MRC-NIHR Overview of Global Maternal and Neonatal Health Research Priorities
In 2015 the UK Government allocated Official Development Assistance (ODA) budget to, among others, the Department for Business, Energy and Industrial Strategy and the Department of Health and Social Care.

As part of this allocation the departments support global health research addressing the challenges faced by low and middle income countries (LMICs) through the Global Challenge Research Fund (GCRF) and the National Institute for Health Research (NIHR) Global Health Research Programme. The Medical Research Council (MRC) is a GCRF delivery partner for ODA funding.
1 Purpose and scope
This document sets out an overview of research priorities to improve maternal and neonatal health in LMICs. The document aims to:

i. Highlight global research themes in maternal and neonatal health (MNH);
ii. Promote a holistic approach that considers the health of mother and baby both together and as individuals;
iii. Present a cohesive overview that:
   - Incorporates clinical, molecular, social, applied and epidemiological disciplines in accordance with the range and complexity of problems affecting mothers and babies in LMICs.
   - Promotes research that leads to improved interventional strategies and faster transition from bench to bedside and
   - Accounts for wide-ranging influences on the health of mother and baby before, during, and after pregnancy.

This overview of research priorities will inform the remit of future funding calls for ODA eligible research proposals for the MRC and NIHR Global Health Research Programme in the area of MNH. The document has been the subject of consultation with external expert stakeholders in the UK and internationally. This consultation has highlighted specific research gaps that need to be addressed and general objectives for the long-term improvement of global MNH outcomes.

2 Introduction
Every year, worldwide, 2.7 million babies die during the first 28 days of life (neonatal death) and 2.6 million babies are stillborn. 98% of this combined total occurs in LMICs, along with 99% of maternal deaths. Neonatal preterm birth complications are now the leading cause of death in children under five.

There has been global progress in reducing child and maternal mortality over the past 25 years. However, this progress has neither been at the level required to meet global targets nor has it been uniform across health outcomes: for instance, the number of stillbirths has reduced more slowly than maternal mortality or mortality in children under five. Even those outcomes that have shown marked reductions still occur at unacceptably high levels: despite the 44% decrease in maternal deaths between 1990-2015, to meet the Sustainable Development Goal (SDG) 3 target of 70 deaths per 100,000 in 2030, a 68% reduction in maternal mortality rates is needed. For comparison, the current maternal mortality ratio in developed countries is 12 per 100,000. Importantly, despite overall reductions in childhood mortality, the burden has shifted earlier in life and is now concentrated around high-risk pregnancy, the perinatal period and the first months of life.

4. Osrin, D, Frost, A. Perinatal interventions and survival in resource-poor settings: which work, which don’t, which have the jury out? Arch Dis Child. 2010, 95: 1039-1046.
There remains a major need to improve neonatal and maternal mortality outcomes, but also a need to address morbidity, to have a transformative effect on health throughout the life-course. Despite some gains, poor pregnancy outcomes remain a major global issue, and a major global inequality.

This document attempts to break down the broad spectrum of MNH to inform future funding calls. Provisionally, this delineation distinguishes:

- Research focused on pre-conception health and contraception;
- Research addressing problems during pregnancy, the birth process, immediate post-partum care, and care for mother and child during the first month of the newborn’s life;
- Research with a longer-term postpartum focus, including the reduction of morbidity in mother and child (with an acknowledgement that postpartum health outcomes are strongly linked to pre-conception health prior to subsequent pregnancy).

This separation enables particular MNH time periods to be highlighted in funding calls whilst acknowledging that there will be inevitable areas of overlap between them, and cross-cutting themes relevant to all areas (see Figures 1 and 2). We encourage exploration of the entire research pathway within each area linking basic research to epidemiology to clinical research and health systems integration. This is depicted in Figure 1. This depth of exploration is best achieved by interdisciplinary and multi-funder collaboration promoting the consideration of medical, social, cultural, environmental, and engineering perspectives. Over time, collaborative funding will build up a network of programmes that spans the spectrum of reproductive health and wider influences on MNH.

**Figure 1.** Pathway delineating research areas across the reproductive lifespan from pre-conception to post-partum health. **Examples** of specific topics within each time-period are provided ranging from mechanistic science to health systems research – the list is illustrative but not exhaustive, and topics not included but clearly relevant to improving MNH outcomes will be considered. Cross-cutting themes that input to all areas are discussed in section 3.1. Cross-cutting themes relevant to two time-periods span the dashed line separating the time periods. The looping arrow represents issues important in the postpartum period that influence pre-conception health for subsequent pregnancies. Abbreviations: HCW: Healthcare worker; IUGR: Intra-uterine growth restriction; MSP: miscarriage, stillbirth, prematurity; NCDs: Non-Communicable Diseases.
3 Outlook
The goal of this document is to provide an overview of global MNH research priorities to improve global knowledge of the scale, cause, prevention, prediction, detection, and treatment of MNH problems. We emphasise that such a wide-ranging challenge can only be met through interdisciplinary engagement and via a range of research methods promoting both innovation and better implementation of existing interventions.

3.1 Cross-Cutting Research Themes
In addition to the MNH sub-topics outlined below, there are cross-cutting research themes that feed into all areas, as depicted in figure 2.

![Cross-cutting research themes diagram](image)

**Figure 2.** Cross-cutting research themes that are relevant to pre-conception, during pregnancy and birth, and postpartum.

3.2 Pre-conception
Research into factors affecting maternal and neonatal health outcomes prior to conception are included in this sub-area in addition to research surrounding contraception. There are also issues listed in section 3.3 that apply to a lesser extent here, such as prophylactic intervention prior to conception and the development of biomarkers that predict risks during pregnancy prior to conception. The following topics are research priorities and consideration should also be given to the cross-cutting themes in section 3.1, particularly sociocultural factors, maternal multimorbidity, and humanitarian settings:

- **Contraception:** e.g., drug-drug interactions, acceptability of contraceptive methods, provision of accurate information, implementation of and access to known interventions, including access to emergency contraception and school-based interventions, etc.
- **Use of targeted intervention to improve pre-conception health:** e.g. promoting and improving access to healthy lifestyle choices, improved health literacy, and better nutrition.
- **Sociocultural research around women’s reproductive rights:** e.g. the barriers preventing women and girls from having control of their reproductive health and timing of pregnancies and how these barriers can be overcome.


3.3 Pregnancy and Birth

Research into miscarriage (loss of a foetus up to 23 weeks of pregnancy), stillbirth (a baby born with no signs of life at, or after, 28 weeks’ gestation), neonatal death (death of a baby within 28 days of life), and maternal mortality, (the death of a woman during pregnancy, childbirth, and the puerperium) as defined by the World Health Organisation (see footnote5), fits within the scope of this sub-area. Keeping in mind potential interplay with the cross-cutting themes highlighted above, the following areas are research priorities:

- Better understanding of cellular and molecular mechanisms operating during placental formation.
- Underlying aetiology of factors contributing to adverse foetal, neonatal, and maternal outcomes.
- Innovative, cost-effective, efficient detection techniques that can be used both within and outside of healthcare settings to facilitate early diagnosis and management of maternal and neonatal conditions.
- Identification of biomarkers and risk factors that allow prediction of complications that may occur during pregnancy and delivery.
- Interventions for the prevention of adverse birth outcomes based on known risk factors and predictive markers including reducing the rate of pre-term birth, a major risk factor for stillbirth and neonatal death.
- Detection, treatment and management of obstetric complications.
- Epidemiology and impact of maternal NCDs on miscarriage, stillbirth and neonatal death.
- Epidemiology, diagnosis, and treatment of comorbid infection.
- Implementation of best practice and existing interventions in LMIC healthcare settings to reduce preventable causes of death.
- Safe abortion including the prevention of unsafe abortion.
- Digital technology solutions for effective dissemination of information on reducing pregnancy risks.
- Big data collection including mechanisms for standardised collection of MNH outcomes.
- Healthcare worker experience of challenges faced by low-resource health systems in implementing quality MNH care and the feasibility of implementing proposed interventions in both health facilities and the community.

3.4 Postpartum

Research to understand and reduce the burden of maternal and neonatal morbidity after birth is urgently needed.

Neonatal morbidity encompasses the lasting disability or impairment of the infant due to factors occurring during pregnancy, birth and the neonatal period. As such, this ranges from maternal malnutrition during pregnancy, through intrapartum related encephalopathy, and infections in the neonatal period.

Maternal morbidity refers to any physical or mental illness or disability directly related to pregnancy and/or childbirth. Morbidities are not necessarily life-threatening but can have a significant impact on

5. Note that there is a ‘grey zone’ of four weeks between WHO definitions of miscarriage which ends at 23 weeks and stillbirth which starts at 28 weeks. For details on the ‘grey zone’ and its importance for measuring the scale of burden see McGready et al. Miscarriage, stillbirth and neonatal mortality in the extreme preterm birth window of gestation in a limited-resource setting on the Thailand-Myanmar border: a population cohort study. Wellcome Open Research 2016, 1:32.
quality of life and future reproductive health (hence the looping arrow in figure 1). Here, the focus is on chronic postpartum morbidities – the long-term physical or mental health consequences resulting from pregnancy, childbirth, and acute maternal morbidities – with acute morbidities themselves (i.e. obstetric complications such as sepsis or eclampsia) covered in 3.3 Pregnancy and Birth. Indirect effects of maternal morbidity, such as unemployment, the health of her other children, and the social and economic standing of her family are outside the scope of the current document.

This document acknowledges the value of sustainable cohorts to follow mother-newborn pairs from pre-conception to term and beyond. Projects including cohorts should commence prior to the end of the postpartum period (i.e. within six months of birth) with work after this point falling under the remit of potential future programmes on early child development. Cohort studies will allow the follow-up of mother and baby during pregnancy, ongoing morbidity beyond the immediate postpartum period, and the impact of intervention provided before and during pregnancy on MNH outcomes.

Again, bearing in mind the cross-cutting themes outlined in section 3.1 (particularly sociocultural factors, maternal multimorbidity, maternal experience, and mother-child transmission), the following areas are research priorities:

- **Post-abortion care**
- **Management and treatment of neonatal morbidity** to minimise the impact on the quality of life of the child and ensure that the predisposition to stunting and poor health outcomes is not realised.
- **Management and treatment of chronic maternal morbidity** caused by the birthing process (e.g. fistula, uterine prolapse, post-traumatic stress disorder, dyspareunia).
- **Implementation of high-quality maternal and neonatal care in community settings.**
- **Perinatal mental health** of mother and father.
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