*) were to blame. The opinions related to evil spirits were divided, and some young mothers and husbands strongly opposed the notion, mentioning that these were myths and old tales, whilst others said this might result in miscarriage or inability to get pregnant but not premature births. Those who believed in the notion mentioned that pregnant women are to follow certain norms during their pregnancy e.g., not leaving the house in the evening, afternoon, prayer times, or not roaming in the garden with big trees. It was said that an inability of the pregnant women to do so may result in early birth or even loss of pregnancy, as the excerpt below reveals:

> *"…Women are prone to curses and evil spirits, for this reason some babies get aborted at eight months. These babies may be born alive for some women but for others they die before birth…for example today is full moon, a lot of things (sprits) are outside during this time…if I am a new pregnant woman (kacha poyati), the evil spirits can attract me… when it attracts a pregnant woman, the pregnant women loses appetite, becomes thin. Sometimes she starts having abdominal pains. That is why she delivers early or loses her pregnancy." (KII06 Untrained birth attendant).*

An adult woman with a PTB strongly believed that she was possessed by *Jinn. In her words*: *"While I was sleeping, I used to feel that there's someone else sleeping beside me…the kabiraj [traditional healer] said that a huge Jinn is after me but wasn't courageous enough to harm… the kabiraj gave me an amulet that I wore till seven days after delivery…"* (*IDI13 Adult mother of a preterm baby*). Now she believes that her newborn is possessed by the *Jinn* as the baby cries a lot and turns black. Similarly, two participants with prior history of PTBs believed that their womb was cursed, and another woman with two PTBs and whose husband's second wife had seven miscarriages believed that someone had cast an evil eye on their house.

Unable to explain the cause of PTB, some participants opined that it was God's will. A husband mentioned that: *"I don't know the reason. Life and death depend on The One. We don't have the ability to know when one will be born or die!"* (*IDI36 with a Husband*). Another grief-stricken young mother said, *"People used to ask me, what I have done that the baby was born at seven months. But I did not do anything…God took away whatever was His in the way He wanted…"* (*IDI07 Adolescent mother of a preterm baby*).

A few husbands/fathers during in-depth interviews as well as in the focus groups mentioned that a lower maternal age to be a cause of PTB as well as other complications for the mother and child, including miscarriage and early c-sections. According to these men, young mothers are usually poorly nourished which makes it difficult for them to bear a child, as one husband stated, *"girls who deliver early get pregnant at young age…nowadays girls are married at 12 or 13 years of age…if someone is married at a young age, they are not fully nourished, how will she bear a fully nourished child (FGD06 A participant of FGD with fathers)."* Unexpectedly, the two traditional birth attendants interviewed strongly believed that it is easier for adolescent mothers to deliver since their bone structures were believed to be very flexible and not rigid like those of older women. Other infrequently mentioned causes included infections, vaginal discharge problems, low-lying placenta, convulsions, domestic violence, and stress.

5.4.3 Care of preterm babies

In our study we asked participants about the care a preterm baby would need with an aim to elicit information on knowledge and practices related to three important aspects of preterm babies' care: temperature management, frequent feeding, and weight monitoring. In general, care practices did not vary by mothers' age (adolescent or adult) but rather on the status of the baby.

Having identified preterm babies to be small, under-nourished and weak, both adolescent and adult mothers mentioned the need to provide extra care to preterm babies. However, it was difficult for participants – especially adolescents – to describe what this extra care should entail, especially when physical problems were not present. For example, a baby who was born a month earlier was perceived to be under-nourished but otherwise well if there were no visible signs of illnesses or

problems/anomalies and cared for like term babies: *"…baby was otherwise healthy and beautiful at birth. Baby was under-nourished and hence was not so active…" (IDI03 Adolescent mother of a preterm baby).* For these babies, the routine care at home included feeding the child well, keeping them warm, clean and dry, maintaining cleanliness including timely bathing so that the baby becomes healthy or so that the baby does not fall sick. An untrained birth attendant mentioned the need for a three-way approach for care of preterm babies that included (i) extra care by mother, (ii) traditional/spiritual care for dealing with evil eyes/spirits and (iii) treatment from doctors depending on the condition of the baby:

> *"If you enclose the house, then the baby will be free from evil eyes or curses – this is spiritual or traditional treatment; If the child is under-nourished, or has cough and cold or gas, you need advice from doctors. In addition, mother needs to take extra care such as timely feeding, bathing, sleeping etc. In this way the child will become healthy in a few days." (KII06 Untrained birth attendant).*

The recommendation for babies that were born too early, or babies born too small was that advice should be sought from formal health care providers and care provided accordingly. Although participants could not mention the benefits or purpose of using incubators, a few recollected instances where babies born early were kept in glasshouses and treated till they could be brought home.

Findings also highlight that adolescent mothers were dependent on various members in their network for support and care for the preterm/term newborn. These sources varied by the type of support needed and the roles of natal and marital kins were found to be prominent in their narratives. While the role of the adolescent's mother in providing instrumental and emotional support was a constant theme, other members such as mothers-in-law, aunts and sisters were also important. These are highlighted in the excerpts below:

> *"My mother taught me this (how to breastfeed). I did not know how to. She told me the proper way to hold when breastfeeding so that the flow of milk is slow. Otherwise, the baby will choke." (IDI01 Adolescent mother of a term baby).*

> *"I was afraid to take care of baby, my mother used to do everything, from bathing to cleaning. Now I have learnt" (IDI03 Adolescent mother of a preterm baby).*

Temperature management

In rural Baliakandi, all newborns (preterm and term) were considered to be susceptible to cold and hence need to be kept warm: *"Newborns come from the womb, they need to be kept warm."* The threat of *"catching cold"* was more imminent among preterm babies since they are small and under-nourished. Several practices were followed to keep them warm and prevent the babies from catching a cold.

Our findings reveal that, in general, management of temperature depended on the weather or external temperature. Whilst all newborns are wrapped using a *katha* (traditional cloth made from old sarees) or towel immediately after birth, as days progressed newborns or babies were cared for according to the external temperature which included wearing warm clothes or covering the child with layers of cloth during rainy or winter days or during evenings and wearing thin clothes or using the fan during hot days. Among mothers with preterm babies particularly small or early preterms, practices included wrapping them in blankets, cotton, or holding the baby in mother's arms (to receive mother's warmth – *mayer om*) often at the advice of health care providers or elders. However, participants could not clearly specify how long they did this for and gradually started dressing newborns as per temperature.

Regardless of the communities' awareness about keeping newborns warm, traditional practices of immediate bathing after birth were prevalent. An adolescent mother of a preterm baby mentioned: "*We didn't bathe her for nine days. It is customary to bath babies after they are born, to clean all the impurities. So, on the 9th day my cousin sister-in-law shaved her hair off. We did not bath her fully but sprinkled some water over her body. That night the baby developed slight cough and cold*" (IDI07 *Adolescent mother of a preterm baby*). The adolescent mother then explained that her baby died on the way to the hospital.

A few mothers of preterm babies who experienced facility births or births with health care worker mentioned delaying first bathing to seven or 12 days as the doctor or health worker had suggested that their baby was too small. Some mothers and grandmothers whose babies were born at health facilities expressed discontent that in the absence of any bathing facility they had to bathe the baby once they returned home. Almost all babies were massaged with mustard oil on their skin before bathing. The mustard oil was seen to act as a protective barrier between the baby and the water, insulating the baby from cold. Almost all babies were bathed with lukewarm water, around mid-day. The water was warmed either by placing the container under the hot sun or over a hot stove during cloudy days. Babies were bathed almost every day except for cloudy, rainy or cold days, when bathing would be skipped, or they would be wiped with a wet cloth.

Feeding

Participants in our study widely shared the view that for under-nourished and weak preterm babies to grow healthy and regain their strength they must be fed well. For extremely preterm babies, who were not able to suckle, the practice was to express milk and feed with a dropper or spoon. For other preterm babies, feeding practices varied and some participants also mentioned pre-lacteal and non-exclusive breastfeeding. Honey and warm water ("to clear the stomach") were the two common pre-lacteal feeds mentioned. The common reason for non-exclusive breastfeeding with formula or cow or goat's milk was that the mother was not producing enough milk. On the other hand, mothers with hospital deliveries also recollected instances where they were told off by doctors for pre-lacteal feeding or had to stop

feeding babies formula milk based on the doctor's advice. One mother mentioned, *"I started feeding after a day…the doctor scolded us a lot for feeding the baby some warm water (IDI27 Adolescent mother of a preterm baby)"* while another mother mentions, *"…we used a dropper to feed the baby powder milk (formula milk)…everyone else was feeding so we thought it would be okay… but the doctor told us that it is not good for baby, so we stopped (IDI22 Adolescent mother of a term baby)."* In terms of interval or frequency, most participants mentioned that they fed their babies when they cried while some mentioned that they fed at regular intervals.

Weight monitoring

Although service providers were aware of the importance of weight monitoring, none of the interviewed participants was aware of the need to regularly monitor the weight of preterm babies. Birth weight was measured only for babies born in health facilities or when care was sought from formal health care providers.

5.4.4 Care-seeking for preterm babies and illnesses

Several factors influenced appropriate care-seeking for preterm babies as well as those with illnesses. These included a lack of knowledge about prematurity and perceived severity of illness, low decision-making ability and autonomy at the societal level, influence of family members and neighbours at the interpersonal level and several health systems factors such as unavailability of services and poor quality of care. These factors affected illness recognition, caused delays in decision-making regarding choice of care and uptake of appropriate services at the health facility. Adolescents were found to have low decision-making ability and often consulted family members before care-seeking.

Many mothers and family members frequently mentioned that preterm newborns were small, weak, and less mobile. In the absence of any visible signs of illnesses they considered that with appropriate feeding these babies would recover. As such, care was only sought when the babies presented with illnesses. A mother who was unable to understand the severity of the child's condition who was placed in an incubator mentions that initially they did not want to take her (now deceased) baby to a specialised hospital, despite being referred. In her words: *"My mom said baby was well, was moving and looking unlike her older grandchild. So, she did not want to take her to hospital"* (IDI09 Adult mother of a preterm baby).

Participants mentioned a range of health care providers for the treatment of their babies, including untrained traditional and spiritual healers, herbalists, homeopaths and village doctors. Participants claimed that they were often the first point of contact, and care was sought from qualified providers when the illness became severe or prolonged, as a father participating in a FGD highlights: *"If the baby cries a lot or has gas we go to kabiraj…For minor illnesses there is community clinic where services are free, people are poor here…then some also go to village doctors…if the baby does not recover we go to shishu hospital."* Mothers were also often found to use amulets and spiritual water to ward off

evil spirits or if the child was too cranky. Adolescent mothers also had little decision-making authority – the decision to seek care was usually made by the husband, in-laws or parents, or in consultation with them: "*I wanted to take my baby to the big hospital. But my in-laws did not approve. So, I went to the nearby doctor (village doctor) instead…*" *(IDI08 Adolescent mother of a preterm baby).*

Cost was another factor that was repeatedly mentioned by mothers and community members during the interviews. During the interviews, several participants highlighted that some preterm babies need specialised care or need to be kept in incubators (*glass-houses*) which were considered to be expensive. An adult mother of a preterm baby described two instances where one of them survived as the family was able to seek advanced and expensive care while the other was not: "*…see he was rich, do you understand…he took his child to Dhaka (the capital) and saved the baby by putting him inside the glass house (incubator)…whereas the other family used to live from hand-to-mouth…they waited for seven days and saw the baby was fine and stayed at home, but the baby died…*" *(IDI31 Adult mother of a preterm baby).* An adult mother mentioned that they were denied care at a health facility based on the assumption that they might not be able to afford the cost of the treatment whilst another adolescent mother waited for her in-laws to come and help because she had already spent a lot of money: "*The baby was very small and malnourished (pusto chilo na), but the doctor said if you take care well, she might survive. The doctor also told us to put the baby in a glass-house. However, we brought her home before we took her there. My in-laws were not at home, and we had already spent a lot of money at the hospital. So, we waited for them to come before admitting her in the glasshouse…*" *(IDI07 Adolescent mother of a preterm baby).*

At the health facility level, health care providers interviewed mentioned several challenges affecting service provision. For example, several service provider highlighted the lack of equipment and trained staff, as highlighted in the following excerpt: "*We are supposed to keep one baby in SCANU/warmer, sometimes I put in three babies…we have CPAP, but don't have the disposable equipment for it…we can't provide up to the mark service all the time…I also don't have enough trained staff…*"*(KII01 - Trained service provider).* Related to this was the unavailability of a KMC ward, particularly in public hospital settings which demotivated mothers to practice KMC in front of other patient and families: "*In the absence of dedicated KMC ward, mothers don't want to do KMC…*" *(KII01-Trained service provider).* In addition, another service provider highlighted the ineffectiveness of the referral system and pointed out the challenges of parents and families in arranging their own transport causing delays: "*If we cannot provide treatment, we refer…but the patient has to arrange the transport…we do not have a system…*" *(KII02-Trained service provider).*

Other challenges that service providers mentioned were related to availing services by the users and included late presentation or delay in care-seeking from the health facility, wanting to leave quickly from the health facility due to cost or other responsibilities and not coming back for regular follow-ups. These are highlighted in the excerpts below:

Late presentation. *"Preterm babies are brought to the hospital very late…we receive a lot of cases…"(KII03 Trained service provider).*

Early discharge. *"Patients here are poor, they want to leave early…they don't stay to see if weight of baby is steadily increasing or not…" (KII-04 Trained service provider).*

Lack of follow-up. *"Some patients come for follow-up others don't unless the baby is ill" (KII05 Trained service provider).*

On the other hand, mothers and family members who sought care at health facilities mentioned a lack of responsive and respectful care including poor communication, denial of care, verbal abuse, and non-consented care. Among these, verbal abuse was commonly mentioned. Two mothers reported that it was difficult to reach doctors and nurses who used to get angry if the patients' family enquired about them or asked them to come and check on their baby: *"We had to call the doctor to come…if you called them more than twice, they would get angry and scold us…" (IDI08 Adolescent mother of a preterm baby).* Other mothers reported being confused about the care given or not taking appropriate consent before initiating treatment. For example, an adult mother was not happy when her baby was kept in the same incubator with another child: *They put another baby in the same glass house (incubator) as mine… was that right? Different children have different illnesses, other beds (incubators) were empty" (IDI09 Adult mother of a preterm baby).* Similarly, a grandmother left the hospital with the baby when the service providers-initiated treatment without asking: *"The grandmother started arguing why the baby was given the medicine. She removed all the equipment, washed the baby's head, and left next morning…" (IDI09 Adult mother of a preterm baby).* Surprisingly, another mother of a preterm baby also mentioned how they were forced to move from one health facility to another, causing delays, based on the assumption that wouldn't be able to pay for the treatment as the excerpt below reveals:

"They (private hospital) said my baby is too small and the costs are too high here. We said we will pay, but they said they don't want to take the risk and asked us to take baby to the government hospital." (IDI33 Adult mother of a preterm baby).

5.5   Discussion

5.5.1 Main findings

The findings from this study contribute to our understanding of newborn health and care of preterm babies among mothers including adolescents in rural Baliakandi from the perspectives of the parents themselves, as well as family and community members, and health care providers. The findings have been categorized into two major areas of exploration: (i) perceptions and understanding of PTB and (ii) care practices and care-seeking for preterm babies. In general, findings highlight poor understanding of PTB, with major gaps in care and care-seeking practices among all, including adolescents. We observed gaps and variations in understanding of preterm birth (length of gestation, appearance, causes, problems

faced) and care practices (thermal management, feeding, weight monitoring) among all, but particularly among adolescents. Adolescents were found to be largely dependent on family members for these care practices for their preterm babies. The use of multiple providers and delays in care-seeking from trained qualified providers for sick preterm babies was noted. Factors affecting appropriate care seeking included perception of severity of illness, cost, convenience, and quality of services. Health systems challenges included lack of equipment, supplies and trained staff in facilities to provide special care to preterm babies. These findings can enable public health practitioners and policy makers to design the health systems' response to PTB in a locally relevant way.

5.5.2 Findings in the context of the literature

The findings revealed variations and gaps in knowledge among the participants about various pregnancy issues including normal pregnancy duration, and perceived causes and consequences of PTB. The perceptions regarding normal pregnancy duration varied between nine months and 10 months and 10 days. A baby born in the 7th or 8th month was considered preterm. This finding is similar to reports from Malawi, Ghana and Uganda, where gestational age at the community level was quantified in months with babies born before nine months being considered to be preterm (46-49, 60). Accurately estimating the gestational age is crucial for facilitating care-seeking for PTB and the provision of life saving and time-sensitive interventions. The prevalence and preference for home births (51%) in Bangladesh is still high, and unless mothers are educated about PTB and the risks it poses, care-seeking and facility birth even for preterm labour will continue to be low (61, 62). In addition, like other studies in Bangladesh, our findings also reveal a high acceptance and usage of ultrasonography (80% in 2017). However, USG is mostly utilized in the latter trimesters when its accuracy for estimating the due date of delivery is less than in the first trimester even though it may still provide some information about foetal growth and wellbeing (61). Therefore, educating mothers about the value of early pregnancy USG will improve the accuracy of gestational age estimation and consequently the diagnostic accuracy of premature labour and birth. This would ultimately lead to more prompt care-seeking for threatened preterm labour, leading to improved risk mitigation by interventions such as antenatal corticosteroid and magnesium sulphate therapy to reduce the risk of respiratory distress syndrome and neurological sequelae respectively.

Most of the mothers (adults and adolescents) in this study had limited knowledge of the causes of PTB. Those who demonstrated some awareness volunteered a mix of bio-medical and supernatural/spiritual explanations and practices for PTB. The commonly perceived causes e.g., heavy work/stress, inadequate nutrition/food intake, trauma to the abdomen etc., were in line with qualitative studies conducted in similar resource poor settings (46, 47, 63). While this is encouraging, participants either failed to identify some potential associations with PTB or held beliefs that could deter appropriate antenatal or newborn health care-seeking. For example, contrary to the studies in Malawi, young maternal age was highlighted as a risk factor only by a few fathers in IDIs and FGDs (46, 47, 63).

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Participants did not appreciate that previous history of miscarriage or PTB, and multiple pregnancy were risk factors for PTB, often attributing it to supernatural causes such as evils spirits or God's will (46, 47, 63). This is consistent with the findings from previous studies in rural Bangladesh and elsewhere, all of which deter women from antenatal care-seeking and encourage resort to spiritual treatments from religious leaders and faith-healers and traditional practitioners (39, 49, 64, 65). The misperception of the mothers regarding PTB requires concerted efforts at culturally congruent education to improve care seeking in their future pregnancies. Indeed, Legare et al. (2012), highlights the pivotal role of understanding the extent to which traditional perinatal explanations and practises compete, conflict and coexist to provide unique insight into cultural ecologies of health, and asserts that this is critical to improving the efficacy of health education interventions and policies (66, 67). In addition, the social capital associated with traditional medicine could also be capitalised to improve knowledge of the community regarding PTB and appropriate referral for high-risk preterm babies.

In general, breastfeeding improves neurodevelopmental outcomes and protects preterm babies from sepsis, necrotizing enterocolitis, and retinopathy of prematurity (68-70). Breastfeeding was highly valued by the community in our study, primarily, to improve the health of the weak and under-nourished preterm babies. Despite this, we also observed non-recommended practices such as prelacteal feeding, and non-exclusive breastfeeding. Several studies exploring care in newborn or low-birth-weight newborns in Bangladesh and similar settings also report that newborns or babies are primarily supplemented with either formula milk, cow or goats' milk or porridge (rice, sugar and water) when the mothers feel that they are not producing enough milk or are insufficiently lactating, whereas prelacteal feeds are usually introduced as a ritual practice, "to help keep baby's throat and stomach clear", or due to a delay in the flow of breastmilk (71-75). Often, the suggestion of the formula feed is made upon consultation with formal or informal care providers (75). Overall, in Bangladesh, 87% of women who experienced facility births were counselled on exclusive breastfeeding. This has resulted in a decrease in the proportion of children who are given prelacteal feed and an increase in non-exclusive breastfeeding (61). Even so, about 29% of children under-2 years are given prelacteals and 35% of children 0–5 months are not exclusively breastfed, according to the 2017-18 BDHS report (61). This highlights that further improvements can be made, especially among young mothers or mothers of preterm babies, for example by training neonatal nurses or health workers to provide home or facility-based evidence-informed breastfeeding support (76-78).

The community in Baliakandi did not recognize hypothermia to be a separate entity but were conscious that newborns, and specifically preterm babies, are at high risk of "catching cold" and indicated preventative practices such as bathing babies at noon with warm water, the use of emollients, and appropriate dressing of babies according to the external temperature (39, 74, 75, 79, 80). None of the participants, including those who gave birth in facilities, was aware of or had practiced KMC. The community still valued early bathing, but bathing was more likely to be delayed by three or more days

for neonates born at health facilities or upon advice of health care providers. While these practices do not fully protect newborns from hypothermia, it is evident that the community in Baliakandi as well as those in Sylhet, Gopalgonj (65, 72, 74), placed a high value on keeping babies warm. Efforts to implement and improve the implementation and adoption of appropriate thermal care and KMC for preterm babies can capitalize on this pre-existing awareness (65, 72, 74). However, KMC has been scaled up in only 314 facilities in Bangladesh, with less than 5% of preterm newborns receiving KMC in 2021 (80). Our findings highlight the need for further concerted effort to accelerate training and scale up of KMC in rural communities and facilities by addressing health systems challenges and demand-side barriers.

Although programming often targets interventions to preterm babies, the emergent themes in this study suggest that the local explanatory model of PTB does not always consider being preterm as a determinant or stimulus for health care-seeking. Instead, community members considered various observable characteristics and illnesses of the baby or newborn to first judge the overall health. According to the participant narratives, it was natural for preterm babies to be small and weak. In the absence of any visible illnesses or symptoms, many of these babies were considered to be healthy babies who would grow well if fed appropriately. As a result, many at-risk babies, especially late PTBs, in this community are overlooked or care-seeking delayed due to the inability of caregivers to identify risk factors, spot danger signs and assess severity. In agreement with studies in Uganda and Malawi babies were considered at high risk and more likely to receive care when they were very small, had fused eyelids, thin or wrinkled skin, or breathing problems etc. (45, 46, 48, 63). Similarly, studies in Bangladesh and similar settings have associated recognition of symptoms of illness and danger signs with increased care-seeking for sick preterm children. This reiterates the need to educate caregivers on recognition of risk factors for mortality and morbidity (49, 81, 82).

A few prior studies in rural Bangladesh and other low-resource settings also highlighted perception of inevitability or fatalism in preterm or sick newborns as a deterrent for care seeking (83-85). Although, participants in our study repeatedly mentioned that babies born as early as seven months may not survive, their views were not fatalistic but rather the overall opinion was to seek care from qualified/formal health care providers for such babies. Several participants also mentioned the use of incubators or challenges of having to spend a lot of money for formal care, indicating a shift in beliefs towards acknowledging that extremely preterm babies can also survive.

The local explanatory model for newborn illness in Baliakandi, as in other parts of Bangladesh, or other low-resource settings is largely influenced by a wider ecological framework including the management options available and other factors related to the local health system. In Baliakandi, participants reported several barriers to accessing formal health care - financial constraints, quality issues (lack of services, trained staff and equipment, inadequate referral system etc.) and disrespectful care. They demonstrated a preference for informal care by unqualified providers, consistent with prior studies that have

highlighted that only a small proportion of families sought care from formal providers (49, 83, 86, 87). Equally, there is ample evidence regarding the limited availability of good quality care at health facilities including in Bangladesh (45, 46, 88-90). Care-seeking decisions regarding newborns and children is often influenced by family members, relatives, neighbours and peers whose narratives often reinforce reports of mistreatment in facilities in contradistinction to positive views regarding traditional care (90, 91). Improving access to and quality of preterm and newborn care at health facilities, delivered respectfully, is therefore an imperative to drive shifts in the care-seeking behaviour and subsequently the local explanatory model (90, 92).

Our study also revealed that most adolescents lived with their extended families and were highly dependent on their social network particularly natal and marital kins for support (39, 73). Instrumental and informational support for care of their baby was provided primarily by their mother and mother-in-law, whereas financial support was provided by their husband and other family members. As such, decision making related to care and care-seeking for sick babies was never made in isolation but rather jointly taken with husbands and family members. In rural Bangladesh where adolescents lack knowledge and decision-making authority, health education on preventative practices and management practices of the preterm babies should, therefore, be provided at the family level involving women, their husbands, and the mother/mothers-in-laws (39, 73).

5.5.3 Strengths and limitations

One of the strengths of this study is the inclusion of different methods and participants to triangulate the findings. We conducted IDIs, FGDs and KII with participants from different ages (adults and adolescents), birth status (preterm, term), genders, and relationship with the babies, allowing us to report similarities and differences in values and beliefs. Despite the benefits, summarising perspectives of multiple groups of participants and reporting their findings was challenging. In order to ensure that we do not over emphasise or marginalise any group and to refine our interpretations, we conducted a thematic analysis revisiting the data and summaries, and conducting regular discussions with the team involved in data collection and analysis to enhance the depth of the summary. Participants with preterm and term births were identified from the existing surveillance system and birth status (preterm, term) were also verified during interviews. However, data was collected retrospectively and may be subject to recall bias. To minimize recall bias, we included participants within 6 months of birth.

5.6 Positionality of the researcher

As the lead researcher in this study, my academic and professional experiences had provided me with a deep understanding of the socio-economic and health-related challenges faced by communities in resource-limited settings. I have a background in development studies and public health (from Bangladesh), with a strong focus on maternal and child health research at the community level. My first research study, which explored postpartum depression in women living in urban slums in Bangladesh,

along with my subsequent involvement in evaluating community-based maternal, newborn, and child health interventions in rural Bangladesh, expanded my understanding of maternal and newborn health issues in rural communities, including the socio-cultural and health system barriers affecting healthcare access and outcomes. These experiences, along with my personal experience as a Bangladeshi woman and mother of two, shaped my research approach and my understanding of PTB from a public health perspective.

That said, I was very aware of my own privileged background and how my educational and professional opportunities had shaped the way I see the world. While I shared cultural ties with many of the women interviewed, I knew my experiences were different from theirs, especially for those from rural areas, young mothers, or those who had experienced PTB. To stay mindful of this, I made it a point to be reflexive throughout the research process—constantly checking my own assumptions, biases, and engaging with colleagues to get a broader perspective.

Building trust and rapport with adolescent mothers and community members was crucial for gathering meaningful insights. My familiarity with the language and cultural nuances in Bangladesh was essential in establishing rapport with participants, but I was also careful to avoid making assumptions based on my own cultural understanding. Being a married woman with children allowed me to connect more easily with the mothers in the communities. I was often asked if I was married or had children, which helped foster open and honest discussions. Also, coming from a social science background rather than a medical one helped ease power dynamics during interviews and focus group discussions, making participants feel more comfortable sharing their thoughts.

I was also conscious of the ethical responsibilities tied to this research, ensuring that participants fully understood the study's purpose, provided informed consent, and were assured of confidentiality. Each interview or discussion was conducted in a private location at a time convenient for the participants, which created a comfortable and secure environment for open conversation. Additionally, I was particularly sensitive to the experiences of mothers and families who had experienced PTB or the loss of a newborn, approaching these discussions with empathy and care to ensure they felt supported and respected.

Because of all these factors, my background, experiences, and reflexive approach, I felt I was well positioned to conduct this research in a way that was both sensitive and impactful.

5.7 Conclusion

A combination of factors including local knowledge, socio-cultural practices and health systems challenges influenced awareness of, and care for, preterm babies among adolescent and adult mothers and the community. Strategies to improve birth outcomes will require increased awareness among adolescents, women and their families about PTB and improvement in the quality of, and access to,

PTB services at health facilities – especially for adolescent mothers. In addition, intervention strategies to improve care of preterm babies should account for social, cultural, and economic reasons for current practices. Additionally, improved quality and competence of health facilities in managing care for preterm babies is likely to motivate appropriate care-seeking and improve chances of survival for those who do seek care.

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6   Chapter 6: General discussion and conclusion

Around 2.3 million newborn deaths were recorded in 2022, mainly concentrated in Sub-Saharan Africa, Central, and South Asia (1). Despite a 44% decline in neonatal deaths since 2000, 64 countries are projected to miss the SDG target for neonatal mortality by 2030 without immediate action (1). PTB remains the primary cause of neonatal deaths, with roughly 900,000 children dying due to complications of PTB in 2019 (2). In 2020, an estimated 13.4 million babies were born prematurely, highlighting a global issue with significant survival rate disparities between high and low resource settings (3).

My PhD aims to bridge the knowledge gap surrounding PTB in LMICs by identifying and prioritising future research areas for preventing and managing PTB and PE/E that are contextually relevant to the specific needs of these regions. By combining research prioritisation with insights from high-risk groups, especially adolescents in low-resource settings, the study seeks to inform policy and practice in order to address maternal and newborn health disparities. Ultimately, the goal is to align research with the SDGs that will aid in the development of impactful, context-specific interventions and strategies to reduce maternal and neonatal mortality in LMICs.

6.1   Summary

I employed the well-established CHNRI method for setting research priorities related to PTB and PE/E in LMICs involving partners in four countries – Sheffield (UK), Cape Town and Pretoria (South Africa), Dhaka (Bangladesh), and Ilishan-Benin-Kano (Nigeria). Study 1 detailed the research priority setting process and outcomes for preventing and managing PTB in LMICs, with a specific focus on Bangladesh in the post-MDG era and highlighted considerations for their successful implementation. Seventy-six experts contributed 490 research questions, which were collated into 95 unique questions for scoring by 109 experts. The top twenty priorities for LMICs primarily emphasized health systems and policy research, including improving Kangaroo Mother Care uptake, promoting breastfeeding, enhancing referral systems, and evaluating skilled attendant use, quality improvement activities, and exploring barriers to antenatal steroid use. These priorities aligned closely with those for Bangladesh, which also highlighted community-level care improvements and epidemiological inquiries related to measuring developmental outcomes, gestational age estimation, antepartum complications, and nutrition.

In study 2, I outlined the research priority setting process and outcomes for PE/E in LMICs, focusing on Sub-Saharan Africa and South Asia. Forty-nine experts provided a total of 254 research questions through online submissions. These questions were then condensed into 76 distinct queries and distributed to all experts for evaluation. Sixty-nine experts participated in scoring these questions, assessing them based on five predetermined criteria: answerability, potential for translation, deliverability, maximum potential for burden reduction, and effect on equity. Experts prioritised health systems and delivery research to improve the detection, transfer, and management of PE/E, including reducing care delays, enhancing supply availability, assessing provider readiness, implementing

guidelines, and improving referral systems. Additionally, priorities included early identification and follow-up of at-risk women. While most priorities were consistent across LMICs and Sub-Saharan Africa, specific regional priorities for Sub-Saharan Africa included improving postpartum screening and management of hypertension, exploring barriers to early identification of high-risk women, evaluating digital technologies, and assessing anti-hypertensive medication effectiveness. Substantial variation was seen in the priorities identified for South Asia and the overall LMIC priorities, possibly due to the low number of experts participating for South Asia.

During the CHNRI research priority setting process, initial stakeholder engagement was conducted in Bangladesh to garner support for the exercise. During that workshop, stakeholders expressed keen interest in investigating evidence gaps related to PTB among adolescents, given the high rates of adolescent motherhood and PTB in Bangladesh. In response, Study 3 was conducted, focusing on exploring the perceptions and experiences of adolescents in caring for their preterm babies. Additionally, other groups such as adult mothers with PTB experience, family, and community members were included in the study to provide a comprehensive community-level perspective. Various factors, including local insights, socio-cultural norms, and obstacles within healthcare systems, impacted the awareness and management of preterm babies among both adolescent and adult mothers, as well as within the community. Study participants primarily referred to babies born 'before time' as undernourished, weak, or underdeveloped. There was discordance about the 'normal' length of gestation. Poor maternal nutrition, infection, heavy work, evil spirits and God's will were mentioned as reasons for PTB. Breast-feeding was considered crucial for the growth of under-nourished preterm babies, but practices of pre-lacteal feed and non-exclusive breastfeeding were common. Newborns were kept warm mainly to prevent them from catching cold or cough and participants were not aware or had practiced KMC. Use of multiple providers and delay in care-seeking from trained providers for sick preterm babies was observed often influenced by the perception of severity of illness, cost, convenience and quality of services. Health systems challenges included lack of equipment and trained staff to provide special care to preterm babies. To address these findings, we proposed two recommendations: Firstly, implement awareness-raising strategies targeting adolescents, women, and families regarding preterm birth (PTB). Second, enhancing the accessibility, quality, and capabilities of healthcare facilities in managing preterm baby care, which is not only important for improving survival rates among those seeking care but is also crucial for reinforcing appropriate care-seeking behaviour in the long run. In addition, we also noted that, intervention strategies to improve care of preterm babies should account for social, cultural, and economic reasons for current practices.

6.2 Implications of findings and lessons learnt

The top research priorities identified through the exercises primarily aim to enhance care at various stages, focusing on addressing the burden in LMICs in the short term. These questions emphasise health systems and implementation research rather than discovery and basic science research, which still

typically require substantial commitments from stakeholders, including donors and funders (4-6). In addition, these priorities aim not only to identify barriers and implement strategies to streamline the care pathway for high-risk women and newborns but also to facilitate the implementation of international guidelines and recommendations on antenatal care (7), PTB (8-10), and pre-eclampsia management (11). Consequently, our research outcomes should inform researchers, funders, programme developers, and policy implementers in LMICs and Bangladesh on future research investments needed to achieve SDG targets in this critical area. A common limitation in research priority setting is the lack of implementation of identified research priorities (12) (13, 14). Research prioritisation, therefore, should align with, not undermine, national health goals and engaging well-defined stakeholders ensures ownership and integration of priorities into national health research systems instead of creating parallel priorities (15, 16). In 2014, WHO established global research priorities for newborn health until 2025 using the CHNRI method (17). A recent review assessing progress found that 40% of these priorities had seen high research uptake, while 55% had moderate uptake and one priority remained unaddressed (18). Another study highlighted that, implementation research, crucial for evidence-based interventions at scale, consistently received insufficient funding, with the authors stressing that the proper allocation of these resources could significantly hasten local progress in newborn survival, contributing to meeting the SDGs by 2030 (6). These findings underscore the importance of directing attention and resources towards areas with less research, ensuring comprehensive progress in tackling newborn health challenges. To this end, we conducted extensive stakeholder engagements to enhance ownership and uptake of prioritised areas. We involved local stakeholders including policy and programme implementers from the outset, and findings were widely disseminated through local and international workshops and conferences. The benefits of stakeholder engagement were directly evident in the community-based adolescent study (study 3). As noted, during the CHNRI process, stakeholders emphasised the need to address evidence gaps PTB among adolescents. After sharing the study's findings with local stakeholders, including programme managers and service providers, a follow-up study funded by NIHR was initiated. This small-scale study, focused on designing, co-developing, and piloting an intervention with the Government to raise awareness about PTB prevention and management among mothers in rural Bangladesh. As an outcome, national maternal and newborn Behaviour Change and Communication (BCC) materials were updated to include messages about KMC and care-seeking for preterm infants.

Since the endorsement of ENAP and EPMM in 2014, several CHNRI exercises were carried out related to maternal, perinatal, and newborn health. These studies varied in context and included studies to identify global priorities on maternal, perinatal or newborn health (19-21); or local or regional priorities on maternal, newborn, child health in India (22, 23), Ethiopia (24), Africa (25), Uganda (26), LMIC (27); child nutrition including wasting (28-30); child development (31-34); child health in crisis setting (35, 36); private sector delivery (37); paediatric HIV (38, 39); prevention of mother-to-child

transmission (PMTCT) (Africa) (40); and integrated community case management (iCCM) (41). These exercises identified 13 research questions focused on addressing issues related to PTB (Chapter 2, Table 2-6). A recent priority setting exercise using methods similar to CHNRI was also conducted as a complementary exercise to the development on WHO guideline on PTB and LBW in 2023 and recommended 12 new priority areas for research. The variations in priority-setting exercises reflect the needs of differing contexts and countries, regions. It indicates that global bodies have distinct research priorities shaped by factors such as disease burden, healthcare system capacity, policy agendas, funding availability, and stakeholder perspectives. While these priorities may differ based on the contexts, they often overlap. Global bodies like the WHO provide guidelines and frameworks that many countries align with, ensuring a shared focus on the most pressing health challenges. As a result, while local needs and conditions influence priorities, broader global health objectives help create alignment in research efforts. In addition, national priority setting often include implementation research, addressing how the globally recommended interventions can be adapted and delivered in real-world settings. For example, promotion of exclusive breastfeeding, post discharge follow-up visits, scaling up KMC in health facilities were identified as a priorities in our exercise as well as the recent WHO led exercise. However, our exercise also prioritised the effectiveness of community-based initiation of KMC (cKMC), a topic that the WHO-led exercise had already addressed and recommended in the guideline. Despite the global recommendations, cKMC is not yet practiced in Bangladesh, and challenges persist in scaling up facility-based KMC. This is also a problem in other LMIC settings highlighting the need for further research to identify challenges in the implementation, scale-up and coverage of facility-based KMC, improve utilisation of cKMC, improve the quality of KMC counselling, and increase the overall acceptability and compliance of KMC. We should bear in mind that research priority setting is not a one-time event; ongoing analysis is necessary to assess whether researchers are adopting the priorities (12) (13, 14). Future evaluations and revisions are essential to ensure that research investments remain relevant and aligned with emerging needs and guidelines.

One of the key challenges we encountered in our exercise was the low response rates, an issue that has been consistent across many previous CHNRI exercises. This led to concerns about response bias, as the majority of participants were self-selected. While increasing the number of participants could help reduce some of this bias, it does not fully address the issue. To increase participation, we included structured and unstructured methods were used to list a large and diverse pool of experts for the study, sent regular requests and reminders, invited the larger pool of experts, not only those who submitted research questions to the scoring process. Although still underrepresented, we also made an effort to include policy and programme implementers, particularly at the national level in Bangladesh, to ensure a broader range of perspectives. Additionally, drawing from our experience with the PTB prioritisation exercise, we reduced the number of criteria to be scored for the PE/E exercise from 15 to seven. This was aimed at increasing participation while also reducing scorer fatigue. Research questions were

randomly assigned to experts to ensure each question had an equal likelihood of being scored, allowing us to include incomplete scoring in the analysis. Other methods which could not be implemented in our exercise include tracking completion using software tools like SurveyMonkey to send targeted reminders and analysing whether scoring varied based on the characteristics of those who responded versus those who did not (42). That said, lessons can be learnt from other users of the method who engaged about 1000 experts in their priority setting exercises (25, 43).

In my experience with the CHNRI method, I found that consolidating research questions was the most time-consuming component of the process. The research ideas submitted by participants varied greatly in their level of specificity and clarity, which created challenges and may even result in bias when trying to consolidate them (44). This also led to a dilemma about how specific or broad individual research questions should be (44). Although we consolidated the research questions based on discussions with the project management team (to reduce bias), we noticed a difference in how they were scored by the experts. For example, consider the following three questions focused on early screening of women at risk of PE/E in our study, arranged based on the research priority scores, high to low:

- Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.

- What factors influence the use of simple interventions, such as BP measurement, to detect hypertensive disorders in LMICs?

- Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?

In the analysis, the more specific question ranked lower in comparison to more general one. Yoshida et al. (2019) argues that detailed questions like the latter one appeal to a smaller group with a particular focus, while broader questions tend to attract more attention and support (44). There should, therefore, be clear guidance on how to address this challenge. Balancing specificity and generality are key for ensuring both targeted expertise and wider support for research priorities, and clear frameworks should be developed to guide participants in formulating balanced research questions.

Another notable challenge in both the research priority setting exercises worth reiterating is the limited stakeholder engagement, which deviates from the guidelines set by CHNRI. A large, diverse and heterogeneous group of stakeholders (funders, international and regional organisations, researchers, policy makers, service users, or advocacy groups, journalists, lawyers, economists, experts in ethics etc) is needed to "weigh" and set "thresholds" for minimum acceptable scores for each predefined criteria (16, 45). Among 102 reviewed exercises (chapter 2, Annex 1), only 28 engaged stakeholders, with most (15 exercise) national-level efforts involving small, non-representative groups (20–79 participants). Additionally, applying weights and thresholds had minimal impact on research rankings. Yoshida et al. (2017) suggested a sample of 500–1000 stakeholders for national exercises to ensure representativeness

(46). Studies in Zambia and Iran showed that funders had disproportionate influence, while rural communities, women, and young professionals were underrepresented. Digital tools like Telegram and Amazon Mechanical Turk have been explored to expand engagement, with mixed success. (15, 47-49) Overcoming this challenge requires further investigation to understand potential solutions and to improve stakeholder inclusion, CHNRI exercises should diversify participation, leverage digital platforms, and refine methods for incorporating stakeholder input into prioritisation.

Although the qualitative exploratory study among adolescents was prioritised by stakeholders during the initial CHNRI workshops, it was not conducted to align with the CHNRI results or to inform its research priorities, as both took place almost simultaneously. Instead, the study aimed to identify gaps in knowledge and care practices, offering contextual insights that could help shape future research priorities for this high-risk and vulnerable group in Bangladesh.

However, some gaps identified in the qualitative study may directly or indirectly correspond with the research priorities established through the CHNRI process. The qualitative study identified several other critical gaps in maternal and newborn care practices among adolescents, particularly in pre-lacteal feeding and non-exclusive breastfeeding. Many mothers introduced liquids or foods to their newborns before initiating breastfeeding, increasing the risk of infections and compromising infant nutrition. Additionally, the study highlighted issues of poor and disrespectful care in health facilities, with mothers reporting judgmental attitudes from healthcare providers, and dismissive behaviour discouraging them from seeking facility-based care. Financial constraints and inadequate referral and transport systems further compounded these challenges, leading to delays in accessing emergency care. Findings indicated that hospital care was primarily sought only in emergencies or based on severity of the condition, and many families relied on multiple healthcare providers, including traditional healers and informal practitioners. Inconsistencies in how preterm birth was understood and measured in terms of gestational age also often led to the misclassification of preterm births, affecting the timely provision of essential interventions and potentially impacting newborn survival and long-term health outcomes. Although these issues closely align with the research priorities identified in the CHNRI exercise including promoting early and exclusive breastfeeding, improving the quality of care in health facilities, strengthening referral networks, identifying barriers to gestational age estimation, and enhancing community-based newborn care and support for community health workers, involving mothers and communities in the process of identifying research priorities could have further highlighted research priorities based on their direct needs, making the research process more grounded in the lived experiences of those most affected. For example, although advocated widely nowadays, implementing respectful care was a research question that was not prioritised in the top-20. Similarly, while mothers and communities recognised the importance of thermal management for preterm newborns, they were largely unaware of Kangaroo Mother Care (KMC) and relied on traditional practices to keep babies warm. Service providers, however, highlighted challenges, such as the lack of dedicated spaces for

KMC and reluctance among mothers to practice and this corresponded to CHNRI-identified priorities focused on addressing barriers to implementing facility-based KMC, improving the quality of KMC counselling, and enhancing acceptability and adherence to KMC.

Meaningful community engagement in research priority-setting ensures that research aligns with the needs and experiences of those most affected, particularly people with lived experience and disadvantaged or vulnerable groups (50-52). It enhances the relevance, impact, and equity of research by incorporating diverse perspectives, identifying knowledge gaps, and addressing barriers to care (52). Several barriers to engagement have been identified for community engagement at personal, relational, and organisational levels (52-54). Personal challenges include a lack of knowledge, awareness, and feelings of intimidation, while relational issues involve power dynamics, cliques, and internalised powerlessness. Researchers may struggle with limited engagement experience, insufficient commitment, and the undervaluing of community knowledge whereas organisational barriers include funding shortages, lack of diversity, bureaucracy, logistical constraints, time limitations, technological issues, and inadequate compensation (52-54). Example of research priority setting involving patients and caregivers and lay public can be seen in initiatives like the James Lind Alliance and NIHR Public Involvement, Dialogue Method (Netherlands), Global Evidence Mapping (Australia), and the Deep Inclusion Method/Choosing All Together (US), however they are more practiced in high income countries (55-57). Although community engagement is more commonly practiced in high-income countries, Participatory Action Research (PAR), developed in the 1940s, has been a longstanding approach in LMICs where researchers and participants—particularly those from the community—work together to understand and improve their practices and situations (58). However, despite its long history, several studies indicate that community engagement in LMICs still faces barriers, and much of the engagement remains ad-hoc or inconsistent (59-61). This suggests that while community engagement in LMICs is possible, achieving meaningful participation in research priority setting will require structured guidance and support to overcome these challenges and ensure its effectiveness.

6.3   Conclusion

My PhD project has produced research, care, and policy recommendations tailored to the specific context of the studies, aiming to enhance care for preterm babies in resource poor settings, particularly Bangladesh. Through the CHNRI research prioritisation method, I have identified key areas for improvement, guiding the execution and definition of outputs that can be implemented to enhance maternal, perinatal, and newborn health outcomes. The implementation of research ideas stemming from priority setting exercises and addressing gaps in care practices for preterm babies at the community level holds promise for alleviating the burden of PTB in Bangladesh and LMICs. This effort is crucial for accelerating progress towards achieving the maternal and newborn health targets outlined in the SDGs. By translating the research ideas into practical interventions and policies, we can work towards

reducing the burden of PTBs and improving the health outcomes of mothers and newborns, thereby contributing to the broader global health agenda.

6.4   References

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7 Annexures

Annex 1 Summary of CHNRI exercises conducted (2007-2024)

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
1	(D'Mello-Guyett, Heylen et al. 2024)	Water, sanitation and hygiene (WASH) in humanitarian crises	Global, regional, country and local levels	6	All countries, communities affected by or at-risk of humanitarian crises	Morbidity, mortality, hygiene practoces, sustainability etc.	5	1500+	128	286	Y
2	(Song, Adeloye et al. 2024)	Global pandemic preparedness	Global	-	-	-	5	1000	163	42	N
3	(Ssendagire, Mohamoud et al. 2023)	Context specific knowledge to advance universal health coverage	National (Somalia)	-	-	Strengthening the Somalia national health research system	2	200+	231	42	N
4	(Korte, Teklie et al. 2023)	MNCH	National (Ethiopia)	5-10'	Women, newborns, children, and adolescents	Mortality, morbidity	1-4'	236	56	62	Y
5	(Kapilashrami, John et al. 2023)	Migration health research priorities	India/South Asia	10	Migrant population	Health of migrants and migration health challenges	5	123	59	34	N
6	(Lelijveld, Wrottesley et al. 2023)	Nutrition	LMICs	10	School-aged children and adolescents	Malnutrition, including micronutrient deficiencies	4	285+	48	116	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
7	(Abalos, Adanu et al. 2023)	World Health Organization Labour Care Guide	Global	2-5'	Pregnant women experiencing labour and childbirth by skilled health personnel in facilities	Maternal and perinatal health, experience of care and process outcomes around the time of birth	5	220	70	75	N
8	(Tine, Herrera et al. 2023)	Malaria control and elimination	Sub-Saharan Africa	-	-	Malaria control and elimination	6	128	33	46	N
9	(Sadeghi-Bazargani, Razzaghi et al. 2022)	National road safety	National (Iran)	-	-	National road safety	5	--	145	25	Y
10	(Polašek, Wazny et al. 2022)	Impact of COVID-19	LMICs	Urgent	All populations living in LMICs	Impact of COVID-19	5	642	192	52	N
11	(WHO 2022)	Communicable, noncommunicable diseases,injuries; reproductive, maternal, newborn, child and adolescent health; health systems services; mental health	National (Pakistan)	-	-	-	5	80+	155	-	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
12	(Fasina, Nanyingi et al. 2022)	One Health: Improving capacities in public and animal health systems	National (Kenya)	-	-	-	5	183	193	60	N
13	(Chapman, Browning et al. 2022)	Difficult to treat Depression	National(UK)	5	All adults (16+)	Difficult-to-Treat Depression	5	90	99	42	Y
14	(Weobong, Ae-Ngibise et al. 2022)	Mental health and disability	National (Ghana)	0-5'; >5	All	Mental health and disability	5	153	55	40	N
15	(Siefried, Ezard et al. 2022)	Methamphetamine and emerging drugs of concern	National (Australia)	-	--	-	12	59	-	-	N
16	(Paskins, Farmer et al. 2022)	Rheumatic musculoskeletal diseases	UK; beyond UK	0-3; >3	People>18y with, at risk of, musculoskeletal disorders, families, carers, and health-care providers	Enhance prevention, early detection, and treatment and care; to improve the quality of life and wellbeing; to reduce personal, social, and economic burden	3	285+	68	285	N
17	(Ko, Cherian et al. 2022)	Cholera	Global, regional, national, and sub-national	10	Cholera endemic or at epidiemic risk countries, communities	Prevalence and morbidity as well as any economic or social impact of cholera	5	245 (?)	93	138	Y
18	(Groom, Mossinger et al. 2022)	Clinical trials, cohort studies addressing health and healthcare for mothers/ babies	Aotearoa New Zealand	-	-	Maternal and perinatal health and healthcare	5		358		Y

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
19	(COVID-19 Research Prioritization Group on MNCAH 2021)	COVID-19 on MNCAH	Global	2	MNCAH	Direct and indirect effects of the COVID-19 pandemic on MNCAH	6	264	220	121	N
20	(Tudor Car, Teng et al. 2021)	Family physician, general practitioner recruitment and retention	National (Singapore)	Long term		Improves recruitment/retention	4	50	33	50	N
21	(Francis-Oliviero, Bozoki et al. 2021)	Vaccination coverage	Europe	3-5'	All ages	Vaccine and vaccination research (Measles, Pertussis, Influenza and HPV)	8	100+	27	7	N
22	(Adeloye, Agarwal et al. 2021)	Chronic obstructive pulmonary disease (COPD)	Global	10	Physicians, researchers, policymakers, funders, patients, support groups	COPD	6	432	230	34	N
23	(Zwaan, El-Kareh et al. 2021)	Diagnostic Safety	Global	3-5'		Reduce patient harm in the diagnosis process	5	207	51	49	Y
24	(Evans, Janiszewski et al. 2021)	Covid-19 pandemic in the local maternity setting	UK	Urgent	Pregnant women and families or women in the postnatal period	Physical health, psychological wellbeing, women's (and families) experiences, women's choice and control	5	58	8	58	NC

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
25	(Alobo, Mgone et al. 2021)	Maternal and neonatal health	Africa	-	-	Maternal and newborn morbidity, mortality, and disability	4	700	46	319	Y
26	(Angood, Kerac et al. 2021)	Treatment of child wasting	Global	Till 2020	Children<5y	Treatment of wasting in children <5y	4	394+	53	394	N
27	(Kobeissi, Nair et al. 2021)	Sexual, reproductive, maternal, newborn, child and adolescent health in humanitarian settings	Global (humanitaria n setting)	5	Women, Children, adolescent, newborn, men	Sexual, reproductive, maternal, newborn, child and adolescent health (SRMNCAH) domains in humanitarian settings	4	1000+	280	69	N
28	(Ouedraogo, Nkurunziza et al. 2020)	Sexual and Reproductive Health and Rights Services in Humanitarian Settings	Africa	-	Humanitarian Settings	Sexual and Reproductive Health and Rights	6	80	21	4	N
29	(Frison, Angood et al. 2020)	Prevention of child wasting	LMICs	5	Children <5y	Prevention of child wasting	4	828	40	146	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
30	(Clarence, Shiras et al. 2020)	Private sector child health service delivery	Global		Children<5y	Management of sick child care, with an emphasis on children< 5y	4	129	50	49	No
31	(Gomes, Bourassa et al. 2020)	Multiple micronutrient supplementation (MMS) during pregnancy	LMIC	5-10'	Foetus and infants 0–11 months old; Pregnant women	Adverse pregnancy and birth outcomes; MMS defficiency	4	87	35	35	Y
32	(Ashley, McLean et al. 2020)	Patient-centered surveillance of drug-resistant infections	LMIC	3-5'	-	Drug resistant infections	5	500	107	2-6'	N
33	(Chan, Storey et al. 2020)	Social, behavioural and community engagement interventions for maternal, newborn and child health	Global	10	-	-	4	1296	444	281	N
34	(Waiswa, Okuga et al. 2019)	Newborn health	National (Uganda)	10		Newborn health and mortality	5	300	41	82	N
35	(Li, Bamidis et al. 2019)	Healthcare workforce IT skills competence improvement	EU		Healthcare workforce	Deficiency of IT skill competence	4	280	23	34	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
36	(Tomlinson, Darmstadt et al. 2019)	Early Childhood Development	LMICs	10	Children, parents, care providers	Early Childhood Development	5	348	54	69	N
37	(Wazny, Arora et al. 2019)	Child health	National (India)	10	Children <5y; <18 years	Mortality and morbidity	5	212+233	101	233	Y
38	(Fun, Sararaks et al. 2019)	advancing universal access andquality healthcare research	Nat (Malaysia)	5	-	-	3		67		Y
39	(Sheikh, Rudan et al. 2019)	Medication safety	Global	-	-	improving medication safety	6	637	333	42	N
40	(Woodward, Griekspoor et al. 2018)	Cash programming for health & nutrition in humanitarian settings	Global (humanitarian setting)		All	Cash programming for health and nutrition in humanitarian settings	4	167	189	2	N
41	(Penazzato, Irvine et al. 2018)	Pediatric HIV	Global	10	Children <20y with HIV & those who need testing	mortality, morbidity, biological markers, psychosocial well-being program outcomes	4	3631	51	45	N
42	(Mansoori, Majdzadeh et al. 2018)	Long-term health targets in Iran	National (Iran)	5	All population	Achievement of national targets and SDGs	5	68	128	48	Y

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
43	(Irvine, Armstrong et al. 2018)	Paediatric HIV	Global	10	Children (0-18 Y)	Mortality, morbidity, biological markers, psychosocial well-being & programme outcomes	8	375	181	112	N
44	(Bermudez, Williamson et al. 2018)	Child protection in humanitarian settings	Humanitarian	435 29	Children (0-18 Y)	Understand risks and vulnerabilities & guide donor investment	4	47	90	41	N
45	(Ball, Barnes et al. 2018)	Physical activity and nutrition	National (Australia)	-	-	Health lifestyle behaviour	5	10	13	13	N
46	(Armstrong, Nagata et al. 2018)	HIV	Global	12	Adolescents	testing, treatment, and service delivery HIV	4	323	61	66-107	Y
47	(Abu-Rmeileh, Ghandour et al. 2018)	Reproductive heath	National (Palestine)	-	-	Reproductive health	5	45	232	30	N
48	(Ali, Farron et al. 2018)	Family planning	Global	10	Reproductive age	Unmet need for family planning	5	102	47	66	N
49	(Sharma, Buccioni et al. 2017)	Maternal, newborn, child and adolescent health	LMICs	15	Maternal, newborn, child and adolescent	Maternal, newborn, child and adolescent health	5	32	45	20	N
50	(Sharma, Gaffey et al. 2017)	Integrated implementation of early childhood development and maternal, newborn, child	LMICs	15	All ages	Improve development, health and well-being across the life course	5	67	57	20	No

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
		and adolescent health and nutrition									
51	(Tomlinson, Jordans et al. 2017)	Integrated ECD & violence prevention	LMIC	-	-	ECD and Violence	5	186	50	55	N
52	(McNeely, Morland et al. 2017)	Healthy development for Adolescents in Schools	National (US)	5	Immigrants and refugee adolescents	School success	3*	132	36	58	Y
53	(Gordon, Rotheram-Borus et al. 2017)	Alcohol and HIV/AIDS	LMICs	10	HIV and alcohol users	HIV and alcohol interaction	5	174	48	59	N
54	(Arora, Mohapatra et al. 2017)	MNCH and nutrition	National (India)	10	Women - reproductive age , newborns, Children <18y	Mortality and morbidity burden in MNCH and Nutrition in India 2012–2013	5	1178	400 3	1536	Y
55	(Shah, Albanese et al. 2016)	Dementia	Global	10	Old persons	Dementia	5	740	59	154	N
56	(Nagata, Ferguson et al. 2016)	Adolescent health	LMICs	10	Adolescents	Communicable diseases, injuries, violence, mental health, NCD, nutrition, physical activity, substance use and health policy)	5	450	303	160	Y
57	(Read, Fernandez-	Education in LMICs	LMICs	10	School children	Suboptimal education	4	84	89	37	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
	Hermosilla et al. 2016)										
58	(Velayutham, Nair et al. 2015)	Drug-resistant TBC	Global	10	Children (0-9 years)	Drug-resistant tuberculosis	5	304	53	81	N
59	Li X et al	Health policy research direction	National (China)	5	All age groups	All cause morbidity and mortality	5	33	50	29	Y
60	(Angood, McGrath et al. 2015)	Acute malnutrition in infants	Global	10	Infants< 6 months	Management of acute malnutrition and child mortality	6	64	60	64	Y
61	(Campbell, Higginnbottom et al. 2014)	Family planning	Global	10	Women of reproductive age	Family planning - maternal and perinatal health	6	80	53	80	N
62		Maternal and child health services	Sub-national (W China)	10	Mothers and children (0-4 years)	Morbidity and mortality of mothers and children	10	17	24	17	Y
63	(Rollins, Chanza et al. 2014)	PMTCT in 3 African countries	Nat (Zim, Malawi, Nigeria	435 95	People living with HIV/AIDS	PMTCT implementation barriers and child mortality	6	191	90	191	Y
64	(Wazny, Sadruddin et al. 2014)	Integrated community case management (iCCM)	LMICs	10	Children (0-4 years)	Mortality & morbidity from childhood diseases that could be prevented, treated through iCCM	4	133	61	75	N
65	(Tomlinson, Yasamy et al. 2014)	Developmental and intellectual disabilities and autism	Global	435 95	All age groups	Intellectual disability and autism	5	72	69	49	N

Sl	Author	Topic	Level (Global/Regional/National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
66	(Morof, Kerber et al. 2014)	Neonatal survival in humanitarian emergencies	Global	435 95	Newborns	Mortality and disability in humanitarian emergencies	4	97	28	35	N
67	(Souza, Widmer et al. 2014)	Maternal and perinatal health	Global	10	Pregnant and post-partum women	Maternal and perinatal health	5	339	190	140	N
68	(Yoshida, Rudan et al. 2014)	Newborn health	LMICs	437 53	Newborns	Mortality and morbidity in newborns	5	132	205	91	N
69	(Morof, Kerber et al. 2014)	Reproductive health in crisis settings	Crisis settings	435 95	Women, adolescents & couples-reproductive age	Mortality and severe morbidity in mothers, fetuses, newborns and children	5	68	94	16	N
70	(Bhutta, Zipursky et al. 2013)	Emerging interventions for childhood diarrhoea	LMICs	10	Children (0-4 years)	Childhood diarrhoea	9	12	10	12	N
71	(Dean, Rudan et al. 2013)	Pre-conception care	LMICs	10	Women, adolescents & couples-reproductive age	Mortality and severe morbidity in mothers, fetuses, newborns, children	6	130	37	48	N
72	(Wazny, Zipursky et al. 2013)	Childhood diarrhoea	Global	15	Children (0-4 years)	Mortality and morbidity from diarrhoea	5	200	466	150	N
73	(Hindin, Christiansen et al. 2013)	Adolescent sexual and reproductive health needs	LMICs	10	Adolescents	Sexual and reproductive health problems	5	296	280	144	N
74	(Nair, Lau et al. 2013)	Influenza	LMICs	10	Children (0-4 years)	Mortality from influenza	9	20	1	20	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
75	(Collins, Tomlinson et al. 2013)	Impaired mental health	Global	10	All age groups	Mental health	4	422	164	33	N
76	(Arbour, Murray et al. 2012)	Developmental risk	National (Chile)	1	Children (5-7 years)	Child development assessment	13	21	22	12	N
77	(Gregorio, Tomlinson et al. 2012)	Impaired mental health in Brazil	Natl (Brazil)	10	All age groups	Mental health	5	28	35	17	N
78	(Rudan, Theodoratou et al. 2012)	Emerging intervention	LMICs	10	Children (0-4 years)	Childhood pneumonia,	9	20	29	20	N
79	(Bahl, Martines et al. 2012)	Preterm birth and low birth weight	LMICs	10	Newborns	Preterm birth and low birth weight	5	21	82	21	Y
80	(Jordans, Tol et al. 2011)	Mental health care	National (Nepal)	10	All age groups	Mental disorders and psychosocial issues	3	26	13	26	N
81	(Jordans, Tol et al. 2011)	Children in adversity	LMICs	435 95	Children <10 years	Mental health	3	60	17	31	N
82	(Lawn, Blencowe et al. 2011)	Stillbirths	LMICs	10	Stillbirths	Stillbirths	5	50	279	50	N
83	(George, Young et al. 2011)	Implementation for stillbirths and preterm births	LMICs	435 95	Children <5years	Preterm births and stillbirths	5	85	55	29	N
84	(Tol, Patel et al. 2011)	Psychosocial support in	Global	10	All age groups	Mental disorders and psychosocial issues	5	136	74	82	N

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
		humanitarian settings									
85	(Rudan, El Arifeen et al. 2011)	Childhood pneumonia	LMICs	10	Children <5y	Mortality from pneumonia	5	45	156	45	Y
86	(Lawn, Bahl et al. 2011)	Birth asphyxia	LMICs	10	Newborns	Mortality from birth asphyxia	5	26	61	21	Y
87	(Sekar, Shah et al. 2011)	Zoonotic diseases in India	National (India)	5	All age groups	11 major zoonotic diseases	5	17	103	5	Y
88	(Higginson, Theodoratou et al. 2011)	Measles	LMICs	10	Children <5y	Morbidity and mortality from measles	9	20	1	20	N
89	(Nair, Verma et al. 2011)	RSV-associated respiratory infections	LMICs	10	Children <5y	Morbidity and mortality from RSV	9	20	3	20	N
90	(Choudhuri, Huda et al. 2011)	Meningococcal diseases	LMICs	10	Children <5y	Morbidity and mortality from Meningitidis	9	20	2	20	N
91	(Catto, Zgaga et al. 2011)	Oxygen systems for intensive care	LMICs	10	Children <5y	Mortality from respiratory infections and sepsis	9	20	1	20	N
92	(Huda, Nair et al. 2011)	Staphylococcal diseases	LMICs	10	Children <5y	Morbidity and mortality from S. Aureus	9	20	2	20	N
93	(Webster, Theodoratou et al. 2011)	Pneumococcal diseases	LMICs	10	Children <5y	Morbidity and mortality from S. Pneumoniae	9	20	2	20	N
94	Lienhardt et al 2009	Tuberculosis	Global	5	All age groups	Tuberculosis	5	50	250	50	No

Sl	Author	Topic	Level (Global/ Regional/ National)	Time frame	Population	Target burden	Criteria	Experts (approached)	Ideas (final)	Scorers	Stakeholders
95	(Fontaine, Kosek et al. 2009)	Childhood diarrhoea	LMICs	10	Children <5y	Mortality from diarrhoea	5	25	154	13	Y
96	(Bahl, Martines et al. 2009)	Neonatal infections	LMICs	10	Newborns	Mortality from infections	5	20	61	13	Y
97	(Kosek, Lanata et al. 2009)	Diarrhoeal disease	Global	10	Children <5y	Morbidity and mortality related to diarrhoea	5	17	46	10	N
98	(Brown, Hess et al. 2009)	Zinc interventions	LMICs	10	Children <5y	Morbidity and mortality related to Zn deficiency	5	7	31	7	N
99	(Tomlinson, Rudan et al. 2009)	Impaired mental health	Global	10	Persons mental health issues	Schizophrenia; Depression; Substance abuse & alcoholism; Adolescent & children's disorders	5	39	55	39	Y
100	(Tomlinson, Swartz et al. 2009)	Disabilities	Global	10	Persons with disabilities	Global burden of disability	5	82	83	50	N
101	(Walley, Lawn et al. 2008)	Primary health care	LMICs	20	All age groups	NCDs and maternal & child health	6	27	69	20	N
102	(Tomlinson, Chopra et al. 2007)	Child mortality in South Africa	National (South Africa)	10	Children <5y	Child mortality (all cause)	5	6	63	6	Y

Annex 2 Ranked research questions for scorers who had experience in working in Sub-Saharan Africa (SSA) (n = 35) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	1.000	1.000	0.980	0.980	0.920	0.976	0.975	0.949
2	3	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	1.000	1.000	0.964	0.955	0.938	0.971	0.971	0.939
3	2	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	1.000	0.963	0.942	0.990	0.962	0.971	0.970	0.956
4	4	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.981	0.981	0.980	0.960	0.910	0.962	0.961	0.909
5	5	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	0.981	0.981	0.963	0.954	0.917	0.959	0.958	0.915
6	6	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.946	1.000	0.963	0.954	0.889	0.950	0.950	0.905
7	7	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	0.981	0.963	0.923	0.941	0.933	0.948	0.948	0.890
8	8	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	0.983	0.948	0.929	0.920	0.939	0.944	0.943	0.884
9	9	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.946	0.964	0.981	0.981	0.843	0.943	0.942	0.895
10	10	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	0.981	0.958	0.927	0.850	0.943	0.941	0.884
11	11	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.964	0.964	0.963	0.963	0.852	0.941	0.939	0.910

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
12	12	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.907	0.898	0.861	0.933	0.932	0.873
13	13	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	0.950	1.000	0.879	0.948	0.862	0.928	0.927	0.887
14	14	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	0.950	0.967	0.931	0.914	0.868	0.926	0.925	0.881
15	15	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	0.950	0.933	0.914	0.922	0.905	0.925	0.924	0.873
16	16	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.931	0.948	0.929	0.946	0.866	0.924	0.923	0.873
17	17	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.981	0.923	0.940	0.900	0.860	0.921	0.918	0.875
18	18	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.917	0.966	0.914	0.905	0.879	0.916	0.916	0.872
19	19	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	0.929	0.914	0.946	0.929	0.860	0.915	0.914	0.844
20	20	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	1.000	0.942	0.854	0.890	0.878	0.913	0.911	0.820
21	21	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.952	0.917	0.900	0.892	0.890	0.910	0.909	0.814
22	22	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	0.952	0.935	0.900	0.900	0.861	0.910	0.908	0.845
23	23	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	0.983	0.966	0.929	0.861	0.809	0.909	0.907	0.834

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
24	24	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.963	0.926	0.926	0.898	0.833	0.909	0.907	0.820
25	26	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.914	0.931	0.944	0.813	0.898	0.900	0.901	0.809
26	25	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.926	0.889	0.923	0.913	0.856	0.901	0.900	0.842
27	27	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.942	0.923	0.920	0.880	0.830	0.899	0.897	0.813
28	28	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	0.968	0.952	0.933	0.825	0.817	0.899	0.897	0.796
29	29	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.982	0.907	0.923	0.833	0.845	0.898	0.896	0.845
30	30	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.875	0.929	0.889	0.907	0.868	0.894	0.894	0.831
31	31	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	0.880	0.900	0.896	0.938	0.854	0.894	0.893	0.865
32	32	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	0.914	0.983	0.911	0.833	0.809	0.890	0.890	0.798
33	33	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium Sulphate for pre-eclampsia/eclampsia in LMICs.	Del	0.893	0.929	0.893	0.866	0.866	0.889	0.890	0.862
34	34	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.904	0.904	0.880	0.854	0.900	0.888	0.889	0.833
35	35	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.935	0.919	0.917	0.873	0.797	0.888	0.886	0.808

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
36	36	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.946	0.870	0.870	0.750	0.887	0.884	0.826
37	37	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.875	0.893	0.893	0.898	0.813	0.874	0.873	0.799
38	39	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.900	0.880	0.854	0.890	0.827	0.870	0.869	0.779
39	38	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.940	0.865	0.900	0.850	0.800	0.871	0.868	0.773
40	40	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	0.944	0.875	0.796	0.861	0.870	0.869	0.868	0.827
41	41	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	0.911	0.885	0.860	0.880	0.800	0.867	0.865	0.797
42	43	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.907	0.875	0.889	0.815	0.824	0.862	0.861	0.805
43	44	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.946	0.911	0.827	0.798	0.824	0.861	0.860	0.796
44	42	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing PRE-ECLAMPSIA and improving neonatal outcomes in LMICs?	Desc	1.000	0.885	0.880	0.770	0.780	0.863	0.859	0.795
45	45	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.926	0.911	0.870	0.852	0.731	0.858	0.855	0.747
46	46	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.827	0.904	0.846	0.890	0.769	0.847	0.847	0.778
47	47	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.903	0.867	0.900	0.733	0.758	0.832	0.830	0.696
48	48	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.962	0.880	0.827	0.800	0.683	0.830	0.826	0.727
49	49	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.917	0.820	0.780	0.790	0.820	0.825	0.823	0.742

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
50	50	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.821	0.857	0.788	0.833	0.796	0.819	0.819	0.742
51	51	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.944	0.852	0.750	0.809	0.700	0.811	0.807	0.738
52	52	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.923	0.788	0.760	0.813	0.755	0.808	0.804	0.670
53	53	Can (self) home-based BP monitoring improve identification of women at risk of Pre-eclampsia and Eclampsia in LMICs?	Del/Desc	0.917	0.867	0.690	0.802	0.733	0.801	0.799	0.750
54	54	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.773	0.854	0.813	0.793	0.739	0.794	0.795	0.703
55	55	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.827	0.827	0.771	0.781	0.750	0.791	0.790	0.721
56	56	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.923	0.885	0.722	0.740	0.685	0.791	0.788	0.655
57	57	What are the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.880	0.846	0.692	0.808	0.721	0.789	0.787	0.691
58	58	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.796	0.827	0.827	0.783	0.704	0.787	0.786	0.662
59	59	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.848	0.818	0.771	0.781	0.700	0.784	0.781	0.654
60	60	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	0.957	0.738	0.714	0.798	0.698	0.781	0.775	0.697
61	61	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.771	0.840	0.760	0.780	0.690	0.768	0.768	0.695
62	62	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.900	0.763	0.625	0.786	0.720	0.759	0.755	0.642
63	63	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.818	0.771	0.740	0.686	0.750	0.753	0.752	0.623

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
64	64	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.923	0.813	0.667	0.690	0.608	0.740	0.735	0.639
65	65	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.907	0.800	0.720	0.620	0.640	0.737	0.734	0.602
66	66	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.720	0.792	0.729	0.727	0.688	0.731	0.732	0.582
67	67	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	0.771	0.750	0.727	0.728	0.652	0.726	0.724	0.600
68	68	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.761	0.760	0.696	0.638	0.716	0.714	0.714	0.592
69	69	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.840	0.800	0.600	0.740	0.550	0.706	0.702	0.600
70	70	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.788	0.750	0.720	0.590	0.640	0.698	0.696	0.580
71	71	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.778	0.722	0.731	0.620	0.637	0.698	0.696	0.583
72	72	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.741	0.704	0.712	0.635	0.673	0.693	0.692	0.586
73	73	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.771	0.813	0.604	0.587	0.543	0.663	0.662	0.544
74	74	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.816	0.711	0.400	0.569	0.442	0.588	0.582	0.558
75	75	How can MRI aid in the diagnosis of foetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.705	0.643	0.429	0.538	0.404	0.544	0.539	0.504
76	76	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.500	0.540	0.521	0.433	0.510	0.501	0.502	0.460

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 3 Ranked research questions for scorers who had experience in working in South Asia (SA) (n = 19) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium Sulphate for pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.962	1.000	0.981	0.988	0.988	0.978
2	2	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	1.000	1.000	1.000	1.000	0.942	0.988	0.988	0.967
3	3	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	1.000	0.979	0.904	0.977	0.975	0.933
4	4	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	1.000	0.967	0.967	0.983	0.950	0.973	0.972	0.943
5	5	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	1.000	1.000	0.933	0.967	0.933	0.967	0.966	0.924
6	6	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	1.000	1.000	1.000	0.917	0.917	0.967	0.966	0.905
7	7	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	0.964	0.964	0.964	1.000	0.929	0.964	0.964	0.929
8	8	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.967	0.967	0.883	0.963	0.962	0.933
9	9	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.967	1.000	0.967	1.000	0.867	0.960	0.959	0.924
10	10	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.962	0.962	0.962	0.962	0.923	0.954	0.953	0.901

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation ... RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
11	11	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.967	0.967	0.967	1.000	0.867	0.953	0.952	0.914
12	12	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	0.962	0.962	0.923	0.962	0.904	0.942	0.941	0.879
13	13	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.933	0.967	0.933	0.983	0.867	0.937	0.936	0.886
15	14	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.958	0.958	0.958	0.958	0.833	0.933	0.931	0.869
14	15	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.964	0.933	0.900	0.933	0.933	0.933	0.932	0.866
16	16	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	1.000	0.962	0.885	0.923	0.885	0.931	0.929	0.846
17	17	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	1.000	0.923	0.885	0.923	0.917	0.929	0.928	0.853
18	18	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.967	1.000	0.900	0.900	0.867	0.927	0.926	0.876
19	19	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.958	0.962	0.885	0.923	0.904	0.926	0.926	0.856
20	20	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	0.962	0.962	0.885	0.923	0.885	0.923	0.922	0.846
23	21	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	1.000	0.958	0.875	0.923	0.827	0.917	0.914	0.821
22	22	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.944	0.950	0.889	0.944	0.850	0.916	0.914	0.821
21	23	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.923	0.962	0.923	0.923	0.846	0.915	0.915	0.835

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
24	24	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	0.929	0.893	0.929	0.821	0.914	0.911	0.867
25	25	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.929	0.929	0.893	0.929	0.857	0.907	0.906	0.878
26	26	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	1.000	0.900	0.900	0.909	0.825	0.907	0.903	0.805
28	27	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	1.000	0.893	0.893	0.929	0.808	0.904	0.900	0.830
27	28	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	1.000	0.889	0.861	0.882	0.882	0.903	0.900	0.869
29	30	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.923	0.923	0.923	0.885	0.846	0.900	0.899	0.802
30	29	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.923	0.788	0.788	0.900	0.898	0.835
31	31	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.929	0.929	0.893	0.893	0.846	0.898	0.897	0.852
32	32	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.923	0.923	0.885	0.923	0.808	0.892	0.891	0.769
33	33	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.900	0.900	0.867	0.933	0.833	0.887	0.885	0.790
34	34	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.917	0.875	0.875	0.875	0.875	0.883	0.882	0.764
35	35	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.962	0.962	0.792	0.808	0.865	0.878	0.877	0.810
36	36	Can (self) home-based BP monitoring improve identification of women at risk of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.962	0.962	0.731	0.904	0.827	0.877	0.876	0.802
37	37	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.972	0.889	0.833	0.847	0.838	0.876	0.874	0.831

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
38	38	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.923	0.923	0.833	0.846	0.833	0.872	0.871	0.725
39	39	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	0.923	0.846	0.808	0.885	0.885	0.869	0.868	0.824
40	40	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.875	0.885	0.846	0.923	0.808	0.867	0.866	0.811
41	41	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.909	0.864	0.850	0.850	0.850	0.865	0.863	0.818
42	42	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.846	0.885	0.885	0.860	0.808	0.857	0.856	0.756
43	43	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.923	0.885	0.846	0.857	0.769	0.856	0.854	0.763
45	44	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.923	0.846	0.846	0.846	0.788	0.850	0.847	0.824
46	45	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.923	0.923	0.846	0.846	0.712	0.850	0.847	0.714
44	46	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.833	0.929	0.857	0.844	0.786	0.850	0.850	0.679
48	47	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.917	0.846	0.846	0.846	0.750	0.841	0.838	0.723
47	48	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.875	0.875	0.813	0.889	0.750	0.840	0.838	0.700
49	49	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.885	0.885	0.808	0.846	0.769	0.838	0.837	0.736
50	50	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	0.923	0.846	0.808	0.808	0.808	0.838	0.836	0.725
51	51	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.885	0.923	0.808	0.846	0.712	0.835	0.833	0.791

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
52	52	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.958	0.885	0.846	0.731	0.750	0.834	0.831	0.680
54	53	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.885	0.731	0.769	0.750	0.827	0.823	0.773
53	54	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.800	0.792	0.846	0.914	0.778	0.826	0.825	0.696
57	55	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.933	0.821	0.750	0.804	0.817	0.825	0.822	0.721
55	56	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.867	0.821	0.800	0.833	0.800	0.824	0.823	0.644
58	57	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.846	0.846	0.846	0.846	0.731	0.823	0.821	0.780
56	58	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.727	0.917	0.792	0.917	0.750	0.820	0.823	0.710
59	59	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.846	0.821	0.857	0.722	0.750	0.799	0.798	0.636
60	60	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.857	0.821	0.700	0.827	0.768	0.795	0.793	0.620
62	61	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.967	0.781	0.781	0.719	0.719	0.793	0.788	0.714
61	62	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	0.885	0.808	0.846	0.731	0.692	0.792	0.789	0.670
63	63	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.769	0.808	0.808	0.792	0.750	0.785	0.785	0.711
64	64	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.786	0.786	0.821	0.759	0.732	0.777	0.776	0.650

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
65	65	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.850	0.750	0.750	0.800	0.722	0.774	0.771	0.630
66	66	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.846	0.846	0.714	0.750	0.688	0.769	0.767	0.576
67	67	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.773	0.864	0.792	0.688	0.708	0.765	0.766	0.576
68	68	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.833	0.792	0.708	0.750	0.688	0.754	0.752	0.583
69	69	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.900	0.813	0.625	0.813	0.617	0.753	0.748	0.632
70	70	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.885	0.846	0.538	0.788	0.615	0.735	0.731	0.637
71	71	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.875	0.769	0.615	0.727	0.673	0.732	0.728	0.560
72	72	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.778	0.722	0.722	0.688	0.667	0.715	0.713	0.524
73	73	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.885	0.708	0.654	0.667	0.583	0.699	0.693	0.532
74	74	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.800	0.778	0.450	0.778	0.600	0.681	0.678	0.630
75	75	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.885	0.636	0.542	0.545	0.480	0.618	0.610	0.490
76	76	How can MRI aid in the diagnosis of foetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.708	0.654	0.385	0.591	0.423	0.552	0.548	0.511

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 4 Comparison of ranks within by geographical location of work

sl	Research question	Domain	Rank (weighted): All (n=69)	Rank (weighted): Sub Saharan Africa (n=35)	Rank (weighted): South Asia (n=19)
1	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	1	3	10
2	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	2	5	8
3	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	3	4	32*
4	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	4	1	15*
5	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	5	8	6
6	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	6	9	13
7	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	7	11	9
8	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	8	13	3
9	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	9	2	12
10	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	10	6	11
11	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	11	19	28*
12	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	12	10	24
13	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	13	18	19
14	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	14	22	5
15	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	15	7	39*

sl	Research question	Domain	Rank (weighted): All (n=69)	Rank (weighted): Sub Saharan Africa (n=35)	Rank (weighted): South Asia (n=19)
16	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	16	17	25
17	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	17	26	29*
18	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	18	31	7
19	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	19	12	30*
20	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	20	24	21
21	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	21	14	20
22	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	22	32	16
23	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	23	21	14
24	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	24	25	34
25	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	25	29	37*
26	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	26	30	33
27	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	27	40*	27
28	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	28	15*	2*
29	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	29	23	50*
30	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	30	35	18*
31	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	31	28	4*

sl	Research question	Domain	Rank (weighted): All (n=69)	Rank (weighted): Sub Saharan Africa (n=35)	Rank (weighted): South Asia (n=19)
32	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	32	20*	49*
33	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	33	38	22*
34	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	34	33	1*
35	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	35	27	48*
36	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	36	45	31
37	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	37	41	23*
38	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	38	42	45
39	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	39	46	51*
40	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	40	36	54*
41	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	41	16*	58*
42	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	42	50	56*
43	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	43	54*	41
44	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	44	37*	40
45	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	45	47	55
46	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	46	39	52
47	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	47	44	61*
48	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	48	43	35

sl	Research question	Domain	Rank (weighted): All (n=69)	Rank (weighted): Sub Saharan Africa (n=35)	Rank (weighted): South Asia (n=19)
49	Can (self) home-based BP monitoring improve identification of women at risk of pre-eclampsia /eclampsia in LMICs?	Del/Desc	49	53	36
50	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	50	34	68*
51	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	51	56	38
52	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	52	51	60
53	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	53	49	65*
54	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	54	67*	17
55	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	55	48	46
56	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	56	52	71*
57	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	57	58	43
58	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	58	59	62
59	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	59	55	63
60	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	60	72*	42
61	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	61	60	26
62	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	62	57	69
63	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	63	68	57
64	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	64	71	64
65	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	65	63	53
66	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	66	62	47
67	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	67	65	73

sl	Research question	Domain	Rank (weighted): All (n=69)	Rank (weighted): Sub Saharan Africa (n=35)	Rank (weighted): South Asia (n=19)
68	How effective is the use of mannitol in unconscious eclamptics?	Desc	68	61	44
69	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	69	70	59
70	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	70	66	72
71	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	71	64	75
72	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	72	73	66
73	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	73	69	70
74	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	74	74	74
75	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	75	76	67
76	How can MRI aid in the diagnosis of foetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	76	75	76

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 5 Ranked research questions for scorers with experience in laboratory science research (n = 6) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
2	2	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
3	3	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
4	4	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
5	5	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
6	6	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
7	7	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
8	8	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
9	9	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
10	10	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
11	11	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
12	12	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
13	13	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
14	14	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.875	1.000	1.000	0.975	0.975	0.958
15	15	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.875	1.000	1.000	0.975	0.975	0.964
16	16	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	1.000	1.000	0.875	1.000	1.000	0.975	0.975	0.964
17	17	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.833	1.000	1.000	0.967	0.967	0.952
18	18	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	1.000	1.000	0.833	1.000	1.000	0.967	0.967	0.952
19	19	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	1.000	1.000	0.833	1.000	1.000	0.967	0.967	0.952
20	20	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.875	0.875	1.000	0.950	0.951	0.893
21	21	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.833	1.000	0.917	0.950	0.949	0.905
22	22	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	1.000	0.875	0.875	1.000	1.000	0.950	0.948	0.929
23	23	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	1.000	0.875	0.875	1.000	1.000	0.950	0.948	0.929
24	24	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	0.833	1.000	0.833	1.000	1.000	0.933	0.938	0.905

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
25	25	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.833	1.000	0.833	1.000	1.000	0.933	0.938	0.905
26	26	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.833	0.833	1.000	1.000	0.933	0.931	0.905
27	27	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	1.000	0.833	0.833	1.000	1.000	0.933	0.931	0.905
28	28	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	1.000	0.833	0.833	1.000	1.000	0.933	0.931	0.905
29	29	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.875	1.000	0.875	1.000	0.875	0.925	0.926	0.857
30	30	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	0.875	0.875	0.875	1.000	1.000	0.925	0.926	0.893
31	31	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.875	0.875	0.875	1.000	1.000	0.925	0.926	0.893
32	32	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	1.000	1.000	0.750	0.875	1.000	0.925	0.926	0.857
33	33	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.800	1.000	0.800	0.920	0.917	0.886
34	34	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	0.750	1.000	0.750	1.000	1.000	0.900	0.907	0.929
35	35	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.875	1.000	0.875	0.875	0.875	0.900	0.902	0.786
36	36	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.875	0.875	0.875	1.000	0.875	0.900	0.899	0.821
37	37	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.750

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Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
38	38	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.750
39	39	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.900	0.900	0.875	0.900	0.750	0.865	0.863	0.736
40	40	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	0.750	0.875	0.875	0.875	0.875	0.850	0.853	0.750
41	41	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.750	0.875	0.875	0.875	0.875	0.850	0.853	0.750
42	42	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.875	0.875	0.750	0.875	0.875	0.850	0.850	0.750
43	43	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	0.875	0.875	0.750	0.875	0.875	0.850	0.850	0.714
44	44	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.900	0.800	0.875	0.900	0.750	0.845	0.841	0.707
45	45	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.833	0.833	0.833	0.833	0.833	0.833	0.833	0.667
46	46	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.833	0.833	0.833	0.833	0.833	0.833	0.833	0.667
47	47	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.833	0.833	0.833	0.833	0.833	0.833	0.833	0.667
48	48	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.800	0.900	0.750	0.850	0.833	0.827	0.829	0.664
49	49	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.750	0.875	0.750	0.875	0.875	0.825	0.828	0.679
50	50	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	1.000	0.800	0.700	0.800	0.800	0.820	0.815	0.800
51	51	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.833	0.667	0.667	1.000	0.833	0.800	0.797	0.762

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
52	52	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.750	0.750	0.750	0.875	0.750	0.775	0.774	0.571
53	53	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.875	0.800	0.750	0.700	0.750	0.775	0.773	0.607
54	54	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.667	0.833	0.667	0.833	0.833	0.767	0.771	0.667
55	55	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.667	0.833	0.667	0.833	0.833	0.767	0.771	0.667
56	56	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.750	0.667	0.833	0.667	0.833	0.750	0.750	0.643
57	57	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
58	58	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
59	59	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.750	0.750	0.625	0.875	0.750	0.750	0.750	0.679
60	60	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	1.000	0.750	0.500	0.750	0.750	0.750	0.745	0.750
61	62	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.750	0.875	0.500	0.813	0.750	0.738	0.740	0.571
62	63	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.667	0.667	0.667	0.833	0.833	0.733	0.735	0.667
63	61	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	1.000	0.600	0.600	0.800	0.700	0.740	0.731	0.686
64	64	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.625	0.750	0.750	0.750	0.750	0.725	0.728	0.714
65	65	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del/Desc	0.750	0.750	0.500	0.750	0.875	0.725	0.728	0.750

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
66	66	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.750	0.750	0.625	0.750	0.750	0.725	0.725	0.714
67	67	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.750	0.750	0.625	0.750	0.750	0.725	0.725	0.714
68	68	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.800	0.600	0.600	0.800	0.800	0.720	0.717	0.743
69	69	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.900	0.500	0.500	0.800	0.700	0.680	0.672	0.657
70	70	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.667	0.667	0.500	0.667	0.750	0.650	0.652	0.619
71	71	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.500	0.667	0.667	0.667	0.667	0.633	0.637	0.643
72	72	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.625	0.625	0.500	0.625	0.625	0.600	0.600	0.500
73	73	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.625	0.625	0.625	0.500	0.500	0.575	0.574	0.500
74	74	How can MRI aid in the diagnosis of foetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.333	0.625	0.500	0.750	0.625	0.567	0.573	0.524
75	75	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.500	0.625	0.250	0.625	0.500	0.500	0.502	0.571
76	76	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	0.625	0.250	0.625	0.375	0.375	0.450	0.442	0.536

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 6 Ranked research questions for scorers with experience in clinical science research (n = 34) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Desc	1.000	0.980	1.000	0.940	0.950	0.974	0.973	0.931
2	2	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Dis	0.977	0.977	0.955	0.966	0.955	0.966	0.966	0.929
3	3	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Dis	1.000	1.000	0.958	0.948	0.917	0.965	0.964	0.923
4	4	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Desc	0.981	1.000	0.981	0.952	0.904	0.963	0.963	0.929
5	6	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Desc	0.978	0.978	0.957	0.957	0.924	0.959	0.958	0.907
6	5	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Desc	0.981	0.981	0.980	0.963	0.889	0.959	0.957	0.904
7	7	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Desc	0.978	0.935	0.935	0.967	0.957	0.954	0.953	0.925
8	9	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Dev/Del	0.981	1.000	0.980	0.913	0.894	0.954	0.953	0.890
9	8	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Desc	1.000	0.981	0.923	0.933	0.933	0.954	0.953	0.912
10	10	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Del	0.981	0.981	0.940	0.933	0.913	0.950	0.949	0.889
11	11	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Desc	0.962	0.962	0.962	0.942	0.913	0.948	0.947	0.896

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
12	12	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Desc	0.981	0.962	0.960	0.942	0.894	0.948	0.946	0.890
13	13	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Desc	0.944	1.000	0.885	0.952	0.904	0.937	0.937	0.896
14	14	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dis	0.980	0.979	0.979	0.906	0.837	0.936	0.934	0.853
15	15	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Desc	0.944	0.962	0.940	0.935	0.877	0.932	0.931	0.849
16	16	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Dis	0.981	0.960	0.920	0.885	0.885	0.926	0.925	0.850
17	17	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Desc	0.958	0.935	0.913	0.917	0.885	0.922	0.920	0.850
18	18	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Desc	0.980	0.979	0.917	0.875	0.857	0.922	0.920	0.841
19	19	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Desc	0.957	0.935	0.935	0.891	0.880	0.920	0.918	0.863
20	20	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc	0.981	0.923	0.904	0.894	0.892	0.919	0.917	0.829
21	21	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Dis	0.958	0.913	0.935	0.896	0.885	0.917	0.916	0.862
22	23	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Dis	0.935	0.913	0.913	0.891	0.913	0.913	0.913	0.882

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Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
23	22	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.981	0.907	0.904	0.880	0.898	0.914	0.912	0.876
24	24	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	0.981	0.942	0.940	0.827	0.856	0.909	0.908	0.802
25	25	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.962	0.926	0.904	0.870	0.858	0.904	0.902	0.807
26	26	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Desc	0.958	0.938	0.864	0.885	0.872	0.903	0.902	0.835
27	27	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Dis/Desc	0.958	0.938	0.932	0.880	0.802	0.902	0.900	0.830
28	28	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Del/Desc	0.981	0.889	0.852	0.917	0.870	0.902	0.899	0.884
29	29	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Del/Desc	1.000	0.904	0.865	0.880	0.840	0.898	0.895	0.825
30	30	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Desc	0.917	0.917	0.935	0.823	0.880	0.894	0.894	0.796
31	31	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Del	0.917	0.958	0.864	0.875	0.833	0.889	0.889	0.795
32	32	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Dis	0.917	0.896	0.935	0.854	0.833	0.887	0.886	0.833
33	33	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.875	0.913	0.891	0.913	0.826	0.884	0.883	0.821
34	34	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Dis	0.891	0.870	0.891	0.891	0.859	0.880	0.880	0.801

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
35	35	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.896	0.891	0.771	0.844	0.880	0.878	0.833
36	36	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Del	1.000	0.875	0.891	0.802	0.833	0.880	0.877	0.815
37	37	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.886	0.886	0.864	0.875	0.864	0.875	0.875	0.799
38	38	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Dis	0.962	0.885	0.885	0.833	0.800	0.873	0.870	0.788
39	39	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Del/Desc	0.958	0.935	0.804	0.872	0.784	0.871	0.868	0.808
40	40	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Desc	0.917	0.880	0.896	0.840	0.810	0.869	0.867	0.770
41	41	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Del	0.938	0.870	0.870	0.815	0.844	0.867	0.866	0.800
42	42	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Desc	0.962	0.885	0.846	0.788	0.794	0.855	0.852	0.762
43	43	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.846	0.885	0.865	0.827	0.808	0.846	0.846	0.819
44	44	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Del	0.940	0.900	0.769	0.798	0.817	0.845	0.844	0.718
45	45	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dev	0.904	0.846	0.846	0.850	0.769	0.843	0.840	0.778
46	46	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Del	0.846	0.813	0.854	0.850	0.820	0.837	0.836	0.741
47	47	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Del	0.952	0.818	0.795	0.807	0.807	0.836	0.833	0.772

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
48	49	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del	0.900	0.900	0.760	0.790	0.800	0.830	0.829	0.783
49	48	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.962	0.827	0.865	0.750	0.760	0.833	0.829	0.703
50	50	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Del	0.875	0.826	0.826	0.773	0.815	0.823	0.822	0.755
51	51	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc/Del	0.865	0.788	0.808	0.808	0.817	0.817	0.816	0.791
52	52	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Del	0.808	0.827	0.800	0.827	0.760	0.804	0.804	0.757
53	53	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dev	0.820	0.800	0.833	0.786	0.770	0.802	0.801	0.694
54	55	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Desc/Del	0.810	0.826	0.783	0.830	0.750	0.800	0.799	0.749
55	54	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.880	0.840	0.846	0.769	0.663	0.800	0.796	0.701
56	56	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.935	0.804	0.739	0.739	0.728	0.789	0.785	0.671
57	57	Can new omics approaches be used to discover better markers of pre-eclampsia?	Del/Dev	0.886	0.762	0.667	0.786	0.720	0.764	0.760	0.693
58	59	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dev/Del	0.860	0.780	0.700	0.760	0.680	0.756	0.753	0.663
59	58	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Desc	0.917	0.717	0.727	0.739	0.689	0.758	0.752	0.675
60	60	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.891	0.739	0.750	0.705	0.674	0.752	0.747	0.607
61	61	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Del	0.896	0.750	0.771	0.646	0.688	0.750	0.746	0.643

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
62	62	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.820	0.740	0.740	0.724	0.710	0.747	0.745	0.632
63	63	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Del	0.804	0.804	0.727	0.702	0.663	0.740	0.739	0.670
64	64	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc	0.870	0.761	0.636	0.716	0.682	0.733	0.730	0.646
65	65	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Dev/Del	0.792	0.731	0.708	0.706	0.683	0.724	0.722	0.612
66	66	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Dev/Del	0.750	0.680	0.740	0.735	0.692	0.720	0.718	0.581
67	67	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Del	0.833	0.696	0.696	0.663	0.686	0.715	0.711	0.565
68	68	How effective is the use of mannitol in unconscious eclamptics?	Desc/Dis	0.727	0.761	0.696	0.707	0.663	0.711	0.710	0.638
69	69	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.909	0.682	0.591	0.682	0.625	0.698	0.692	0.591
70	70	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Dev/Del	0.760	0.700	0.700	0.663	0.602	0.685	0.682	0.589
71	71	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.690	0.684	0.684	0.667	0.618	0.669	0.668	0.601
72	72	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc/Del	0.740	0.646	0.625	0.553	0.594	0.632	0.629	0.534
73	73	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Del	0.737	0.737	0.500	0.595	0.577	0.629	0.628	0.556
74	74	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.740	0.708	0.583	0.521	0.552	0.621	0.619	0.490
75	75	How can MRI aid in the diagnosis of fetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Del	0.684	0.711	0.526	0.653	0.525	0.620	0.618	0.527

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
76	76	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc/Dis	0.522	0.457	0.500	0.422	0.458	0.472	0.470	0.420

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 7 Ranked research questions for scorers with experience in public health and health systems research (n = 20) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	1.000	1.000	0.982	0.996	0.996	0.990
2	2	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	1.000	1.000	1.000	1.000	0.981	0.996	0.996	0.989
3	3	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	1.000	1.000	1.000	1.000	0.962	0.992	0.992	0.978
4	4	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.933	1.000	1.000	1.000	0.946	0.976	0.977	0.960
5	5	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	1.000	1.000	1.000	1.000	0.875	0.975	0.973	0.952
6	7	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.933	0.964	0.964	0.964	0.946	0.955	0.955	0.919
7	6	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	1.000	0.962	1.000	0.896	0.917	0.955	0.953	0.882
8	8	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.906	0.953	0.891	0.950	0.949	0.911

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
9	9	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	1.000	0.964	0.929	0.923	0.929	0.949	0.948	0.896
10	10	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	1.000	1.000	0.938	0.906	0.891	0.947	0.946	0.875
11	11	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	1.000	0.971	0.906	0.922	0.924	0.945	0.944	0.886
12	12	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	1.000	0.900	0.893	1.000	0.929	0.944	0.942	0.920
13	13	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.967	0.967	0.929	0.964	0.875	0.940	0.939	0.869
14	14	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.955	0.955	0.955	0.958	0.875	0.939	0.938	0.866
15	15	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	1.000	0.941	0.938	0.891	0.906	0.935	0.933	0.885
16	16	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.929	0.885	0.852	0.933	0.931	0.882
17	17	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.967	0.967	0.933	0.900	0.883	0.930	0.929	0.838

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
18	18	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	0.923	0.917	0.917	0.875	0.926	0.924	0.906
19	19	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.967	0.933	0.929	0.857	0.911	0.919	0.919	0.818
20	21	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	0.941	0.941	0.875	0.906	0.909	0.915	0.914	0.869
21	20	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.938	0.969	0.900	0.900	0.867	0.915	0.914	0.868
22	23	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	0.941	0.912	0.875	0.906	0.938	0.914	0.914	0.877
23	25	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	0.933	0.933	0.857	0.929	0.911	0.913	0.912	0.899
24	22	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	0.938	0.875	0.933	0.967	0.859	0.914	0.912	0.882
25	24	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	1.000	0.929	0.923	0.846	0.865	0.913	0.910	0.858
26	26	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.923	0.923	0.917	0.917	0.875	0.911	0.910	0.895
27	27	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.941	0.941	0.844	0.906	0.906	0.908	0.908	0.885

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
28	29	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	0.846	0.923	0.923	0.923	0.904	0.904	0.905	0.901
29	32	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.923	0.923	0.917	0.864	0.886	0.903	0.902	0.849
30	28	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	1.000	0.938	0.933	0.800	0.850	0.904	0.902	0.830
31	31	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.900	0.900	0.929	0.929	0.857	0.903	0.902	0.870
32	30	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	1.000	0.875	0.875	0.875	0.891	0.903	0.900	0.795
33	33	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.933	0.900	0.893	0.893	0.875	0.899	0.898	0.859
34	35	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.941	0.912	0.875	0.844	0.891	0.892	0.892	0.795
35	34	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	1.000	0.833	0.833	0.944	0.861	0.894	0.890	0.825
36	36	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.969	0.867	0.867	0.867	0.823	0.878	0.875	0.856

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
37	38	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.833	0.900	0.857	0.857	0.911	0.872	0.874	0.810
38	37	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.933	0.867	0.893	0.893	0.793	0.876	0.873	0.801
39	39	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	0.867	0.938	0.900	0.833	0.817	0.871	0.871	0.773
40	40	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.950	0.833	0.778	0.889	0.861	0.862	0.860	0.795
41	41	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del/Desc	1.000	0.875	0.767	0.867	0.783	0.858	0.854	0.821
42	42	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.875	0.958	0.875	0.854	0.688	0.850	0.848	0.750
43	43	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.792	0.923	0.917	0.833	0.771	0.847	0.848	0.810
44	44	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	0.906	0.844	0.833	0.833	0.806	0.845	0.843	0.816
45	45	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.857	0.857	0.846	0.885	0.769	0.843	0.841	0.816
46	46	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.964	0.821	0.786	0.786	0.821	0.836	0.833	0.755
47	47	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	0.821	0.821	0.846	0.885	0.788	0.832	0.831	0.773

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
48	50	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.833	0.923	0.808	0.769	0.808	0.828	0.830	0.698
49	49	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	0.875	0.818	0.818	0.818	0.818	0.830	0.828	0.742
50	48	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.929	0.846	0.769	0.615	0.832	0.826	0.770
51	51	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.885	0.846	0.792	0.750	0.854	0.825	0.825	0.707
52	54	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.767	0.875	0.750	0.900	0.817	0.822	0.823	0.741
53	52	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.933	0.867	0.821	0.692	0.804	0.823	0.822	0.759
54	53	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.882	0.824	0.813	0.781	0.813	0.822	0.821	0.665
55	55	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.893	0.857	0.846	0.740	0.769	0.821	0.820	0.681
56	57	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.833	0.833	0.821	0.821	0.786	0.819	0.818	0.769
57	56	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.929	0.846	0.769	0.846	0.712	0.820	0.816	0.716

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
58	58	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.833	0.833	0.808	0.808	0.796	0.816	0.815	0.689
59	59	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.900	0.833	0.786	0.750	0.750	0.804	0.801	0.707
60	60	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.885	0.885	0.708	0.769	0.750	0.799	0.798	0.679
61	61	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.750	0.808	0.769	0.846	0.769	0.788	0.789	0.750
62	63	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.821	0.786	0.808	0.740	0.750	0.781	0.780	0.661
63	62	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.900	0.733	0.786	0.821	0.672	0.783	0.777	0.663
64	64	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.958	0.808	0.654	0.846	0.635	0.780	0.774	0.691
65	65	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.885	0.808	0.708	0.688	0.780	0.774	0.772	0.652
66	67	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.750	0.792	0.708	0.773	0.729	0.750	0.751	0.733
67	66	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.917	0.750	0.750	0.692	0.667	0.755	0.750	0.622

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Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
68	69	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.750	0.769	0.750	0.769	0.692	0.746	0.745	0.648
69	68	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.938	0.750	0.688	0.750	0.625	0.750	0.744	0.643
70	70	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.833	0.833	0.667	0.771	0.583	0.738	0.734	0.619
71	71	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.857	0.893	0.615	0.625	0.667	0.731	0.731	0.608
72	73	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.750	0.714	0.731	0.660	0.731	0.717	0.717	0.607
73	72	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.964	0.846	0.708	0.545	0.542	0.721	0.716	0.549
74	75	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.542	0.708	0.682	0.523	0.625	0.616	0.620	0.517
75	74	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.923	0.708	0.500	0.500	0.480	0.622	0.615	0.488
76	76	How can MRI aid in the diagnosis of fetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.818	0.600	0.500	0.500	0.435	0.571	0.564	0.473

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 8 Ranked research questions for scorers with experience in policy and programme implementation (n = 15) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	1	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	1.000	1.000	1.000	1.000	0.900	0.980	0.978	0.943
2	3	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	1.000	1.000	0.950	0.950	0.900	0.960	0.959	0.900
3	2	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.950	0.975	0.875	0.960	0.958	0.900
4	5	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	1.000	1.000	0.958	0.938	0.891	0.957	0.956	0.915
5	4	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	1.000	1.000	0.962	0.962	0.865	0.958	0.956	0.890
6	6	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	1.000	1.000	0.944	0.917	0.889	0.950	0.949	0.873
7	7	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	1.000	0.923	0.962	0.923	0.923	0.946	0.944	0.890
8	9	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.938	0.944	1.000	0.944	0.861	0.938	0.936	0.855
9	8	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	1.000	1.000	1.000	0.909	0.786	0.939	0.936	0.892
10	12	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	1.000	0.955	0.792	0.955	0.958	0.932	0.931	0.889

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
11	10	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	1.000	0.909	1.000	0.977	0.786	0.934	0.930	0.866
12	11	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	1.000	0.900	0.944	0.972	0.850	0.933	0.930	0.854
13	13	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	0.962	1.000	0.885	0.958	0.846	0.930	0.929	0.878
14	14	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	0.958	0.958	0.875	0.938	0.917	0.929	0.929	0.857
15	15	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	1.000	0.958	0.875	0.935	0.864	0.926	0.924	0.874
16	16	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	0.923	0.923	0.962	0.962	0.846	0.923	0.922	0.868
17	17	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	1.000	0.955	0.909	0.932	0.818	0.923	0.920	0.844
18	18	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	1.000	0.962	0.846	0.896	0.885	0.918	0.916	0.854
19	19	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	0.923	0.962	0.958	0.904	0.827	0.915	0.914	0.867
20	21	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.850	0.950	0.950	0.950	0.850	0.910	0.911	0.829
21	20	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.955	0.909	0.864	1.000	0.833	0.912	0.909	0.866
22	22	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	0.944	0.929	0.929	0.882	0.844	0.906	0.904	0.805
23	23	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.938	0.833	1.000	0.933	0.813	0.903	0.900	0.841

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
24	24	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.923	0.846	0.923	0.923	0.885	0.900	0.898	0.821
25	25	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	1.000	0.917	0.875	0.875	0.813	0.896	0.893	0.762
26	26	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.909	0.909	0.955	0.864	0.818	0.891	0.890	0.818
27	27	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.950	0.900	0.900	0.875	0.806	0.886	0.884	0.746
28	28	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	0.833	0.917	0.875	0.875	0.896	0.879	0.881	0.857
29	29	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	1.000	0.885	0.885	0.846	0.769	0.877	0.873	0.791
30	30	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	1.000	0.875	0.917	0.854	0.729	0.875	0.870	0.762
31	32	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.900	0.900	0.900	0.825	0.806	0.866	0.865	0.775
32	31	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	1.000	0.833	0.875	0.833	0.795	0.867	0.863	0.745
33	33	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.800	0.909	0.900	0.909	0.773	0.858	0.859	0.801
34	34	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.923	0.846	0.808	0.846	0.860	0.857	0.855	0.723

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
35	35	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	0.875	0.917	0.833	0.808	0.818	0.850	0.850	0.679
36	36	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.875	0.857	0.813	0.895	0.794	0.847	0.845	0.751
37	37	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.944	0.850	0.850	0.850	0.737	0.846	0.842	0.749
38	38	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	1.000	1.000	0.833	0.750	0.646	0.846	0.842	0.738
39	39	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.917	0.750	0.917	0.854	0.792	0.846	0.842	0.786
40	40	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.944	0.800	0.833	0.850	0.794	0.844	0.840	0.705
41	43	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.864	0.833	0.833	0.896	0.771	0.839	0.837	0.760
42	41	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	0.900	0.700	1.000	0.864	0.750	0.843	0.837	0.724
43	42	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.889	0.833	0.889	0.895	0.694	0.840	0.836	0.702
44	45	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	0.889	0.850	0.800	0.895	0.750	0.837	0.834	0.741
45	44	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	1.000	0.792	0.818	0.826	0.750	0.837	0.831	0.764
46	47	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.833	0.875	0.769	0.827	0.827	0.826	0.827	0.743

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
47	46	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del/Desc	0.962	0.885	0.731	0.827	0.731	0.827	0.823	0.758
48	49	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	0.875	0.864	0.833	0.813	0.729	0.823	0.821	0.700
49	48	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	1.000	0.958	0.750	0.826	0.591	0.825	0.819	0.722
50	51	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.833	0.944	0.778	0.844	0.667	0.813	0.812	0.756
51	50	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.929	0.929	0.813	0.813	0.600	0.816	0.812	0.699
52	52	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.833	0.833	0.792	0.875	0.688	0.804	0.802	0.738
53	53	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.750	0.875	0.833	0.813	0.676	0.789	0.790	0.602
54	54	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.885	0.708	0.808	0.750	0.769	0.784	0.780	0.599
55	55	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.813	0.889	0.722	0.806	0.656	0.777	0.776	0.647
56	56	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.938	0.929	0.625	0.821	0.563	0.775	0.770	0.668
57	57	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.857	0.786	0.714	0.846	0.643	0.769	0.765	0.626
58	58	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.950	0.727	0.700	0.765	0.694	0.767	0.761	0.633
59	60	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.850	0.800	0.667	0.775	0.711	0.760	0.758	0.629
60	59	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.958	0.792	0.727	0.630	0.696	0.761	0.756	0.653

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
61	61	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.944	0.800	0.750	0.625	0.658	0.755	0.751	0.605
62	62	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.944	0.929	0.500	0.750	0.633	0.751	0.748	0.651
63	64	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.833	0.833	0.722	0.639	0.694	0.744	0.744	0.587
64	63	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	1.000	0.864	0.792	0.571	0.524	0.750	0.743	0.560
65	65	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.938	0.833	0.500	0.778	0.625	0.735	0.730	0.569
66	66	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.889	0.750	0.600	0.781	0.650	0.734	0.729	0.600
67	67	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.900	0.667	0.750	0.667	0.667	0.730	0.724	0.538
68	68	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.875	0.688	0.611	0.694	0.611	0.696	0.690	0.528
69	69	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.750	0.900	0.450	0.850	0.425	0.675	0.672	0.629
70	70	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.688	0.875	0.556	0.633	0.533	0.657	0.658	0.543
71	71	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.571	0.571	0.750	0.688	0.594	0.635	0.634	0.515
72	72	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	1.000	0.611	0.591	0.474	0.386	0.612	0.600	0.535
73	73	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.556	0.625	0.667	0.618	0.528	0.599	0.599	0.508

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
74	74	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.714	0.583	0.417	0.500	0.769	0.597	0.597	0.541
75	75	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.389	0.611	0.600	0.400	0.523	0.505	0.510	0.460
76	76	How can MRI aid in the diagnosis of fetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.650	0.450	0.200	0.433	0.333	0.413	0.407	0.580

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 9 Ranked research questions for scorers with experience in clinical services (direct health care) (n = 41) with intermediate scores for each criterion, overall unweighted and weighted research priority scores (RPS), and average expert agreement (AEA)

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
1	2	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	0.960	0.980	0.960	0.971	0.971	0.968	0.969	0.938
2	1	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	0.969	0.984	0.968	0.984	0.938	0.969	0.968	0.937
3	3	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	0.950	0.967	0.967	0.975	0.942	0.960	0.960	0.929
4	4	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	0.964	0.964	0.946	0.963	0.954	0.958	0.958	0.917
5	5	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	0.963	0.944	0.944	0.973	0.964	0.958	0.958	0.933
6	6	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	0.983	0.983	0.931	0.948	0.940	0.957	0.957	0.911
7	7	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	0.966	0.983	0.948	0.929	0.939	0.953	0.953	0.915
8	8	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	0.953	0.969	0.952	0.938	0.919	0.946	0.946	0.891
9	9	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	0.950	0.950	0.966	0.905	0.955	0.945	0.946	0.885
10	10	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	0.969	0.969	0.922	0.914	0.935	0.942	0.942	0.892
11	11	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	0.969	0.984	0.887	0.927	0.935	0.941	0.941	0.899

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
12	12	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	0.953	0.953	0.953	0.938	0.905	0.940	0.940	0.879
13	13	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	0.950	0.933	0.950	0.908	0.950	0.938	0.938	0.871
14	14	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	0.948	0.948	0.966	0.938	0.877	0.935	0.934	0.865
15	15	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	0.938	0.969	0.935	0.930	0.881	0.930	0.930	0.856
16	16	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	0.929	0.911	0.929	0.946	0.929	0.929	0.928	0.872
17	18	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	0.903	0.950	0.935	0.919	0.919	0.925	0.926	0.884
18	17	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	0.914	0.914	0.914	0.948	0.940	0.926	0.926	0.892
19	19	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	0.953	0.938	0.906	0.919	0.903	0.924	0.923	0.859
20	21	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	0.919	0.938	0.935	0.906	0.914	0.923	0.923	0.851
21	20	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	0.952	0.935	0.903	0.927	0.895	0.923	0.922	0.853
22	22	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	0.969	0.938	0.887	0.906	0.913	0.922	0.922	0.879
23	23	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	0.907	0.926	0.907	0.933	0.904	0.915	0.916	0.838
24	24	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	0.911	0.893	0.911	0.920	0.938	0.914	0.914	0.872

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
25	25	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	0.983	0.931	0.914	0.862	0.845	0.907	0.905	0.847
26	26	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	0.984	0.891	0.839	0.922	0.889	0.905	0.903	0.878
27	27	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	0.950	0.917	0.914	0.871	0.850	0.900	0.899	0.836
28	28	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	0.900	0.900	0.900	0.900	0.892	0.898	0.898	0.857
29	29	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	0.875	0.929	0.889	0.907	0.880	0.896	0.897	0.832
30	30	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	0.883	0.917	0.883	0.900	0.883	0.893	0.894	0.857
31	31	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.946	0.929	0.833	0.866	0.891	0.893	0.893	0.814
32	32	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	0.967	0.897	0.857	0.875	0.857	0.891	0.888	0.818
33	34	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	0.931	0.914	0.879	0.836	0.879	0.888	0.888	0.803
34	33	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	0.935	0.922	0.859	0.906	0.820	0.889	0.887	0.825
35	35	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	0.906	0.906	0.900	0.865	0.844	0.884	0.884	0.792
36	36	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	0.911	0.893	0.875	0.866	0.875	0.884	0.883	0.796

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
37	37	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	0.938	0.891	0.875	0.881	0.825	0.882	0.880	0.784
38	38	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	0.953	0.906	0.891	0.817	0.823	0.878	0.876	0.765
39	39	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	0.953	0.875	0.859	0.847	0.847	0.876	0.874	0.740
40	40	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	0.804	0.929	0.875	0.926	0.813	0.869	0.870	0.821
41	41	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	0.857	0.839	0.875	0.893	0.875	0.868	0.868	0.781
42	42	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	0.919	0.887	0.839	0.823	0.831	0.860	0.858	0.765
43	43	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	0.926	0.857	0.839	0.813	0.852	0.857	0.856	0.778
44	44	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	0.860	0.865	0.827	0.870	0.840	0.852	0.852	0.797
45	46	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	0.857	0.857	0.857	0.827	0.858	0.851	0.852	0.772
46	45	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del/Desc	0.935	0.871	0.806	0.839	0.806	0.852	0.849	0.779
47	48	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	0.931	0.929	0.793	0.827	0.759	0.848	0.846	0.751
48	47	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	0.931	0.833	0.850	0.800	0.825	0.848	0.846	0.800

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
49	50	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	0.850	0.850	0.817	0.853	0.800	0.834	0.833	0.755
50	49	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	0.906	0.935	0.766	0.815	0.750	0.834	0.833	0.697
51	51	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	0.938	0.844	0.844	0.750	0.766	0.828	0.825	0.692
52	52	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	0.857	0.827	0.827	0.817	0.784	0.823	0.821	0.731
53	53	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	0.893	0.839	0.750	0.795	0.768	0.809	0.807	0.673
54	54	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	0.911	0.810	0.776	0.767	0.759	0.805	0.802	0.704
55	55	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	0.800	0.800	0.783	0.833	0.783	0.800	0.800	0.738
56	56	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	0.911	0.815	0.778	0.779	0.717	0.800	0.796	0.694
57	57	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.875	0.796	0.810	0.767	0.727	0.795	0.792	0.675
58	58	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	0.828	0.857	0.786	0.760	0.710	0.788	0.787	0.665
59	59	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	0.883	0.817	0.800	0.708	0.717	0.785	0.782	0.690
60	60	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	0.790	0.774	0.774	0.720	0.750	0.762	0.761	0.650

Rank (weighted)	Rank (unweighted)	Research question	Domain	Answerability intermediate RPS	Potential for translation intermediate RPS	Deliverability intermediate RPS	Impact on burden intermediate RPS	Equity intermediate RPS	Unweighted RPS	Weighted RPS	AEA
61	61	How effective is the use of mannitol in unconscious eclamptics?	Desc	0.804	0.828	0.741	0.742	0.692	0.761	0.760	0.651
62	62	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	0.883	0.790	0.645	0.763	0.683	0.753	0.749	0.654
63	64	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	0.846	0.760	0.660	0.769	0.716	0.750	0.748	0.642
64	63	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	0.867	0.800	0.758	0.700	0.629	0.751	0.747	0.635
65	65	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	0.793	0.696	0.767	0.725	0.721	0.741	0.738	0.601
66	66	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	0.845	0.750	0.741	0.643	0.679	0.732	0.729	0.574
67	68	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	0.742	0.742	0.742	0.658	0.650	0.707	0.706	0.608
68	67	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	0.893	0.750	0.672	0.629	0.603	0.710	0.705	0.594
69	70	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	0.704	0.729	0.720	0.717	0.646	0.703	0.703	0.583
70	71	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	0.759	0.700	0.655	0.698	0.702	0.703	0.701	0.581
71	69	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	0.839	0.750	0.625	0.705	0.598	0.704	0.700	0.602
72	72	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	0.742	0.694	0.677	0.559	0.625	0.659	0.658	0.536
73	73	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	0.724	0.707	0.633	0.586	0.585	0.647	0.646	0.498
74	74	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	0.708	0.700	0.500	0.592	0.549	0.610	0.608	0.519
75	75	How can MRI aid in the diagnosis of fetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	0.692	0.673	0.519	0.596	0.510	0.598	0.596	0.468
76	76	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	0.500	0.482	0.518	0.433	0.509	0.488	0.488	0.420

Annex 10 Comparison of ranks within by expertise of scorers

sl	Research question	Domain	Rank (weighted) All (n=69)	Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
53	Evaluate strategies to reduce delays across the care pathway for women with pre-eclampsia/eclampsia in LMICs.	Del	1	37	7	1	2	5
51	Develop and test innovative strategies to improve the availability of supplies (e.g., drugs, blood etc.) to manage pre-eclampsia/eclampsia in LMICs.	Del	2	33	9	9	1	10
66	Evaluate strategies to improve follow-up and management of women with pre-eclampsia/eclampsia in LMICs.	Del/Dev	3	11	5	13	49	4
52	What are the determinants of type-3 delay in the treatment of pre-eclampsia/eclampsia in LMICs?	Del/Desc	4	47	2	3	31	1
74	Evaluate strategies to motivate and facilitate early antenatal care check-ups for women in LMICs.	Del	5	12	1	11	36	13
48	Investigate availability, adherence and barriers to implementation of pre-eclampsia/eclampsia guidelines in health facilities in LMICs.	Del	6	48	15	4	41	15
47	Assess the readiness of health facilities and service providers for the treatment of pre-eclampsia/eclampsia in health facilities in LMICs?	Del	7	39	6	33	52	2
42	Develop and evaluate strategies for early diagnosis/screening of women at risk of pre-eclampsia/eclampsia in LMICs.	Del	8	34	13	8	70	11
27	What factors influence the utilisation of Magnesium Sulphate at different tiers of health facilities in LMICs?	Del/Desc	9	6	4	2	21	3
49	Assess the effectiveness of quality improvement initiatives such as death registration, auditing, introduction of protocols and training in improving management of pre-eclampsia/eclampsia in health facilities.	Del	10	44	12	6	28	8
16	Develop and test prediction models for pre-eclampsia/eclampsia that are suitable for use in LMICs.	Dis	11	5	11	24	12	12
23	When is it best to commence low dose Aspirin in women with previous history of pre-eclampsia/eclampsia in LMICs?	Desc	12	40	27	18	10	27

sl	Research question	Domain	All (n=69)		Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
							Rank (weighted)		
46	Asses the effectiveness of community health workers in monitoring BP to improve identification of women with pre-eclampsia/eclampsia in LMICs?	Del	13		10	8	27	75	17
37	Assess gaps in knowledge and skills of health care providers in managing pre-eclampsia/eclampsia in LMICs.	Del/Desc	14		32	16	20	54	19
54	Will scaling up of midwifery services improve screening and management of pre-eclampsia/eclampsia in LMICs?	Del	15		23	21	23	3	24
24	What is the effect of low dose Aspirin on minimization of pre-eclampsia or preventing recurrent pre-eclampsia in high-risk women in LMICs?	Desc	16		41	32	26	4	28
55	What are the challenges encountered in referring a pre-eclamptic/eclamptic patient from one health facility to another?	Del/Desc	17		38	34	19	6	41
26	Assess the feasibility, safety and efficacy of loading dose magnesium sulphate at the primary care level in the treatment of pre-eclampsia and eclampsia in LMICs.	Del/Desc	18		30	22	5	17	18
9	What are the maternal, foetal and newborn outcomes in women with pre-eclampsia/eclampsia in LMICs?	Desc	19		1	3	16	69	6
56	Develop and evaluate strategies to improve emergency transfer/referral of critically ill women and neonates to tertiary health centres in LMICs.	Del/Dev	20		49	17	17	57	16
44	How can we improve screening, detection and management of hypertension and pre-eclampsia postpartum?	Dev	21		43	42	10	73	42
58	Establish pre-eclampsia/eclampsia registry in LMICs to better understand the disease.	Del	22		18	18	39	22	7
38	Evaluate the impact of education and awareness of mothers and communities regarding pre-eclampsia/eclampsia and appropriate care-seeking on the burden and adverse outcome of pre-eclampsia/eclampsia in LMICs.	Desc/Del	23		16	20	32	19	39
76	Evaluate the feasibility and effectiveness of targeted antenatal care in improving outcomes in women with pre-eclampsia.	Del	24		13	30	34	45	9

sl	Research question	Domain	All (n=69)	Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
				Rank (weighted)				
1	What is the burden of hypertensive disorders including pre-eclampsia/eclampsia in LMICs?	Desc	25	14	23	36	24	22
50	What are the barriers and opportunities for improved health systems to deliver effective evidenced care for pre-eclampsia/eclampsia in LMICs?	Del	26	53	25	37	14	20
2	Are there clinical, demographic or other factors in LMICS that affect the rates, severity, and time of onset (early/late) of pre-eclampsia/eclampsia?	Desc	27	22	28	44	27	26
43	What are barriers and challenges to early identification women at high risk of pre-eclampsia/eclampsia in LMICs?	Desc/Del	28	9	10	22	71	21
57	How can we standardise and improve data collection regarding maternal and newborn indices and outcomes in relation to pre-eclampsia/eclampsia in LMICs?	Dev	29	24	14	30	8	14
41	What factors influence the use of simple intervention such as BP measurement to detect hypertensive disorders in LMICs?	Desc/Del	30	35	38	21	51	37
39	Explore knowledge, attitude and practices of women, their families and communities in LMICs regarding pre-eclampsia/eclampsia, its risk factors and prevention and treatment.	Desc	31	8	24	15	34	38
63	Evaluate the use of m and eHealth or digital technologies in improving diagnosis and monitoring of pre-eclampsia/eclampsia in LMICs.	Dev/Del	32	67	26	12	40	31
61	What is the optimal duration for stabilisation in pre-eclampsia/eclampsia before embarking on delivery?	Desc	33	19	37	14	44	23
28	Assess the feasibility and effectiveness of primary level/lower-level health care workers in administering Magnesium sulphate for pre-eclampsia/eclampsia in LMICs.	Del	34	15	43	28	26	30
65	Evaluate the use of m and eHealth or digital technologies in improving quality of care for the management of pre-eclampsia/eclampsia at health facilities in LMICs.	Dev/Del	35	58	19	31	62	36
14	Which biomarkers are predictors of pre-eclampsia and at which stage in pregnancy should such markers be assessed?	Dis	36	3	40	56	59	34

sl	Research question	Domain	Rank (weighted)					
			All (n=69)	Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
19	Develop novel point of care biomarker testing for pre-eclampsia in LMICs.	Dis	37	50	29	47	25	32
20	What is the impact of low dose calcium supplementation during pregnancy on pre-eclampsia in LMICs?	Desc	38	68	51	25	48	48
70	Which is the best form of anaesthesia to employ for emergency c/s in a patient that has had a seizure for better neonatal outcomes?	Desc	39	29	33	66	72	40
11	Investigate the association between pregnancy related hypertensive disorders and other cardiovascular disease in women in LMICs.	Desc	40	26	35	50	20	25
30	Assess the effectiveness of anti-hypertensive medications for the treatment of pre-eclampsia/eclampsia in LMICs?	Desc/Dis	41	57	52	45	9	55
60	Evaluate the effectiveness of conservative management vs immediate delivery of pre-eclampsia/eclampsia at different gestational ages on perinatal outcomes in LMICs?	Desc/Del	42	25	31	52	67	29
59	Establish pre-eclampsia/eclampsia biobanks in LMICs to better understand the disease.	Del	43	28	54	43	42	44
29	Investigate novel therapeutics for the treatment of pre-eclampsia/eclampsia in LMICs.	Dis	44	31	45	61	11	49
40	What measures are taken by pregnant women to prepare for delivery and complications related to pre-eclampsia/eclampsia in LMICs?	Desc	45	36	49	54	16	51
62	Evaluate the use of m and eHealth or digital technologies in increasing awareness about pre-eclampsia/eclampsia and its prevention and management in LMICs.	Dev/Del	46	66	41	38	43	43
22	What is the role of complimentary nutrient supplementation during pregnancy (e.g., calcium, iron, folate, protein, vitamin-D etc.) in reducing pre-eclampsia and improving neonatal outcomes in LMICs?	Desc	47	76	61	7	39	59
10	What are the socio-economic impacts of pre-eclampsia/eclampsia in LMICs?	Desc	48	21	36	53	58	33
45	Can (self) home-based BP monitoring improve identification of women at risk of PE/E in LMICs?	Del/Desc	49	65	48	41	63	46

sl	Research question	Domain	Rank (weighted)					
			All (n=69)	Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
21	What is the association between dietary factors and pre-eclampsia/eclampsia among women in LMICs?	Desc	50	64	50	51	30	45
12	Do angiogenic markers (e.g., sFlt-1/PlGF) accurately predict pre-eclampsia/eclampsia in women who have higher risk of developing the disease in LMICs?	Dis/Desc	51	2	44	60	37	50
67	What is the role of preconception care in the prevention of pre-eclampsia/eclampsia?	Desc	52	61	39	59	60	47
75	How does insulin and the metabolic syndrome affect the prevalence and progression of pre-eclampsia?	Desc/Dis	53	62	47	46	32	54
13	Evaluate the performance of a glycosylated fibronectin (GlyFn) point-of-care (POC) diagnostic test in women at high risk of pre-eclampsia in LMICs.	Dev/Del	54	27	46	49	66	52
36	How useful is measurement of Oxygen Saturation (SpO2) in the assessment of severity of pre-eclampsia/eclampsia in LMICs?	Desc	55	46	55	57	29	64
64	Evaluate the use of m and eHealth or digital technologies in promoting healthy lifestyle for the prevention of pre-eclampsia/eclampsia in LMICs.	Dev/Del	56	72	56	63	35	53
15	Develop novel biomarkers for early prediction and diagnosis of pre-eclampsia in LMICs.	Dis	57	4	53	68	61	35
6	What is the association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	58	20	67	67	76	57
25	What is effect of continuation of low dose Aspirin in puerperium on pre-eclampsia outcomes?	Desc	59	73	63	29	15	58
34	Evaluate the effect of early diagnosis and treatment of sub-clinical infections on pre-eclampsia/eclampsia in women in LMICs?	Desc/Del	60	54	62	72	18	60
18	What is the role of placenta-derived exosomes as possible biomarkers for the diagnosis/prognosis of pre-eclampsia in women in LMICs?	Dis	61	63	59	35	23	56
4	What is the genetics and genomics of early onset pre-eclampsia in LMICs?	Dis	62	59	58	64	53	62

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sl	Research question	Domain	Rank (weighted)					
			All (n=69)	Laboratory science research (n=6)	Clinical science research (n=34)	Public health and health systems research (n = 20)	Policy and programme implementation (n = 15)	Clinical services (direct health care) (n = 41)
5	What is the effect of air pollution on incidence of pre-eclampsia/eclampsia in LMICs?	Desc	63	42	65	65	55	70
33	Assess the effect of infectious diseases and sub-clinical infections on pre-eclampsia in women in LMICs.	Desc	64	45	70	62	5	67
3	What is the effect of maternal mental health disorders on the onset or severity pre-eclampsia/eclampsia in LMICs?	Desc	65	52	66	58	7	65
17	Can new omics approaches be used to discover better markers of pre-eclampsia?	Dis	66	69	57	40	33	63
8	What is the effect of age of the father on onset of pre-eclampsia/eclampsia?	Desc	67	51	60	73	56	66
72	How effective is the use of mannitol in unconscious eclamptics?	Desc	68	55	68	42	74	61
32	Evaluate the association of urinary infection in the first, second and third trimester and pre-eclampsia in women in LMICs.	Desc	69	56	72	55	47	72
73	Does early weaning influence later development of pre-eclampsia/eclampsia?	Desc	70	71	71	48	65	69
7	What is the relationship between weather seasons and development of pre-eclampsia/eclampsia in LMICs?	Desc	71	17	69	75	50	68
35	What is the effect of regimented physical exercise on the prevention of pre-eclampsia/eclampsia in LMICs?	Desc	72	70	74	71	13	73
68	Evaluate the use of Uterine Artery Doppler Sonography for the prediction of pre-eclampsia and other adverse pregnancy outcomes in LMICs.	Desc/Dis	73	60	64	70	38	71
69	Evaluate the use of plasmapheresis in the management of pre-eclampsia in LMICs.	Desc/Del	74	75	73	69	64	74
31	Do herbal/traditional medicines benefit pre-eclampsia/eclampsia?	Desc	75	7	76	74	46	76
71	How can MRI aid in the diagnosis of fetal neurological abnormalities resulting from pre-eclampsia/eclampsia?	Desc	76	74	75	76	68	75

[1]Dis=Discovery; Desc=Descriptive; Del=Delivery; Dev=Development; RPS=Research Priority Score; AEA= Average Expert Agreement; LMICs=Low- and middle-income countries; MRI=Magnetic Resonance Imaging

Annex 11 Published paper: Perception and experiences of adolescent mothers and community in caring for their preterm babies: Findings from an in-depth study in rural Bangladesh Published in BMC Pregnancy and Childbirth

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Authors' accepted copy of the paper is included in this thesis, pages 247 to 275.

Perception and experiences of adolescent mothers and community in caring for their preterm babies: Findings from an in-depth study in rural Bangladesh

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Abstract

Background

A significant concern for Bangladesh is the high prevalence of adolescent pregnancy and the associated negative consequences for mother and baby, including a teen-related increased risk of preterm birth (PTB). Bangladesh also has one of the highest incidences of PTB (19%). Despite these high numbers of adolescent pregnancies and PTB, little is reported about the experiences of adolescent mothers in caring for their preterm babies, and the interventions needed to support them. The aim of this study was to explore gaps and opportunities for improved care for preterm babies among adolescent mothers and communities in rural Bangladesh.

Methods

We conducted a qualitative study in rural villages of Baliakandi sub-district of Bangladesh. Data collection involved in-depth interviews with adolescent mothers of premature and term babies, adult mothers with premature babies, and family members (n = 36); focus groups with community members (n = 5); and key informant interviews with healthcare providers (n = 13). Adolescent mothers with term and adult mothers with PTBs were included to elicit similarities and differences in understanding and care practices of PTB. A thematic approach was used for data analysis.

Results

We explored two major themes- perceptions and understanding of PTB; care practices and care-seeking for illnesses. We observed gaps and variations in understanding of preterm birth (length of gestation, appearance, causes, problems faced) and care practices (thermal management, feeding, weight monitoring) among all, but particularly among adolescents. Immediate natal and marital-kins were prominent in the narratives of adolescents as sources of informational and instrumental support. The use of multiple providers and delays in care-seeking from trained providers for sick preterm babies was noted, often modulated by the perception of severity of illness, cost, convenience, and quality of services. Health systems challenges included lack of equipment and trained staff in facilities to provide special care to preterm babies.

Conclusion

A combination of factors including local knowledge, socio-cultural practices and health systems challenges influenced knowledge of, and care for, preterm babies among adolescent and adult mothers. Strategies to improve birth outcomes will require increased awareness among adolescents, women, and families about PTB and improvement in quality of PTB services at health facilities.

Keywords: Adolescents, Preterm birth, Bangladesh, Maternal, Newborn

Background

Adolescent pregnancy and motherhood continue to be considered a priority public health and human rights issue because of its profound consequences and long-term negative effects on young individuals, their families, and entire communities. Globally, 16 million adolescent mothers aged 15–19 years and 2 million below the age of 15 experience the physically and emotionally demanding journey of pregnancy and childbirth every year [1, 2]. More than 90% of these births occur in low- and middle-income countries (LMICs) and within marginalized communities – commonly driven by poverty, lack of education and employment opportunities in these areas [3–5]. Adolescent childbearing is generally associated with negative health consequences for both the mother and baby including increased risks of maternal and neonatal deaths, stillbirths, preterm births (PTB), small-for gestational-age (SGA) babies, severe neonatal complications, pregnancy and childbirth complications, and maternal undernutrition, as compared to child-bearing for those older than 19 years [6–10]. In addition, adolescent mothers must simultaneously adapt to the demanding role of being a mother and nurturing a baby while they are still going through their own biological, physical, emotional, and psychological development as an adolescent [11–13]. Without the necessary knowledge, skills, and resources to deal with early parenthood, they face several social, economic, personal and relational challenges [11–13].

Both hospital and population-based studies in high and low resource settings consistently report that adolescent mothers are at an increased risk for PTB compared with mothers aged above 19 years of age [6, 7, 9, 14–16]. Multi-country studies conducted in LMICs also identified that adolescent mothers aged less than 20 years are at increased risk of PTB, after controlling for country, health facility effects and for potential confounding factors [7, 10]. The risk of PTB is especially high among adolescent mothers less than 16 years of age [7, 10]. Although all babies are vulnerable in the first few days after birth and require essential newborn care, premature babies are especially vulnerable to temperature instability, feeding difficulties, low blood sugar, infections, and breathing difficulties [17]. Since preterm babies are high-risk neonates requiring special attention and care, early recognition and health care-seeking is very important for these mothers and babies, to reduce morbidity and mortality. However, this extra care might be challenging for adolescent mothers. Thus, already higher risks posed to adolescent motherhood may be further compounded by a PTB, and vice versa, elevating the vulnerability and distress among adolescent mothers and their high-risk babies.

Despite remarkable progress in health indicators, a significant concern for Bangladesh is the high prevalence of child marriages and the subsequent high levels of adolescent pregnancy. According to the recent 2017-18 Bangladesh Demographic and Health Survey (BDHS) the median age at first marriage among women aged 20–49 is 16.3 years and approximately 71% of women in this age group were married by age 18. The report also highlights that almost one-third (28%) of adolescent girls aged 15–19 years have begun child bearing [18]. Moreover, Bangladesh has one of the highest incidences of PTB in the world. An estimated 603,698 babies were born prematurely in 2014 i.e., 19% of the total

number of births that year [19]. The BDHS estimates that about 19% of all neonatal deaths are directly attributed to PTB [18]. Another study in rural Bangladesh found the risk of death in preterm babies to be significantly higher than that of term babies [20]. Given that worldwide, almost half of preterm babies are born at home and that even among those born in facilities critical newborn care is often lacking [17], ensuring that adolescent mothers, their families and communities are well-informed and empowered about care of preterm babies is crucial [17].

In spite of the high rate of adolescent pregnancies and preterm births in Bangladesh, there is a dearth of evidence documenting the understanding and experiences of adolescent mothers in caring for their preterm babies. Equally, little is known about the interventions needed to prepare and assist them in caring for their premature babies. Exploratory studies in African settings, including Malawi, Uganda and Ghana, indicate that inadequate care of preterm babies is commonly driven by a (i) lack or inadequate knowledge about the causes of preterm birth, diseases severity and how to care for preterm babies; poverty which prevented families from buying warm materials, living in properly build warm houses or paying transport costs and costs of health facilities; and (iii) poor quality of care at health facilities due to lack of protocols, skilled service providers and basic equipment, drugs and other supplies [21–24]. In addition, findings from these studies as well as in Bangladesh reveal low rates of care-seeking or using traditional medicines and care-seeking from unqualified providers for complications and illnesses in preterm babies [21–25]. However, whether these factors are important barriers in other settings specially among adolescent mothers in rural Bangladesh is unknown. We, therefore, undertook a qualitative study to explore the perception and caring practices of adolescent mothers, their family and community members regarding PTB, at a rural sub-district in Bangladesh. To gain an in-depth understanding of whether and how the perception and care-practices differ between adolescents with premature births and their term counterparts, data was also collected from adolescent mothers (15–19 years) who gave birth to term babies and older mothers (≥ 19 years of age) who gave birth to premature babies. Information on the perceptions of PTB, access to related health services and subsequent management practices among adolescent mothers and community, will be important for reproductive health programs to better understand their specific needs and to tailor services and strategies to improve perinatal and newborn care in Bangladesh and other resource poor settings.

Methods

Study design

We adopted a qualitative approach involving in-depth interviews (IDI), key informant interviews (KII), and focus group discussions (FGD) to generate a detailed understanding of mothers' and community perspectives regarding PTB and their experiences in caring for a preterm baby within their social context.

Study setting and participants

The study was conducted in rural villages of Baliakandi sub-district in Rajbari District, central Bangladesh. The sub-district was chosen as International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) operates a demographic and health surveillance system among a population of approximately 200,000 in 261 villages in the sub-district. The surveillance system collects information on key demographic and reproductive events every four months including age, births, gestational age at births etc. which facilitated identification of participants for this study. The primary participants for this study were adolescent mothers aged 15–19 years who had given birth to preterm babies (any live birth before 37 completed weeks of gestation) in the 6 months prior to the start of data collection. However, we also aimed to explore whether perception, experiences and care-practices varied by age of mother and gestation of baby i.e., whether perception or experiences of adolescent mothers with a PTB differ or is similar to adolescent mothers with term birth or adult mothers with PTB. As such, data was also collected from adolescent mothers (15–19 years) who gave birth to a term baby and older mothers (> 19 years of age) who gave birth to a preterm baby in the six months prior to the start of data collection. The secondary participants of the study included immediate family members (e.g., fathers and grandmothers of the preterm baby), community members (other mothers, elderly women and fathers) and health care providers. Immediate family members were included to obtain detailed understandings of their experiences surrounding the birth and care of the baby. To understand and obtain more information about cultural norms and social practices regarding PTB in the community, FGDs were conducted with several homogenous groups including young mothers (with preterm or term births), elderly women and fathers. In addition, we conducted key-informant interviews (KIIs) with health care providers selected purposively from public and private health facilities providing newborn and childcare in the area to understand the challenges faced in providing services to preterm babies.

Data collection

Data was collected by trained social science researchers and anthropologists between July 2019 and December 2019. Individual IDIs, FGDs and KIIs were conducted to add breadth to the data and triangulate the findings (Table 1). Interview guides were developed, translated into the local language Bangla and pilot tested. All questions were open-ended with prompts to elicit details and description from the participants. Topics covered in the interview guides included understanding of PTB, experiences with pregnancy and delivery, care practices of preterm babies, care-seeking for illnesses and the associated challenges. We conducted 36 IDIs, including adolescent mothers with preterm or term babies (n = 18), adult mothers with preterm babies (n = 10), family members (n = 8). We conducted KIIs with formal and informal health care providers (n = 12) (Table 1). This included nurses in labour and neonatal wards (n = 3), obstetricians and gynaecologists (n = 2), neonatal consultant (n = 1), health care worker (n = 1) and traditional birth attendants (n = 3). FGDs were conducted with young mothers (n = 1), grandmothers (n = 1), fathers (n = 2), village doctors/community people (n = 1) (Table 1). There

was no overlap in participants of IDIs, FGDs or KIIs. Each interview/discussion was conducted in a private location at a time that was convenient to the participant or group. Prior to starting the interviews or FGDs, written informed consent or assent was administered. Written informed consent was obtained from study participants above 18 years of age. For participants less than 18 years of age, assent from them and informed consent from their legal guardian was obtained. Each FGD had six–eight participants and efforts were directed to keep the groups as homogenous as possible. Each of the interviews and focus groups lasted between 30 and 115 min and, with the permission of the participant or group, the entire discussion was audio-recorded while a note-taker additionally took handwritten notes. Immediately after each interview or FGD, a short summary was prepared, noting any important points or challenges to facilitate with data analysis. Data collection continued until saturation was reached.

Table 1: Data collection methods

Interview type	Number of participants (n=82)
IDIs	
Adolescent women with PTBs	10
Adolescent women with term births	8
Adult women with PTBs	10
Grandmothers	3
Fathers	5
Sub-total	*36*
KIIs	
Birth attendant	3
Trained/Formal health care provider	9
Sub-total	*12*
FGDs	
Elderly women	2 groups (12)
Fathers	2 groups (16)
Young mothers	1 group (6)
Sub-total	*5 groups (34)*

Data analysis

Preliminary data from this qualitative exploration has been analysed using an inductive thematic approach and both data collection and data analysis were conducted simultaneously [26]. Audio recordings of all FGDs and interviews were transcribed verbatim in Bangla, by the respective interviewer immediately after the interview, preventing minimal loss of data. By adding any additional notes (field notes) transcripts were expanded. Transcripts were randomly checked against audio recordings to ensure quality of transcription. An iterative process was used to code and develop themes. To begin with, initial transcripts were read and re-read carefully to familiarise with the data and a coding structure created. Following this, the important and most frequent codes were applied to the new data. Simultaneously, new and emerging codes were added to the coding structure. Finally, codes were grouped together to develop categories and collated into potential themes and sub-categories. Data analysis was carried out using NVivo v 12 Analysis Software.

Results

In this paper we have presented perceptions and experiences of adolescent mothers on PTB, comparing it with the views of adult mothers, family and community members. Information on challenges of caring for PTB at health facilities were obtained from heath care providers. We concentrate on the two major themes emerging from our data: firstly, perceptions and understanding of PTB (length of gestation, causes, appearances); secondly, care practices and care-seeking for preterm babies.

Background characteristics

We had a mix of participants by birthplace (facility or home birth), delivery mode (normal or c-section births), and family type (nuclear or extended) in both groups - adolescent (15–19 years) and adult (20–36 years) women with recent births and their family members (Table 2). However, a majority had six or more years of education, were housewives living with extended families, delivered at health facilities, and had normal vaginal deliveries. The mean gestational age for PTBs was 31 weeks (28–36 weeks). The fathers who participated in the IDIs were between 19 and 35 years (mean 25.2 years old), grandmothers were between 41 and 50 years (mean 46.7) years, whereas the key informants were between 30 and 86 years (mean 51.6 years) old.

Table 2: Background characteristics of women with recent preterm/term births

	Adolescents with PTB	Adults with PTB	Adolescents with term birth
	n=10	n=10	n=8
Education			
No/Primary (1-5 y)	4	3	1
Secondary + (6+ y)	6	7	7
Religion			
Islam	9	9	7
Others (Hindu)	1	1	1
Child status			
Alive	8	7	8
Dead	2	3	-
Occupation			
Housewife	10	9	2
Student	-	1	-
Family type			
Nuclear	2	5	2
Extended	8	5	6
Delivery place			
Home	3	4	4
Facility	7	6	4
Delivery type			
NVD	8	5	5
C/S	2	5	3
Birth Order			
Primiparous	7	1	8
Multiparous	3	9	-
Mean gestational age at birth (weeks)	30.9	31.0	39.4

Perception and understanding of PTB

Length of gestation

The overall concept of babies born preterm was well understood among all mothers and community members in Baliakandi. Locally, PTBs were referred to as *"births that occur before time"* or "*shomoyer age"* and this appropriate time was mostly defined as the time needed for the baby in the womb to become *fully or well-nourished* or "*pushto.*" The length of gestation was always described in months rather than in weeks and we observed variations in participants' opinion as to what that appropriate time or length of gestation should be. The most common responses by adolescents with PTBs included, nine months, nine months 10 days, between nine to 10 months, 10 months, 10 months 10 days whereas other

adolescent mothers with term births or adult mothers with PTBs mostly mentioned 10 months. Any births at the 8th or 7th month were considered by all to be early.

> *"Elders say that a baby is healthy if born at 10 months 10 days and doesn't have problems with being undernourished." (IDI03 Adolescent mother with a preterm baby).*

> *"When the baby is nourished… if the baby stays in the womb for nine months, then it is nourished." (IDI27 Adolescent mother with a preterm baby).*

The responses of family members and other community participants varied like those of adolescent mothers with premature births, with some mentioning that although 10 months is ideal, nine months is also good: *"Baby is nourished if 10 months… but nine months is also not bad, its medium…" (FGD01 Elderly women).*

All participants used or were aware of using the date of last menstrual period (LMP) to estimate the month of pregnancy and birth. However, participants also relied heavily on dates provided during ultrasonography (USG) to estimate their due dates. Often these USGs were done during the 2nd or 3rd trimester to know the status of the baby or to estimate the gestational age in cases where mothers were confused with their LMP date, for example those with irregular periods or spotting during pregnancy, as one participant mentioned:

> *"I couldn't remember clearly when I became pregnant. So, I went to do an ulta (USG) to determine the date…I have heard that you can even tell how many months old the baby is if you do an ulta (USG). I told them I forgot the date of my last menstruation. Accordingly, they gave me a date of delivery." (IDI11 Adult mother of a preterm baby).*

Appearance of PTB

When mothers and community members were asked to describe a preterm baby, they used several external physical features. The most common notion mentioned by all participants was that babies born before time are under-nourished (*opusto*), small (*choto*), weak (*kabu*), have less weight, frail (*finfina*), have long and thin hands, and legs *(haat pa. noli noli)*. The term *opusto*, which literally means being under-nourished, was mentioned by all participants to describe preterm babies and was often synonymously used to mean babies who are not fully grown. For babies born as early as seven months, a common way to identify them, as mentioned by adolescents as well adults, was that the baby's eyelids are fused together (*chokh fute na*). Other terminologies used by older participants and community members who had seen preterm babies included visible veins around the stomach (*pet-er rog dekha jai*), wrinkled skin, sunken forehead, and no hair.

Problems preterm babies may face

Participants highlighted problems that preterm babies may suffer from, or their preterm babies had suffered. Adolescent and adult mothers with preterm babies, recollected problems mainly from their

experience, whilst about half of the adolescent mothers with term babies mentioned that they were not aware. Participants of FGDs, family members and adult mothers, however, could promptly mention problems faced by preterm babies. Several participants including adolescent mothers emphasized that babies born at nine months or later are generally healthy whereas babies born at seven months rarely survive. A mother mentioned, *"babies who are born in the 7th or 8th months are not born with good health. Those who are well-nourished, survive and those who aren't, die"* (IDI14 Adolescent mother of a preterm baby), whilst others highlighted the need to spend a lot of money to ensure survival, or shared recollections of incidents where babies born early were kept in *glass houses* (*Kacher ghor-* incubators), some of whom had survived:

> *"...babies born at seven months may not survive and those at 8 months have more possibility but need to spend a lot of money…"* (IDI12 Adult mother of a preterm baby).

> *"The baby was not nourished as much as he would have been if born after 10 months. His parents took him to hospital where the baby was kept in a glass house [incubator] so that his eyes develop. They returned after three months when the baby started feeding."* (FGD04 A participant of FGD with fathers).

Other problems mentioned include babies are undernourished; eyelids are fused, babies have difficulty breastfeeding; have breathing difficulties requiring hospitalization; baby turns blue or black; more prone to diseases (such as cough and cold, diarrhoea, pneumonia etc.) due to the babies being undernourished; physically and mentally disabled; ongoing poor nutritional state, and that their health doesn't fully recover when they grow up.

> *"Baby may suffer from heart problem or be weak or their eyes may not develop."* (IDI27 Adolescent mother of a preterm baby).

> *"Baby will either be less intelligent or disabled. Or he will have any other parts of his body damaged…he may have underdeveloped eyes, or hands or legs…he may not be talented. He did not complete his full growth."* (FGD04 A participant of FGD with fathers).

> *"After delivery, the two big problems are difficulty in breathing and cough. Makes wheezing sound inside the throat, noses are blocked, and baby cannot breathe. These happen more to babies born in the 7th or 8th month."* (KII06 Untrained birth attendant).

Causes of PTB

Findings revealed that awareness about the causes of PTB is limited in rural Bangladeshi settings and that many of the perceived causes are outside modern medicine. Over half of the adolescent mothers (10 out of 18) and half of the adult mothers (five out of 10) could not explain why babies could be born prematurely or why her newborn was born premature. Other participants, either mothers or family and

community members, mentioned several causes which have been grouped into (i) maternal health related, (ii) lifestyle or behavioural, and (iii) supernatural/spiritual causes (Table 3).

Table 3: Perceived causes for PTB

Maternal health

Less maternal age / less maternal age leading to c-section

Poor nutritional status

Use of medications (fever, deworming etc)

Inadequate sleep

Falls

Trauma to abdomen

Excessive vaginal discharge

Low-lying placenta

Convulsions, eclampsia

Urine infection

Indicated c-section

Sex during pregnancy

Lifestyle and behavioural

Heavy work, lifting heavy objects (using tube-well etc)

Inadequate eating

Not taking recommended vitamins, calcium, folic acid during pregnancy

Being beaten by husband

Stress due to familial issues e.g., disagreement with in-laws, husband's extra marital affairs

Attempted abortion

Elective c-section

Supernatural/spiritual

Evil spirits (being possessed by Jinn, *dosh, chut, upri, groher shomossa, bhoot)*

God's will

Poor nutritional status of the mother or inadequate eating was one of the most mentioned causes for premature birth. Because premature babies were born small and weak, many participants, including mothers, opined that this was because the mother was weak, under-nourished, or because she did not eat enough food or vegetables or take the recommended vitamins, iron, or calcium medications:"

My *baby was born early, as I didn't get enough to eat…"* (IDI08 Adolescent mother of a preterm baby). On the contrary, one young mother mentioned that food or eating habits had no effect on premature birth, as her relative who had a similar outcome used to eat adequately, whilst another mother stated that in order to prevent PTB and unnecessary c-sections, pregnant women should eat smaller but frequent meals, so that the baby does not grow too big in the womb.

Trauma to the abdomen, accidents/falls, risky work, lifting heavy objects were also mentioned by a few participants across the different groups. According to a young man whose child was born premature: *"We are farmers, we go to the field. Then there is rice to look after in the house or five cows. I would ask her to put the rice away. There is always some work at home, she did a lot of risky work…she used to carry heavy items and that is why my child was like this (born preterm)"* (FGD04 A participant of FGD with fathers).

Use of medicines during pregnancy such as for fever, pain or deworming was highlighted during FGDs. A participant of an FGD highlighted that, failed abortions using abortive medications may later result in early delivery or even still-births. Another mother whose twin preterm babies had died, expressed concern and confusion whether taking iron-folic acid and calcium medications had resulted in such an outcome or not.

Many mothers and community participants believed that supernatural or spiritual causes such as God's will or evil spirits (*dosh, chut, upri, groher shomossa, bhoot, Jinn*) were to blame. The opinions related to evil spirits were divided, and some young mothers and husbands strongly opposed the notion, mentioning that these were myths and old tales, whilst others said this might result in miscarriage or inability to get pregnant but not premature births. Those who believed in the notion mentioned that pregnant women are to follow certain norms during their pregnancy e.g., not leaving the house in the evening, afternoon, prayer times, or not roaming in the garden with big trees. It was said that an inability of the pregnant women to do so may result in early birth or even loss of pregnancy, as the excerpt below reveals:

> *"…Women are prone to curses and evil spirits, for this reason some babies get aborted at eight months. These babies may be born alive for some women but for others they die before birth…for example today is full moon, a lot of things (sprits) are outside during this time…if I am a new pregnant woman (kacha poyati), the evil spirits can attract me… when it attracts a pregnant woman, the pregnant women loses appetite, becomes thin. Sometimes she starts having abdominal pains. That is why she delivers early or loses her pregnancy."* (KII06 Untrained birth attendant).

An adult woman with a PTB strongly believed that she was possessed by *Jinn. In her words*: *"While I was sleeping, I used to feel that there's someone else sleeping beside me…the kabiraj [traditional healer] said that a huge Jinn is after me but wasn't courageous enough to harm… the kabiraj gave me*

an amulet that I wore till seven days after delivery…" (*IDI13 Adult mother of a preterm baby*). Now she believes that her newborn is possessed by the *Jinn* as the baby cries a lot and turns black. Similarly, two participants with prior history of PTBs believed that their womb was cursed, and another woman with two PTBs and whose husband's second wife had seven miscarriages believed that someone had cast an evil eye on their house.

Unable to explain the cause of PTB, some participants opined that it was God's will. A husband mentioned that: "*I don't know the reason. Life and death depend on The One. We don't have the ability to know when one will be born or die!" (IDI36 with a Husband).* Another grief-stricken young mother said, *"People used to ask me, what I have done that the baby was born at seven months. But I did not do anything…God took away whatever was His in the way He wanted…" (IDI07 Adolescent mother of a preterm baby).*

A few husbands/fathers during in-depth interviews as well as in the focus groups mentioned that a lower maternal age to be a cause of PTB as well as other complications for the mother and child, including miscarriage and early c-sections. According to these men, young mothers are usually poorly nourished which makes it difficult for them to bear a child, as one husband stated, *"girls who deliver early get pregnant at young age…nowadays girls are married at 12 or 13 years of age…if someone is married at a young age, they are not fully nourished, how will she bear a fully nourished child (FGD06 A participant of FGD with fathers)."* Unexpectedly, the two traditional birth attendants interviewed strongly believed that it is easier for adolescent mothers to deliver since their bone structures were believed to be very flexible and not rigid like those of older women. Other infrequently mentioned causes included infections, vaginal discharge problems, low-lying placenta, convulsions, domestic violence, and stress.

Care of preterm babies

In our study we asked participants about the care a preterm baby would need with an aim to elicit information on knowledge and practices related to three important aspects of preterm babies' care: temperature management, frequent feeding, and weight monitoring. In general, care practices did not vary by mothers' age (adolescent or adult) but rather on the status of the baby.

Having identified preterm babies to be small, under-nourished and weak, both adolescent and adult mothers mentioned the need to provide extra care to preterm babies. However, it was difficult for participants – especially adolescents – to describe what this extra care should entail, especially when physical problems were not present. For example, a baby who was born a month earlier was perceived to be under-nourished but otherwise well if there were no visible signs of illnesses or problems/anomalies and cared for like term babies: *"…baby was otherwise healthy and beautiful at birth. Baby was under-nourished and hence was not so active…" (IDI03 Adolescent mother of a preterm baby).* For these babies, the routine care at home included feeding the child well, keeping them

warm, clean and dry, maintaining cleanliness including timely bathing so that the baby becomes healthy or so that the baby does not fall sick. An untrained birth attendant mentioned the need for a three-way approach for care of preterm babies that included (i) extra care by mother, (ii) traditional/spiritual care for dealing with evil eyes/spirits and (iii) treatment from doctors depending on the condition of the baby:

> *"If you enclose the house, then the baby will be free from evil eyes or curses – this is spiritual or traditional treatment; If the child is under-nourished, or has cough and cold or gas, you need advice from doctors. In addition, mother needs to take extra care such as timely feeding, bathing, sleeping etc. In this way the child will become healthy in a few days." (KII06 Untrained birth attendant).*

The recommendation for babies that were born too early, or babies born too small was that advice should be sought from formal health care providers and care provided accordingly. Although participants could not mention the benefits or purpose of using incubators, a few recollected instances where babies born early were kept in glasshouses and treated till they could be brought home.

Findings also highlight that adolescent mothers were dependent on various members in their network for support and care for the preterm/term newborn. These sources varied by the type of support needed and the roles of natal and marital kins were found to be prominent in their narratives. While the role of the adolescent's mother in providing instrumental and emotional support was a constant theme, other members such as mothers-in-law, aunts and sisters were also important. These are highlighted in the excerpts below:

> *"My mother taught me this (how to breastfeed). I did not know how to. She told me the proper way to hold when breastfeeding so that the flow of milk is slow. Otherwise, the baby will choke." (IDI01 Adolescent mother of a term baby).*
>
> *"I was afraid to take care of baby, my mother used to do everything, from bathing to cleaning. Now I have learnt" (IDI03 Adolescent mother of a preterm baby).*

Temperature management

In rural Baliakandi, all newborns (preterm and term) were considered to be susceptible to cold and hence need to be kept warm: *"Newborns come from the womb, they need to be kept warm."* The threat of *"catching cold"* was more imminent among preterm babies since they are small and under-nourished. Several practices were followed to keep them warm and prevent the babies from catching a cold.

Our findings reveal that, in general, management of temperature depended on the weather or external temperature. Whilst all newborns are wrapped using a *katha* (traditional cloth made from old sarees) or towel immediately after birth, as days progressed newborns or babies were cared for according to the

external temperature which included wearing warm clothes or covering the child with layers of cloth during rainy or winter days or during evenings and wearing thin clothes or using the fan during hot days. Among mothers with preterm babies particularly small or early preterms, practices included wrapping them in blankets, cotton, or holding the baby in mother's arms (to receive mother's warmth – *mayer om*) often at the advice of health care providers or elders. However, participants could not clearly specify how long they did this for and gradually started dressing newborns as per temperature.

Regardless of the communities' awareness about keeping newborns warm, traditional practices of immediate bathing after birth were prevalent. An adolescent mother of a preterm baby mentioned: "*We didn't bathe her for nine days. It is customary to bath babies after they are born, to clean all the impurities. So, on the 9th day my cousin sister-in-law shaved her hair off. We did not bath her fully but sprinkled some water over her body. That night the baby developed slight cough and cold*" (*IDI07 Adolescent mother of a preterm baby*). The adolescent mother then explained that her baby died on the way to the hospital.

A few mothers of preterm babies who experienced facility births or births with health care worker mentioned delaying first bathing to seven or 12 days as the doctor or health worker had suggested that their baby was too small. Some mothers and grandmothers whose babies were born at health facilities expressed discontent that in the absence of any bathing facility they had to bathe the baby once they returned home. Almost all babies were massaged with mustard oil on their skin before bathing. The mustard oil was seen to act as a protective barrier between the baby and the water, insulating the baby from cold. Almost all babies were bathed with lukewarm water, around mid-day. The water was warmed either by placing the container under the hot sun or over a hot stove during cloudy days. Babies were bathed almost every day except for cloudy, rainy or cold days, when bathing would be skipped, or they would be wiped with a wet cloth.

Feeding

Participants in our study widely shared the view that for under-nourished and weak preterm babies to grow healthy and regain their strength they must be fed well. For extremely preterm babies, who were not able to suckle, the practice was to express milk and feed with a dropper or spoon. For other preterm babies, feeding practices varied and some participants also mentioned pre-lacteal and non-exclusive breastfeeding. Honey and warm water ("to clear the stomach") were the two common pre-lacteal feeds mentioned. The common reason for non-exclusive breastfeeding with formula or cow or goat's milk was that the mother was not producing enough milk. On the other hand, mothers with hospital deliveries also recollected instances where they were told off by doctors for pre-lacteal feeding or had to stop feeding babies formula milk based on the doctor's advice. One mother mentioned, "*I started feeding after a day…the doctor scolded us a lot for feeding the baby some warm water (IDI27 Adolescent mother of a preterm baby)*" while another mother mentions, "*…we used a dropper to feed the baby*

powder milk (formula milk)…everyone else was feeding so we thought it would be okay… but the doctor told us that it is not good for baby, so we stopped (IDI22 Adolescent mother of a term baby)." In terms of interval or frequency, most participants mentioned that they fed their babies when they cried while some mentioned that they fed at regular intervals.

Weight monitoring

Although service providers were aware of the importance of weight monitoring, none of the interviewed participants was aware of the need to regularly monitor the weight of preterm babies. Birth weight was measured only for babies born in health facilities or when care was sought from formal health care providers.

Care-seeking for preterm babies and illnesses

Several factors influenced appropriate care-seeking for preterm babies as well as those with illnesses. These included a lack of knowledge about prematurity and perceived severity of illness, low decision-making ability and autonomy at the societal level, influence of family members and neighbours at the interpersonal level and several health systems factors such as unavailability of services and poor quality of care. These factors affected illness recognition, caused delays in decision-making regarding choice of care and uptake of appropriate services at the health facility. Adolescents were found to have low decision-making ability and often consulted family members before care-seeking.

Many mothers and family members frequently mentioned that preterm newborns were small, weak, and less mobile. In the absence of any visible signs of illnesses they considered that with appropriate feeding these babies would recover. As such, care was only sought when the babies presented with illnesses. A mother who was unable to understand the severity of the child's condition who was placed in an incubator mentions that initially they did not want to take her (now deceased) baby to a specialised hospital, despite being referred. In her words: *"My mom said baby was well, was moving and looking unlike her older grandchild. So, she did not want to take her to hospital" (IDI09 Adult mother of a preterm baby).*

Participants mentioned a range of health care providers for the treatment of their babies, including untrained traditional and spiritual healers, herbalists, homeopaths and village doctors. Participants claimed that they were often the first point of contact, and care was sought from qualified providers when the illness became severe or prolonged, as a father participating in a FGD highlights: *"If the baby cries a lot or has gas we go to kabiraj…For minor illnesses there is community clinic where services are free, people are poor here…then some also go to village doctors…if the baby does not recover we go to shishu hospital."* Mothers were also often found to use amulets and spiritual water to ward off evil spirits or if the child was too cranky. Adolescent mothers also had little decision-making authority – the decision to seek care was usually made by the husband, in-laws or parents, or in consultation with

them: *"I wanted to take my baby to the big hospital. But my in-laws did not approve. So, I went to the nearby doctor (village doctor) instead…"* (IDI08 Adolescent mother of a preterm baby).

Cost was another factor that was repeatedly mentioned by mothers and community members during the interviews. During the interviews, several participants highlighted that some preterm babies need specialised care or need to be kept in incubators (*glass-houses*) which were considered to be expensive. An adult mother of a preterm baby described two instances where one of them survived as the family was able to seek advanced and expensive care while the other was not: *"…see he was rich, do you understand…he took his child to Dhaka (the capital) and saved the baby by putting him inside the glass house (incubator)…whereas the other family used to live from hand-to-mouth…they waited for seven days and saw the baby was fine and stayed at home, but the baby died…"* (IDI31 Adult mother of a preterm baby). An adult mother mentioned that they were denied care at a health facility based on the assumption that they might not be able to afford the cost of the treatment whilst another adolescent mother waited for her in-laws to come and help because she had already spent a lot of money: *"The baby was very small and malnourished (pusto chilo na), but the doctor said if you take care well, she might survive. The doctor also told us to put the baby in a glass-house. However, we brought her home before we took her there. My in-laws were not at home, and we had already spent a lot of money at the hospital. So, we waited for them to come before admitting her in the glasshouse…"* (IDI07 Adolescent mother of a preterm baby).

At the health facility level, health care providers interviewed mentioned several challenges affecting service provision. For example, several service provider highlighted the lack of equipment and trained staff, as highlighted in the following excerpt: *"We are supposed to keep one baby in SCANU/warmer, sometimes I put in three babies…we have CPAP, but don't have the disposable equipment for it…we can't provide up to the mark service all the time…I also don't have enough trained staff…"* (KII01 - Trained service provider). Related to this was the unavailability of a KMC ward, particularly in public hospital settings which demotivated mothers to practice KMC in front of other patient and families: *"In the absence of dedicated KMC ward, mothers don't want to do KMC…"* (KII01-Trained service provider). In addition, another service provider highlighted the ineffectiveness of the referral system and pointed out the challenges of parents and families in arranging their own transport causing delays: *"If we cannot provide treatment, we refer…but the patient has to arrange the transport…we do not have a system…"* (KII02-Trained service provider).

Other challenges that service providers mentioned were related to availing services by the users and included late presentation or delay in care-seeking from the health facility, wanting to leave quickly from the health facility due to cost or other responsibilities and not coming back for regular follow-ups. These are highlighted in the excerpts below:

Late presentation. *"Preterm babies are brought to the hospital very late…we receive a lot of cases…"(KII03 Trained service provider).*

Early discharge. *"Patients here are poor, they want to leave early…they don't stay to see if weight of baby is steadily increasing or not…" (KII-04 Trained service provider).*

Lack of follow-up. *"Some patients come for follow-up others don't unless the baby is ill" (KII05 Trained service provider).*

On the other hand, mothers and family members who sought care at health facilities mentioned a lack of responsive and respectful care including poor communication, denial of care, verbal abuse, and non-consented care. Among these, verbal abuse was commonly mentioned. Two mothers reported that it was difficult to reach doctors and nurses who used to get angry if the patients' family enquired about them or asked them to come and check on their baby: *"We had to call the doctor to come…if you called them more than twice, they would get angry and scold us…" (IDI08 Adolescent mother of a preterm baby).* Other mothers reported being confused about the care given or not taking appropriate consent before initiating treatment. For example, an adult mother was not happy when her baby was kept in the same incubator with another child: *They put another baby in the same glass house (incubator) as mine… was that right? Different children have different illnesses, other beds (incubators) were empty" (IDI09 Adult mother of a preterm baby).* Similarly, a grandmother left the hospital with the baby when the service providers-initiated treatment without asking: *"The grandmother started arguing why the baby was given the medicine. She removed all the equipment, washed the baby's head, and left next morning…" (IDI09 Adult mother of a preterm baby).* Surprisingly, another mother of a preterm baby also mentioned how they were forced to move from one health facility to another, causing delays, based on the assumption that wouldn't be able to pay for the treatment as the excerpt below reveals:

"They (private hospital) said my baby is too small and the costs are too high here. We said we will pay, but they said they don't want to take the risk and asked us to take baby to the government hospital." (IDI33 Adult mother of a preterm baby).

Discussion

The findings from this study contribute to our understanding of newborn health and care of preterm babies among mothers including adolescents in rural Baliakandi from the perspectives of the parents themselves, as well as family and community members, and health care providers. The findings have been categorized into two major areas of exploration: (i) perceptions and understanding of PTB and (ii) care practices and care-seeking for preterm babies. In general, findings highlight poor understanding of PTB, with major gaps in care and care-seeking practices among all, including adolescents. We observed gaps and variations in understanding of preterm birth (length of gestation, appearance, causes, problems faced) and care practices (thermal management, feeding, weight monitoring) among all, but particularly among adolescents. Adolescents were found to be largely dependent on family members for these care

practices for their preterm babies. The use of multiple providers and delays in care-seeking from trained qualified providers for sick preterm babies was noted. Factors affecting appropriate care seeking included perception of severity of illness, cost, convenience, and quality of services. Health systems challenges included lack of equipment, supplies and trained staff in facilities to provide special care to preterm babies. These findings can enable public health practitioners and policy makers to design the health systems' response to PTB in a locally relevant way.

The findings revealed variations and gaps in knowledge among the participants about various pregnancy issues including normal pregnancy duration, and perceived causes and consequences of PTB. The perceptions regarding normal pregnancy duration varied between nine months and 10 months and 10 days. A baby born in the 7th or 8th month was considered preterm. This finding is similar to reports from Malawi, Ghana and Uganda, where gestational age at the community level was quantified in months with babies born before nine months being considered to be preterm [21–24, 27]. Accurately estimating the gestational age is crucial for facilitating care-seeking for PTB and the provision of life saving and time-sensitive interventions. The prevalence and preference for home births (51%) in Bangladesh is still high, and unless mothers are educated about PTB and the risks it poses, care-seeking and facility birth even for preterm labour will continue to be low [18, 28]. In addition, similar to other studies in Bangladesh, our findings also reveal a high acceptance and usage of ultrasonography (80% in 2017). However USG is mostly utilized in the latter trimesters when its accuracy for estimating the due date of delivery is less than in the first trimester even though it may still provide some information about fetal growth and wellbeing [18]. Therefore, educating mothers about the value of early pregnancy USG will improve the accuracy of gestational age estimation and consequently the diagnostic accuracy of premature labour and birth. This would ultimately lead to more prompt care-seeking for threatened preterm labour, leading to improved risk mitigation by interventions such as antenatal corticosteroid and magnesium sulphate therapy to reduce the risk of respiratory distress syndrome and neurological sequelae respectively.

Most of the mothers (adults and adolescents) in this study had limited knowledge of the causes of PTB. Those who demonstrated some awareness volunteered a mix of bio-medical and supernatural/spiritual explanations and practices for PTB. The commonly perceived causes e.g., heavy work/stress, inadequate nutrition/food intake, trauma to the abdomen etc., were in line with qualitative studies conducted in similar resource poor settings [22, 23, 29]. While this is encouraging, participants either failed to identify some potential associations with PTB or held beliefs that could deter appropriate antenatal or newborn health care-seeking. For example, contrary to the studies in Malawi, young maternal age was highlighted as a risk factor only by a few fathers in IDIs and FGDs [22, 24, 29]. Participants did not appreciate that previous history of miscarriage or PTB, and multiple pregnancy were risk factors for PTB, often attributing it to supernatural causes such as evils spirits or God's will [22, 24, 29]. This is consistent with the findings from previous studies in rural Bangladesh and

elsewhere, all of which deter women from antenatal care-seeking and encourage resort to spiritual treatments from religious leaders and faith-healers and traditional practitioners [25, 30–32]. The misperception of the mothers regarding PTB requires concerted efforts at culturally congruent education to improve care seeking in their future pregnancies. Indeed, Legare et al. (2012), highlights the pivotal role of understanding the extent to which traditional perinatal explanations and practises compete, conflict and coexist to provide unique insight into cultural ecologies of health, and asserts that this is critical to improving the efficacy of health education interventions and policies [33, 34]. In addition, the social capital associated with traditional medicine could also be capitalised to improve knowledge of the community regarding PTB and appropriate referral for high-risk preterm babies.

In general, breastfeeding improves neurodevelopmental outcomes and protects preterm babies from sepsis, necrotizing enterocolitis, and retinopathy of prematurity [35–38]. Breastfeeding was highly valued by the community in our study, primarily, as a means to improve the health of the weak and under-nourished preterm babies. Despite this, we also observed non-recommended practices such as prelacteal feeding, and non-exclusive breastfeeding. Several studies exploring care in newborn or low-birth-weight newborns in Bangladesh and similar settings also report that newborns or babies are primarily supplemented with either formula milk, cow or goats' milk or porridge (rice, sugar and water) when the mothers feel that they are not producing enough milk or are insufficiently lactating, whereas prelacteal feeds are usually introduced as a ritual practice, "to help keep baby's throat and stomach clear", or due to a delay in the flow of breastmilk [39–43]. Often, the suggestion of the formula feed is made upon consultation with formal or informal care providers [43]. Overall, in Bangladesh, 87% of women who experienced facility births were counselled on exclusive breastfeeding. This has resulted in a decrease in the proportion of children who are given prelacteal feed and an increase in non-exclusive breastfeeding [18]. Even so, about 29% of children under-2 years are given prelacteals and 35% of children 0–5 months are not exclusively breastfed, according to the 2017-18 BDHS report [18]. This highlights that further improvements can be made, especially among young mothers or mothers of preterm babies, for example by training neonatal nurses or health workers to provide home or facility-based evidence-informed breastfeeding support [44–46].

The community in Baliakandi did not recognize hypothermia to be a separate entity but were conscious that newborns, and specifically preterm babies, are at high risk of "catching cold" and indicated preventative practices such as bathing babies at noon with warm water, the use of emollients, and appropriate dressing of babies according to the external temperature [31, 42, 43, 47]. None of the participants, including those who gave birth in facilities, was aware of or had practiced KMC. The community still valued early bathing, but bathing was more likely to be delayed by three or more days for neonates born at health facilities or upon advice of health care providers. While these practices do not fully protect newborns from hypothermia, it is evident that the community in Baliakandi as well as those in Sylhet, Gopalgonj [31, 40, 42], placed a high value on keeping babies warm. Efforts to

implement and improve the implementation and adoption of appropriate thermal care and KMC for preterm babies can capitalize on this pre-existing awareness [31, 40, 42]. However, KMC has been scaled up in only 314 facilities in Bangladesh, with less than 5% of preterm newborns receiving KMC in 2021 [48]. Our findings highlight the need for further concerted effort to accelerate training and scale up of KMC in rural communities and facilities by addressing health systems challenges and demand-side barriers.

Although programming often targets interventions to preterm babies, the emergent themes in this study suggest that the local explanatory model of PTB does not always consider being preterm as a determinant or stimulus for health care-seeking. Instead, community members considered various observable characteristics and illnesses of the baby or newborn to first judge the overall health. According to the participant narratives, it was natural for preterm babies to be small and weak. In the absence of any visible illnesses or symptoms, many of these babies were considered to be healthy babies who would grow well if fed appropriately. As a result, many at-risk babies, especially late PTBs, in this community are overlooked or care-seeking delayed due to the inability of caregivers to identify risk factors, spot danger signs and assess severity. In agreement with studies in Uganda and Malawi babies were considered at high risk and more likely to receive care when they were very small, had fused eyelids, thin or wrinkled skin, or breathing problems etc. [21, 22, 24, 29]. Similarly, studies in Bangladesh and similar settings have associated recognition of symptoms of illness and danger signs with increased care-seeking for sick preterm children. This reiterates the need to educate caregivers on recognition of risk factors for mortality and morbidity [25, 49, 50].

A few prior studies in rural Bangladesh and other low-resource settings also highlighted perception of inevitability or fatalism in preterm or sick newborns as a deterrent for care seeking [51–53]. Although, participants in our study repeatedly mentioned that babies born as early as seven months may not survive, their views were not fatalistic but rather the overall opinion was to seek care from qualified/formal health care providers for such babies. Several participants also mentioned the use of incubators or challenges of having to spend a lot of money for formal care, indicating a shift in beliefs towards acknowledging that extremely preterm babies can also survive.

The local explanatory model for newborn illness in Baliakandi, as in other parts of Bangladesh, or other low-resource settings is largely influenced by a wider ecological framework including the management options available and other factors related to the local health system. In Baliakandi, participants reported several barriers to accessing formal health care - financial constraints, quality issues (lack of services, trained staff and equipment, inadequate referral system etc.) and disrespectful care. They demonstrated a preference for informal care by unqualified providers, consistent with prior studies that have highlighted that only a small proportion of families sought care from formal providers [25, 51, 54, 55]. Equally, there is ample evidence regarding the limited availability of good quality care at health facilities including in Bangladesh [21, 22, 56–58]. Care-seeking decisions regarding newborns and

children is often influenced by family members, relatives, neighbours and peers whose narratives often reinforce reports of mistreatment in facilities in contradistinction to positive views regarding traditional care [58, 59]. Improving access to and quality of preterm and newborn care at health facilities, delivered respectfully, is therefore an imperative to drive shifts in the care-seeking behaviour and subsequently the local explanatory model [58, 60].

Our study also revealed that most adolescents lived with their extended families and were highly dependent on their social network particularly natal and marital kins for support [32, 41]. Instrumental and informational support for care of their baby was provided primarily by their mother and mother-in-law, whereas financial support was provided by their husband and other family members. As such, decision making related to care and care-seeking for sick babies was never made in isolation but rather jointly taken with husbands and family members. In rural Bangladesh where adolescents lack knowledge and decision-making authority, health education on preventative practices and management practices of the preterm babies should, therefore, be provided at the family level involving women, their husbands, and the mother/mothers-in-laws [32, 41].

One of the strengths of this study is the inclusion of different methods and participants to triangulate the findings. We conducted IDIs, FGDs and KII with participants from different ages (adults and adolescents), birth status (preterm, term), genders, and relationship with the babies, allowing us to report similarities and differences in values and beliefs. Despite the benefits, summarising perspectives of multiple groups of participants and reporting their findings was challenging. In order to ensure that we do not over emphasise or marginalise any group and to refine our interpretations, we conducted a thematic analysis revisiting the data and summaries, and conducting regular discussions with the team involved in data collection and analysis to enhance the depth of the summary. Participants with preterm and term births were identified from the existing surveillance system and birth status (preterm, term) were also verified during interviews. However, data was collected retrospectively and may be subject to recall bias. To minimize recall bias, we included participants within 6 months of birth.

Conclusion

A combination of factors including local knowledge, socio-cultural practices and health systems challenges influenced awareness of, and care for, preterm babies among adolescent and adult mothers and the community. Strategies to improve birth outcomes will require increased awareness among adolescents, women and their families about PTB and improvement in the quality of, and access to, PTB services at health facilities – especially for adolescent mothers. In addition, intervention strategies to improve care of preterm babies should account for social, cultural, and economic reasons for current practices. Additionally, improved quality and competence of health facilities in managing care for preterm babies is likely to motivate appropriate care-seeking and improve chances of survival for those who do seek care.

Declarations

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Abbreviations

BDHS Bangladesh Demographic and Health Survey

FGD Focus group discussion

IDI In-depth interview

KII Key informant interview

LMIC Low- and middle-income country

PTB Preterm birth

USG Ultrasonography

Author contributions

AER, SSS, QN, SEA, DA, JB were responsible for conception, design of the study. AER, QN, SEA, DA and JB provided overall guidance to the study. SSS, SM, TM was responsible for overall implementation of the study including development of tools and data acquisition. SSS, SM, SI, TM, TST, RH, ATC were involved in data collection, coding and analysis. SSS developed the manuscript and incorporated the feedback from all the authors. SA, SJ were contributors in writing the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed for the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical clearance for the study was obtained from the Institutional Review Boards (Research Review Committee and Ethics Review Committee) at icddr,b (PR-19024) and The University of Sheffield (alternative ethics application 000275). Written informed consent was obtained from study participants above 18 years of age. For participants less than 18 years of age, assent from them and informed consent from their legal guardian was obtained. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Annex 12 Ethics approval for the community based research in Bangladesh (Signature redacted)

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icddr,b

Memorandum

22 May 2019

To: D. Quamrun Nahar
        Principal Investigator of research protocol # PR-19024
        Health Systems and Population Studies Division (HSPSD)

From: Professor Saria Tasnim ███████████
        Chairman
        Ethical Review Committee (ERC)

Sub: Approval of research protocol # PR-19024

        Approval Date: 22 May 2019
        Expiration Date: 21 May 2020
        Review Type: Full Committee Review
        Risk Level: No more than minimal
        Project type: New Project

Thank you for your memo dated 16 May 2019 attaching the modified version of your research protocol # PR-19024 entitled "Experiences of caring for premature infants at home: an in-depth study among adolescent mothers in rural Bangladesh" addressing the issues raised by the committee in its March 2019 ERC meeting held on 28 March 2019 at the Research Administration Meeting Room, 3rd floor of the icddr,b Main Building, to the satisfaction of the Committee. I am pleased to inform you that your protocol is **approved**. You will be required to observe the following terms and conditions in implementing the research protocol:

1. The research protocol is approved for 12-month period from the date of approval of the protocol by the Ethical Review Committee. The Federal regulations require review of an approved study not less than once per 12-month period. To comply with federal regulations, a continuing review application must be submitted to the IRB Secretariat for this study to continue beyond 21 May 2020.

    All necessary materials for continuing review must be reviewed with sufficient time for review and issuing continued approval before the expiration date. Failure to initiate a continuing review application in a timely fashion may result in discontinuation of study activities until approval can be renewed. Performing study activities, including data analysis, beyond the expiration date results in noncompliance of federal regulations.

2. The ERC approval shall automatically be revoked after one year if the protocol is not started. After one year, you shall have to seek approval for revalidation of the protocol by the ERC before starting.

3. You should notify the IRB Secretariat of the start date of the protocol for updating in the integrated Navision system. The protocol start date will not

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be updated in the Navision system until receiving information from you. Therefore you will not be able to operate budget code and continue spending funds under the research protocol.

4. As Principal Investigator, the ultimate responsibility for scientific and ethical conduct including the protection of the rights and welfare of study participants vest upon you. You shall also be responsible for ensuring competence, integrity and ethical conduct of other investigators and staff directly involved in this research protocol.

5. You shall conduct the study in accordance with the ERC-approved protocol and shall fully comply with any subsequent determinations by the ERC.

6. You shall obtain prior approval from the Research Review Committee and the ERC for any modification in the approved research protocol and/or approved consent form(s), except in case of emergency to safeguard/ eliminate apparent immediate hazards to study participants. Such changes must immediately be reported to the ERC Chairman.

7. You shall recruit/enrol participants for this study strictly adhering to the criteria mentioned in the research protocol.

8. You shall obtain legally effective informed consent (i.e. consent should be free from coercion or undue influence) from the selected study participants or their legally responsible representative, as approved in the protocol, using the approved consent form prior to their enrolment in this study. Before obtaining consent, all prospective study participants must be adequately informed about the purpose(s) of the study, its methods and procedures, and also what would be done if they agree and also if they do not agree to participate in the study.

9. They must be informed that their participation in the study is voluntary and that they can withdraw their participation any time without any prejudice. Signed consent forms should be preserved for a period of at least five years following official termination of the study.

10. You shall promptly report the occurrence of any Serious Adverse Event or unanticipated problems of potential risk to study participants or others to the ERC in writing within 24 hours of such occurrences.

11. Any significant new findings, developing during the course of this study that might affect the risks and benefits and thus influence either participation in the study or continuation of participation should be reported in writing to the participants and the ERC.

12. You shall report progress of research to the ERC for continuing review of the implementation of the research protocol as stipulated in the ERC Guidelines. Relevant excerpt of ERC Guidelines and 'Annual/Completion Report for Research Protocol involving Human Subjects' are attached for your information and guidance.

13. Data and/or samples should be collected and interviews should be conducted, as specified in the ERC-approved protocol, and confidentiality must be maintained. Data/samples must be protected by reasonable security, safeguarding against risks such as their loss or unauthorized

access, destructions, used by others, and modification or disclosure of data. Data/samples should not be disclosed, made available to or use for purposes other than those specified in the protocol, and shall be preserved for a period, as specified under Centre's policies/practices.

14. You shall promptly and fully comply with the decision of the ERC to suspend or withdraw its approval for the research protocol.

15. The ERC should be immediately notified if the protocol is discontinued before the expected date of completion.

Approved documents:

a. Protocol version no 3.0 dated 16 May 2019

b. English and Bangla Informed written consent; version no 3.0 dated 16 May 2019

c. English and Bangla Guides for IDI and FGD; version no 3.0 dated 16 May 2019

The IRB of icddr,b shall take into account the regulations of the Bangladesh Medical Research Council (BMRC), WHO, international guidelines for biomedical research as laid down by the Council of International Organization of Medical Sciences (CIOMS), the Declaration of Helsinki in relation to biomedical research involving human participants, ICH Guidelines on Good Clinical Practice (GCP), National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), and Division of Microbiology and Infectious Diseases (DMID). If there is any new declaration involving human participants, contents of such declaration should be appropriately adhered to and the applicable laws and policies of the local government.

I wish you success in running the above-mentioned study.

Cc: Senior Manager, Budget & Planning, Finance

Annex 13 In-depth interview and FGD guides for the community based study in Bangladesh

PLEASE NOTE: *These are guidelines to shape the conversations. The questions will not necessarily be asked directly, but the respondent will be invited to tell of their experiences, guided by these topics. The interviewer will use their discretion to decide the order and level of detail in which to cover each topic with each informant.*

<u>**A. In-depth interview: Mothers (15-19 years and >19 years) with preterm baby**</u>

1. General situation

The interviewer will inquire about:

- Respondent: age, education level, occupation, age of baby and other children, source of income

- Husband: age, education level, occupation, income

- Household: Other members of household (with relationship) and occupation, condition of household (water, sanitation, electricity, telephone).

2. Social support

- Who do you live with and who do you spend time with?

- Do your family members help out? How do your family members help out? (i.e., domestic chores, cooking etc.)

- Are you also working or studying? Please describe.

- Please tell us who else helps to look after your baby and how? (partner/family member etc.) Are you the main person, or do you have a partner/parents who share the responsibility?

- Please describe if you have any worries or difficulties?

- How do you manage to cover your costs and those of your baby?

3. Pregnancy to birth narrative

- I am interested in hearing about your pregnancy. How did you feel when you realised you were pregnant? Who did you talk to?

- Was this something you had thought about or planned? If unplanned, describe what family planning measures were you taking? if no family planning measures, why not?

- Did you have antenatal check-ups (ANC)? Describe in details all your ANCs. What was that like?

- Did you have any complications during your pregnancy, that you were aware of? If yes, describe in details what complications and what you did for the complications? (Ask details of complication and care-seeking)

- Did you have any particular worries or difficulties during your pregnancy? If yes, describe what kind of worries. Please tell us what you did about those worries or difficulties and if you shared with and how did they help.

- I am interested in hearing about the birth of your baby. How did it start? (Interviewer will ask for the birth story).

- Tell us in details about your delivery (Probe: Where did you deliver? Who was with you? Who delivered your baby?)

- Did you deliver at term or early?

- How did you feel about yourself and your baby -health-wise?

- Did you have any particular worries or difficulties during the delivery? Tell us in details what worried you?

4. Being a mother/ feelings about maternity

- Did you feel you knew how to look after your baby?

- Does anybody help you in taking care of baby? Who helps you? Did /do you have any worries about your health or your baby's health? Who did you go to for advice or treatment? What did your family members do or say? (partner, mother etc).

- Describe what happened in your postnatal period and any post-natal checkups? (and why or why not)?

- What has been the best thing about having a baby? How do you feel? Do you feel you have changed in some ways?

- Do your other friends and family members also have babies now?

- What types of difficulties do your other friends and family members have?

- How did you spend your time before the arrival of your newborn? How has this changed?

- Has your relationship with your partner/family members/friends changed somehow? If yes, how?

- Do you think the role of the father and the mother is different, and how?

- Did your child suffer from any problems or illness? If yes, what happened? (obtain details of all illnesses). Did you seek care? Where and who provided care? What services/treatment did you

receive? Were you happy with the services? Did you receive any help/support when your child was ill? From who and what kind of help? How did you feel during that time?

- Do you know where you can obtain services if your baby is ill? Please tell us what you know. How did you learn about the places/providers? Do anybody you know visits the providers/places? Are you satisfied with the services? How can services for babies be improved?

5. Perceptions surrounding small/preterm babies

- Did you think your baby was smaller than average or was preterm? If yes, how small/preterm did you think your baby was?

- Did anybody tell you your baby was smaller than average/preterm? How did they explain it?

- Why do you think (what are the reasons according to you) that your baby is smaller than average or preterm? Do you think you could have taken any measures to prevent your baby from being small/preterm? If yes, tell us what kind of measures could be taken.

- Did you face any problems because your baby was small/preterm? Describe all problems and what you did?

- Did/do you have to return to the hospital or clinic for extra visits because your baby is small/preterm? Or receive home visits from community health workers? Are there any difficulties for you or your baby, related to being small/preterm ?if yes, describe what difficulties. Did you get any extra help from anyone, because of this? If yes, what kind of help, describe.

- Did/does your baby require different care because he/she is small/preterm? Did you take any special measures to care for your small baby/preterm? describe the special care that your baby received?

- Did you provide Kangaroo Mother Care (explain KMC)? Please describe the KMC process. How did you provide KMC? Who told you/taught you to provide KMC? How long did you provide KMC? Did you face any challenges? What challenges? Did anybody help you with KMC? If yes, who?

- Do you know where you can obtain services for your small/preterm baby? Describe where you can obtain services and what kind of services. How did you know about the places/providers? Do anybody you know visits the providers/places? Are you satisfied with the services? How can services for babies be improved?

- Did/does anybody help you in taking care of your small/preterm baby when s/he was born? Please tell us who helped and how they helped you?

- Did you have to do household chores/work? Describe your routine and how involved are/were you with household chores?

6. *Previous pregnancies*

- How was this experience different from that of your other children? What happened during that pregnancy/birth? Did you feel that you and your baby were fine, health-wise? How have you managed to keep your children healthy (as babies, and as larger children)? Is caring for your small/preterm baby different from how you remember your previous children, in what way?

7. *Seeking health advice and services on family planning and sexual health*

- Before pregnancy or birth, did you ever visit any health facility? For what reason? Did you find it helpful? Did you receive any help or advice on contraception, or sexual health from the health facility? Which other people or places have helped you with sexual health or contraception advice?

- Do you know if your friends or family members have ever visited the health facility? For which type of services? What did they tell you about their experiences? Where do other people go to get contraceptive advice, or care during pregnancy? What was your experience like with the different people who work there?

- What is your plan for future children? Do you think you need to wait before you conceive again? How long and why? Are you using and family planning methods now? Why and why not? What methods are you using? Are there any challenges?

B. In-depth interview: Mothers (15-19 years) with term baby

1. General situation

The interviewer will inquire about:

- Respondent: age, education level, occupation, age of baby and other children, source of income

- Husband: age, education level, occupation, income

- Household: Other members of household (with relationship) and occupation, condition of household (water, sanitation, electricity, telephone).

2. Social support

- Who do you live with and who do you spend time with?

- Do your family members help out? How do your family members help out? (i.e., domestic chores, cooking etc.)

- Are you also working or studying? Please describe.

- Please tell us who else helps to look after your baby and how? (partner/family member etc.) Are you the main person, or do you have a partner/parents who share the responsibility?

- Please describe if you have any worries or difficulties?

- How do you manage to cover your costs and those of your baby?

3. Pregnancy to birth narrative

- I am interested in hearing about your pregnancy. How did you feel when you realised you were pregnant? Who did you talk to?

- Was this something you had thought about or planned? If unplanned, describe what family planning measures were you taking? if no family planning measures, why not?

- Did you have antenatal check-ups (ANC)? Describe in details all your ANCs. What was that like?

- Did you have any complications during your pregnancy, that you were aware of? If yes, describe in details what complications and what you did for the complications? (Ask details of complication and care-seeking)

- Did you have any particular worries or difficulties during your pregnancy? If yes, describe what kind of worries. Please tell us what you did about those worries or difficulties and if you shared with and how did they help.

- I am interested in hearing about the birth of your baby. How did it start? (Interviewer will ask for the birth story).

- Tell us in details about your delivery (Where did you deliver? Who was with you? Who delivered your baby? etc)

- Did you deliver at term or early?

- How did you feel about yourself and your baby -health-wise?

- Did you have any particular worries or difficulties during the delivery? Tell us in details what worried you?

4. Being a mother/ feelings about maternity

- Did you feel you knew how to look after your baby?

- Does anybody help you in taking care of baby? Who helps you? Did /do you have any worries about your health or your baby's health? Who did you go to for advice or treatment? What did your family members do or say? (partner, mother etc).

- Describe what happened in your postnatal period and any post-natal checkups? (and why or why not)?

- What has been the best thing about having a baby? How do you feel? Do you feel you have changed in some ways?

- Do your other friends and family members also have babies now?

- What types of difficulties do your other friends and family members have?

- How did you spend your time before the arrival of your newborn? How has this changed?

- Has your relationship with your partner/family members/friends changed somehow?

- Do you think the role of the father and the mother is different, and how?

- Did your child suffer from any problems or illness? If yes, what happened? (obtain details of all illnesses). Did you seek care? Where and who provided care? What services/treatment did you receive? Were you happy with the services? Did you receive any help/support when your child was ill? From who and what kind of help? How did you feel during that time?

- Do you know where you can obtain services if your baby is ill? Please tell us what you know. Where and from whom? Where did you learn about the places/providers? Do anybody you know visits the providers/places? Are you satisfied with the services? How can services for babies be improved?

5. Perceptions surrounding small babies

- Do you know anything about babies who are born before term or are smaller than average? If yes, what do you know? From where have you heard?

- What kind of care does these babies need? Have you heard about Kangaroo Mother Care (explain KMC)? if yes, what do you know?

- Do you know where you can obtain services for your small or preterm baby? Where and from whom? Where did you learn about the places/providers? Do anybody you know visits the providers/places?

6. Seeking health advice and services on family planning and sexual health

- Before pregnancy or birth, did you ever visit any health facility? For what reason? Did you find it helpful? Did you receive any help or advice on contraception, or sexual health from the health facility? Which other people or places have helped you with sexual health or contraception advice?

- Do you know if your friends or family members have ever visited the health facility? For which type of services? What did they tell you about their experiences? Where do other people go to get contraceptive advice, or care during pregnancy? What was your experience like with the different people who work there?

- What is your plan for future children? Do you think you need to wait before you conceive again? How long and why? Are you using and family planning methods now? Why and why not? What methods are you using?

C. Key informant interview guide: Healthcare staff

1. Situation of healthcare staff

The interviewer will inquire about the healthcare worker's own household, where he/she lives, how he/she came to choose this career, experience in medical training, his/her own challenges, dreams, plans. His/her own experience as a parent, if relevant.

2. Barriers and challenges in offering care

- How does your working day start? What are your main activities? Responsibilities?

- Who do you work with? What are the best things about this job? What are the challenges? For example, what happened yesterday? What went well, and what were the difficulties?

- How is this job different from what you expected?

- What would you recommend so that you could do your job more easily? How has your working situation changed over the years?

3. Relationship with and situation of patients

- Which type of patients usually come? For which reasons? How would you describe your patients?

- Do adolescent mothers face specific challenges? Mothers with small/PTB/LBW babies? Interviewers will ask the staff to detail all the procedures from family planning, to antenatal care, birth, and post-natal care, and explain the challenges.

- Which particularly difficult, sensitive, frustrating cases can you remember, in antenatal, birth or post-natal care, with adolescent mothers? Or with mothers with small/at-risk/preterm birth/low birth weight babies?

- What services do you provide for PTB/small babies? What challenges do you face in caring for PTB/small babies?

- How would you describe your relationship with the different women and/or mothers who come to the health facility? Which patients do you find most difficult to help? Which part is the most rewarding?

- What are the main problems that you think face girls and women, health-wise, or in general, in this community? Are there girls or women in the community who do not visit the health facility (for family planning, antenatal, post-natal, or infant care), and why not?

D. In-depth interview: Family member (parents, in-laws, husband)

These are similar questions as asked to the adolescent mothers, but modified to collect the parent or guardian's opinion. They are aimed at the adolescent respondents' mother but with small adjustments can be used to interview fathers of adolescent girls and husbands as well.

1. General situation

The interviewer will inquire about:

- Respondent: age, education level, occupation, number of children, source of income

- Household: Other members of household (with relationship) and occupation, condition of household (water, sanitation, electricity, telephone).

2. Social support

- Who does your daughter live with and spend time with? How do family members help out? (ie domestic chores, cooking etc.)

- Is your daughter working or studying? Please describe.

- How does she manage to cover the costs of her baby?

- Please tell us who else helps to look after her baby and how? (partner/family member etc.) Who do you feel takes on the main responsibility?

- As a grandparent, and a parent, do you have any worries or difficulties? What does your husband think and how has he reacted?

3. Pregnancy to birth narrative

- I am interested in hearing about your daughters pregnancy. How did you feel when you realised she was pregnant?

- Did she have antenatal check-ups (ANC)? Describe in details.

- Did she have any complications during the pregnancy, that you were aware of? If yes, describe in details what complications and what you did for the complications? (Ask details of complication and care-seeking)

- Did you have any particular worries or difficulties during her pregnancy? If yes, describe what kind of worries. Please tell us what you did about those worries or difficulties and if you shared with and how did they help.

- I am interested in hearing about the birth of your grandchild. How did it start? (Interviewer will ask for the birth story). Tell us in details about the delivery. (Where did you deliver? Who was with you? Who delivered your baby? etc)

- Did your daughter deliver at term or early?

- How did you feel about her and her child -health-wise?

- Did you have any particular worries or difficulties during the delivery? Tell us in details what worried you and what you did?

4. Feelings about your daugther's maternity

- How do you think your daughter felt when she became pregnant? How did you feel?

- How do you feel about your daughter being a mother now?

- How would you say she is coping? And the rest of the family?

- How is her partner involved? How do you see that relationship has changed? Why do you think this situation happened?

- Does she have other friends who also have babies?

- Did her newborn suffer from any problems/illnesses that you are aware of? Describe in details what happened and care-seeking mechanisms.

5. Perceptions surrounding small/preterm babies

- Do you think your grandchild was preterm or smaller than average? If yes, how small/preterm did you think your baby was?

- Did anybody tell you your grandchild was smaller than average/preterm? How did they explain it?

- Why do you think (what are the reasons according to you) that the baby is smaller than average or preterm? Do you think you could have taken any measures to prevent the baby from being small/preterm? If yes, tell us what kind of measures could be taken.

- What problems did the baby or your daughter face because the child was preterm? Describe in details. Did your daughter get any extra help from anyone, because of this? If yes, what kind of help, describe.

- Did/does your grandchild require different care because he/she is small/preterm? Describe any special care that your grandchildreceived?

- Did your grandchild need Kangaroo Mother Care (explain KMC)? Please describe what happened.

- Do you know where you can obtain services or seek care for small/preterm babies? Describe where you can obtain services and what kind of services. How did you know about the places/providers? Do anybody you know visits the providers/places? Are you satisfied with the services? How can services for babies be improved?

6. Seeking health advice and services on family planning and sexual health

- Before pregnancy or birth, had your daughter ever visited the health facility? What is your own experience of the health facility? Do you know if she received any help or advice on contraception, or sexual health, from the clinic? Do you think she found it helpful? Why or why not? How could it be improved so that girls can make use of it?

- Have you yourself made use of those services, and what was your experience? Which other people or places in the community help with sexual health or contraception advice? Or with other health questions? Where do you usually go if you or your children need health advice or treatment? (Ask about any cases within the last year, and how resolved).

E. FGD guide: community/Family members

FGD guiding questions:

- What services should a women receive if she is pregnant? (Probe: ANCs: from whom, where, how many times; medications)
- What is the proper period for delivering a baby? *(Probe: how many months, weeks)*
- Where is it safe to deliver a baby? *(Probe: home or health facility)*
- Did you see/ever hear about any baby who was delivered before time?
- (If 2 is yes) Can you please describe what actually happened with that baby? *(Probe: alive/died, treatment/ care seeking behaviour, who provided care)*
- What are the reasons babies are born preterm? (probe: anything else)
- What cares should a baby receive if s/he is born preterm?
- What problems do babies have if they are born preterm?
- Where can you obtain health services for babies? (probe for all available services)
- Can you obtain services for preterm babies at the same places? Where can you obtain health services for preterm babies?
- What challenges are there for parents/families/communities whose babies are born preterm?
- What is the usual age of marriage and first birth for girls in your community?
- What do you think should be the appropriate age of child-bearing for a women?

- What kind of problems/challenges can a young girl face if she gives birth? (Probe: before, during and after birth?)
- Do you think young girls deliver before term? what problems/challenges may young girls with preterm babies face?
- Where can you obtain family planning and sexual health services in your community?
- What do you think the appropriate gap should be between two children?