Integrating immediate Kangaroo Mother Care into district hospitals with a level 2 neonatal intensive care unit:

Implementation Research Protocol

Version 3.0

9 January 2023

Protocol version

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Abbreviations

AIC: Akaike information criteria
CHWs: community health workers
CI: Confidence intervals
CONSORT: Consolidated Standards of Reporting Trials
COVID-19: coronavirus disease 2019
CPAP: continuous positive airway pressure
CRFs: case report forms
DSMB: data safety monitoring board
ENAP: Every Newborn Action Plan
iKMC: immediate kangaroo mother care
IQR: interquartile range
IRB: institutional review board
KMC: kangaroo mother care
LBW: low-birth-weight
MNH: maternal and newborn health
M-SNCU: mother-special newborn care unit
NICU: neonatal intensive care unit
NMR: neonatal mortality rate
OBGYN: Obstetrics and Gynaecology
OPD: outpatient department
RCT: randomized controlled trial
RR: relative risk
SNCU: special newborn care unit
SoP: standard operating procedure
STAGE- MNCAH&N: Strategic and Technical Advisory Group for maternal, newborn, child and adolescent health and nutrition
StaRI: Standards for Reporting Implementation Studies

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1. Background

1.1 The global burden of low-birth-weight and preterm birth

Annually about 20 million babies are born with low-birth-weight (LBW)[1] as a result of being born as small for gestational age or preterm. About 32 million are born small for gestational age and 15 million are born preterm.[2] These preterm or LBW infants are vulnerable to an increased risk of death and development challenges. These vulnerable newborns not only account for 80% of all neonatal deaths but also are at increased risk of short- and long-term respiratory, infectious, metabolic and neurological morbidities, with higher risks of adverse outcomes seen at lower gestational ages.[3,4]

Approximately 79% of neonatal deaths occur in sub-Saharan African and Asian countries and an equal proportion of the world's preterm births occur in these two regions.[5] Preterm birth is the leading cause of death in children under five years of age globally, accounting for approximately 16% of all under-5 child deaths, and 35% of deaths among newborns.[6] Preterm birth and its sequelae can have negative psychosocial and financial impacts on their families.[7–9] Rates of preterm birth are rising globally as are inequities in survival and morbidity. In low-income settings, half of the babies born at or below 32 weeks die due to a lack of feasible, cost-effective care, whereas most of these same babies survive in high-income countries. [10,11]

1.2 Efficacy of Kangaroo mother care (KMC)

KMC is defined as early, prolonged, and continuous skin-to-skin contact between a mother and her preterm or LBW newborn, and exclusive breastfeeding or breastmilk feeding.[12,13] In 2016 a Cochrane review reported on 21 randomized controlled trials (3042 infants) that compared KMC with conventional neonatal care in health facilities and showed that KMC reduced mortality by 40% (RR 0.60, 95% CI 0.39 to 0.92), nosocomial infections by 65% (RR 0.45, 95% CI 0.27 to 0.76) and hypothermia by 64% (RR 0.34, 95% CI 0.17 to 0.67).[12] It was also reported that KMC increased weight, length, and head circumference, breastfeeding, mother satisfaction with the method of infant care and maternal-infant attachment, and improved early child development.

1.3 Time of initiation of KMC

In almost all studies included in the Cochrane review, KMC was initiated after the baby was clinically stable. The median age at initiation of KMC ranged from 3.2 to 24.5 days for most studies (Table 1). Only in one study, KMC was initiated relatively early, at a mean age of 10 hours.[14] Until recently, WHO's recommendation was to initiate continuous KMC after the baby is clinically stable. However, half to two-thirds of deaths among preterm/LBW babies would have occurred by the time these infants became stable enough to be provided KMC.[15]

Table 1. Studies included in the Cochrane review

Studies reporting impact on mortality	Mean age at enrolment and KMC initiation
Acharya 2014 [16]	n/a
Boo 2007 [17]	24.5 days
Cattaneo 1998 [18]	10 days

Studies reporting impact on mortality	Mean age at enrolment and KMC initiation
Charpak 1997 [19]	4 days
Eka Pratiwi 2009 [20]	n/a
Ghavane 2012 [21]	14.1 days
Kadam 2005 [22]	3.2 days
Rojas 2003 [23]	19 days
Sloan 1994 [24]	13.0 days
Suman 2008 [25]	3.7 days
Whitelaw 1988 [26]	16 days
Worku 2005 [14]	10 hours

KMC cannot have an effect on deaths that happen before its initiation. Thus, the 40% mortality impact of KMC in enrolled infants would only translate in practice to about 13% impact on mortality in all babies with birth weight <2.0kg. The impact of the KMC intervention could be much larger if it could be initiated immediately after birth, and if it would have the same benefits as those when started after stabilization. Although there is a WHO recommendation for newborns without complications to be kept in skin-to-skin contact with their mothers during the first hour after birth to prevent hypothermia and promote breastfeeding[27], this recommendation is rarely followed for babies with birth weight <2.0kg because they are considered to be clinically unstable and are quickly transferred to newborn special care units. Two small randomized controlled trials (RCTs) have evaluated the feasibility, safety, and effect on the stabilization of initiating KMC immediately after birth. In an RCT from South Africa[28], skin-to-skin contact from birth was associated with 100% stability scores in the fifth to sixth hour of life as compared to 46% in the conventional care group in newborns weighing 1.2–2.2kg. Neonates managed in thermo-controlled incubators were significantly more hypothermic in the first hour, and had lower temperatures throughout the 6-hour observation period than those who received KMC immediately after birth.[28] A similar RCT from Vietnam in neonates weighing 1.5-2.5kg reported a significantly better transition to extra-uterine life ($p < 0.02$) in the immediate skin-to-skin contact group. The neonates in the intervention group also had a significantly lower need for respiratory support, intravenous fluids, and antibiotic use during their hospital stay.[29]

1.4 New evidence on efficacy of iKMC and community initiated KMC

The results of a WHO-coordinated randomized controlled trial of the effects of immediate KMC (iKMC) in five hospitals in Ghana, India, Malawi, Nigeria, and Tanzania were recently published.[30] A total of 3211 infants with birth weights weight from 1.0 to 1.799 kg babies to receive either iKMC or conventional care in an incubator or a radiant warmer until their condition stabilized and KMC thereafter. The median time after birth to initiation of skin-to-skin contact in the intervention group was 1.3 hours (IQR, 0.8 to 2.7),) and in the control group was 53.6 hours (IQR 33.8 to 101.4). During the stay in the neonatal intensive care unit (NICU), the median daily duration of skin-to-skin contact in the intervention group was 16.9 hours.

Implementation of the intervention required the mother or a surrogate provider (identified by the mother) to be with the infant 24 hours a day for the duration of the stay in the NICU. Changes in obstetrical and

neonatal care as well as structural changes in the NICUs were necessary for mothers to provide iKMC. These modified NICUs (hereafter referred to as Mother–NICUs), included beds for the mothers and reclining chairs, and were built or converted from existing NICUs. At two sites, completely new Mother–NICUs were built and at the other three sites, modifications were made to convert half the existing NICUs to Mother–NICUs, while the other half served as the control NICU. Infants receiving KMC were secured firmly to the mother's chest with a binder that ensured a patent airway, particularly when the infant was sleeping.[31] All care of the mother and infant, including respiratory support such as Continuous Positive Airway Pressure (CPAP) for the infant, was provided while skin-to-skin contact was maintained. Obstetricians supervised essential postpartum care provided to mothers in the Mother–NICUs. In both the intervention and control groups, once infants were clinically stable (as determined based on prespecified criteria) for 24 hours, they were transferred from the Mother–NICU or the control NICU to the KMC ward, where continuous KMC was provided for all infants until discharge.

Neonatal death occurred in 191 infants in the intervention group (12.0%) and in 249 infants in the control group (15.7%) (adjusted relative risk of death 0.75; 95% CI 0.64 to 0.89). The trial was stopped early on the recommendation of the data and safety monitoring board because of the large reduction in mortality among infants receiving iKMC. The number needed to treat to prevent one neonatal death was 27 (95% CI 17 to 77). iKMC was also found to reduce the incidence of suspected sepsis (22.9% in intervention group vs 27.8% in control group; adjusted RR 0.82, 95% CI 0.73 to 0.93) and hypothermia (5.6% vs 8.3%; adjusted RR 0.65, 95% CI 0.5 to 0.83). Though exclusive breastfeeding rates at the end of the neonatal period in both the groups were similar (about 85%), initiation of breast milk feeding in the first 24 hours after birth (58.5% vs 45.5%) and full breastmilk feeding by 7 days (78.4% vs 69.0%) were higher in the iKMC group. Other secondary outcomes such as time to stabilization, hypoglycaemia, mean duration of hospital stay, maternal satisfaction and maternal depression were similar in both the groups.

In this trial, the WHO minimum care package for small infants[32] was provided to both groups. This focused on essential newborn care at birth, respiratory support including CPAP when required, exclusive breastmilk feeding and early breastfeeding, thermal care, prevention and management of infections, and regular clinical monitoring. The implementation of conventional KMC (initiated after stabilization in the control group) was of high quality. The duration of skin-to-skin contact in the KMC ward was 20.2 hours (IQR 18.6-21.3) per day in the iKMC group and 19.0 hours (IQR 14.1-19.9) per day in the control group. The implementation of the minimum care package and conventional KMC was associated with a reduction in mortality from the baseline of about 25-30% in 2015 to about 16% in the control group during the study period. A new trial is currently ongoing to examine the effect of KMC initiated before stabilization on important clinical outcomes relative to standard care among neonates weighing ≤ 2000gms in Uganda.[33] The study will advance our knowledge on applicability of immediate KMC in hospitals in low-resource settings and will have important policy and programme implications.

A recent large randomized controlled superiority trial in Haryana, India, tested the effect of KMC initiated at home (community-initiated KMC) within 72 hours of birth in babies weighing 1.5-2.3 kg who were stable and feeding.[13] The study enrolled 8402 infants and reported a 30% reduction in neonatal mortality (hazard ratio [HR] 0·70, 95% CI 0·51 to 0·96), and a 25% reduction in mortality in the first half of infancy (HR 0·75, 0·60 to 0·93).

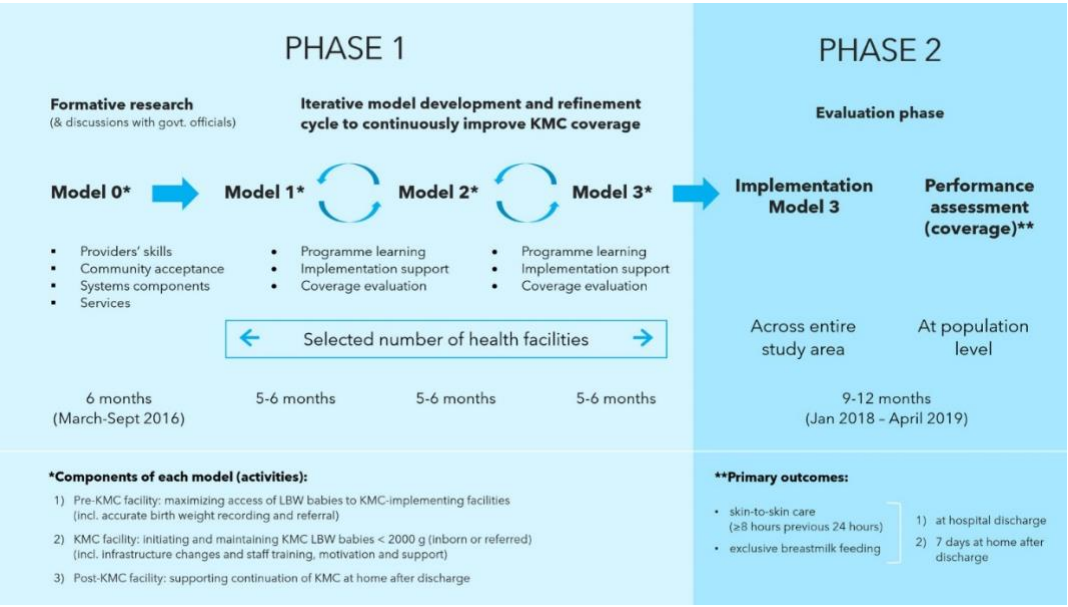
A pragmatic trial, examining the effect of early initiation of KMC (24 hours after admission) on mild to moderately stable newborns (<2000gms) in Gambia, showed no between-arm differences on neonatal survival.[38] The study had lower power to detect effect on newborn survival, it clearly pointed the need for implementation research to better understand how early initiation of KMC can be integrated in routine care setting.

1.5 Lessons learnt from implementation research to scale-up conventional KMC

A wide range of factors that impact the implementation and scale-up of KMC have been identified in recent reviews[34] and analyses of country programmes.[35, 36] They include lack of priority and leadership support within the health system, staff availability and training, inadequate resources, and space allocation, as well as limited community acceptance.

The WHO team recently supported seven sites in Ethiopia and India in an implementation research study that used a mixed-methods design to develop an adaptable strategy to improve KMC implementation.[37] These settings had high numbers of LBW babies and neonatal mortality rate (NMR), and no alternative programmes for increasing KMC coverage. KMC coverage at baseline was very low in all sites. The main outcome was KMC coverage measured as ≥8 hours of skin-to-skin care over 24 hours, and exclusive breastfeeding or exclusive breast milk feeding at discharge. Formative research informed the initial model for: (i) maximizing access to KMC-implementing facilities, (ii) ensuring KMC initiation and maintenance in facilities, and (iii) supporting continuation at home post-discharge (Figure 1 below). The model was refined in three iterative cycles. The evaluation phase included 3804 infants of birth weight under 2000gms who survived the first three days, were available in the study area and whose mothers resided in the study area. KMC was initiated for 68-86% of eligible infants in Ethiopian sites and 87-88% in Indian sites. At discharge from the hospital, effective KMC (defined as skin-to-skin contact for >8 hours in previous 24 hours and exclusive breastfeeding) were provided to 68% infants in Ethiopia and 55% in India. At seven days post-discharge, effective KMC was provided to 53%-65% of infants in all sites. In Oromia (Ethiopia) and Karnataka (India) effective KMC at days was 36 and 38%, respectively.

Figure 1. Iterative model optimization



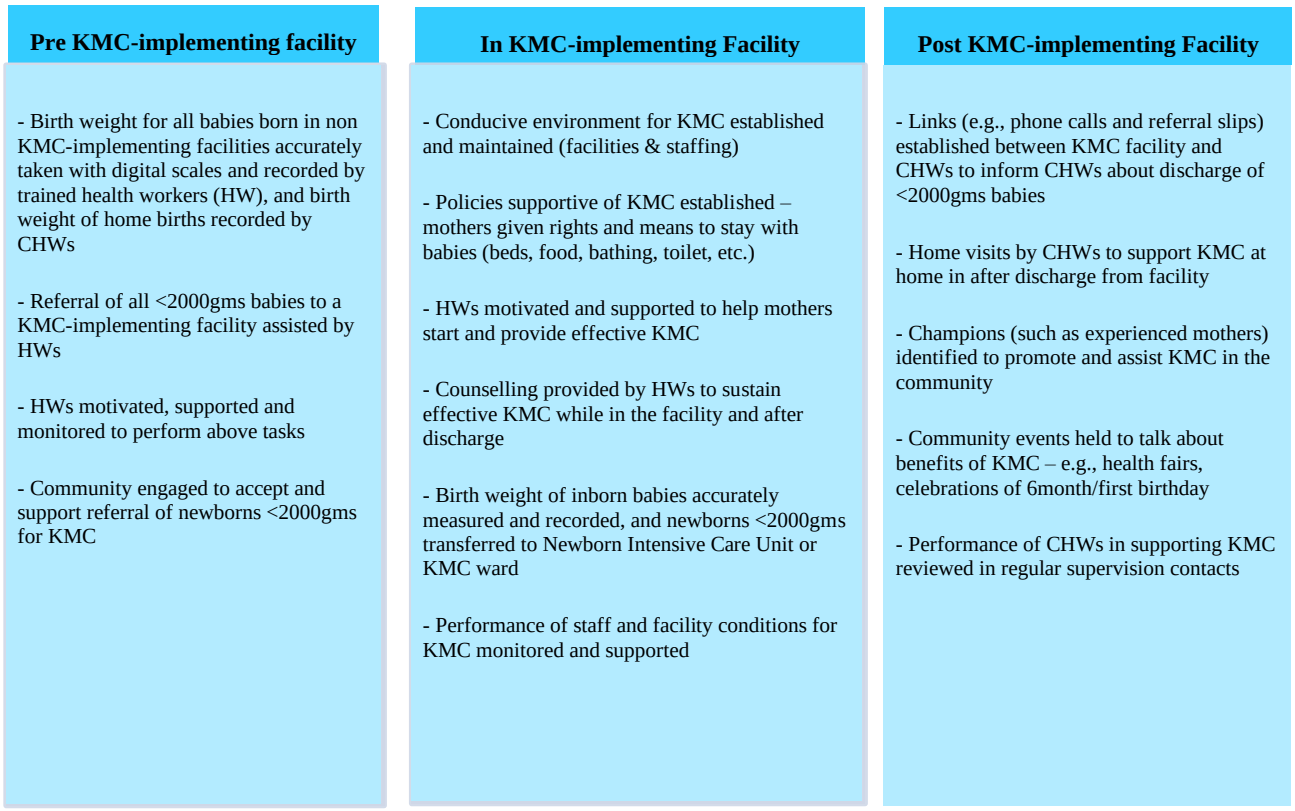
Source: reference 37

The study showed that high coverage of KMC can be achieved using context-adapted models based on implementation science. The following factors were identified as some of the important contributors to successful coverage:

- Identification of all LBW babies at birth
- Facilitated referral of LBW babies to facilities providing KMC care (public and private depending on context)
- Conducive facility environment for providing KMC
- Care for mothers – provision of basic amenities and services (bed, food, toilet, bath) for the mother-baby pair
- Respectful staff attitude to mothers, newborns, and families
- Conviction of staff that KMC is the standard of care
- Staff with the necessary skills to support KMC
- Strengthened links between the hospital, community services and home, to facilitate continued support at home
- Government ownership, responsiveness, and leadership

Key activities are summarized in Figure 2 below.

Figure 2 - Main components of the final model



Source: reference 37

1.6 Rationale to conduct implementation research to scale up iKMC

In summary, KMC initiated immediately after birth for 1.0 to <1.8 kg infants significantly reduced the risk of neonatal death by 25%.[30] The evidence of the efficacy of iKMC is clear. The number needed to treat is 27, which means that the intervention provided to 27 LBW babies will save one life. The key issue is to achieve high-quality, universal coverage of iKMC in the target population. Scale-up KMC study showed that with a package of interventions that included committed workforce, respectful maternity care, and government leadership, KMC coverage could increase to about 80%.[37]

WHO recommendations for the care of the preterm and LBW baby have recently been updated[39], and this update takes into consideration all the new evidence on KMC, including scale-up of facility-KMC, community-initiated KMC, and iKMC as mentioned above.

Currently, 20 years after KMC was first recommended by WHO, coverage of KMC globally remains low[10,11] and iKMC is virtually non-existent. Evidence is often lacking on how to achieve high coverage of newborn survival interventions, and novel approaches to rapidly reach implementation at scale are needed.[3,4,12] The Strategic and Technical Advisory Group for maternal, newborn, child and adolescent health and nutrition (STAGE-MNCAH&N) has set up a global multi-stakeholder working group to develop a joint position paper and implementation strategy for scaling up KMC. While there is sufficient

evidence to develop an implementation strategy for facility-based KMC after stabilization, evidence and experience is still lacking about the optimal ways to scale up iKMC and its potential impact on key outcomes in the target population under programme conditions.

Implementation research on iKMC especially at level 2 newborn care units will provide an opportunity to learn how to improve coverage and effectiveness of iKMC in reducing newborn mortality and improving the health of the most vulnerable babies in low- and middle-income countries. This implementation research proposal aims to support multi-country implementation research focused on learning how to scale up iKMC within programme conditions in multiple districts.

2. Objectives

2.1 Primary objectives

1. To develop an optimized implementation model in six sites in four countries (Bangladesh, Ethiopia, India, and Nigeria) that will add iKMC to functional systems of care for preterm or LBW infants. This model will provide necessary care including iKMC (skin-to-skin contact and breastmilk feeding), respiratory support, warmth, monitoring, and prevention and treatment of infections in newborn care units. The model will transform level 2 NICUs to level 2 M-SNCUs in health administrative areas (e.g., 1-2 districts) in four countries

2. To scale up the model to multiple administrative areas in each country using a stepped-wedge design and evaluate impact of the scale up on health outcomes including neonatal mortality

3. To support the national governments in the four countries to further scale up iKMC at sub-national and national levels

2.2 Secondary objectives

1. To ascertain the costs and cost-effectiveness of iKMC implemented at scale

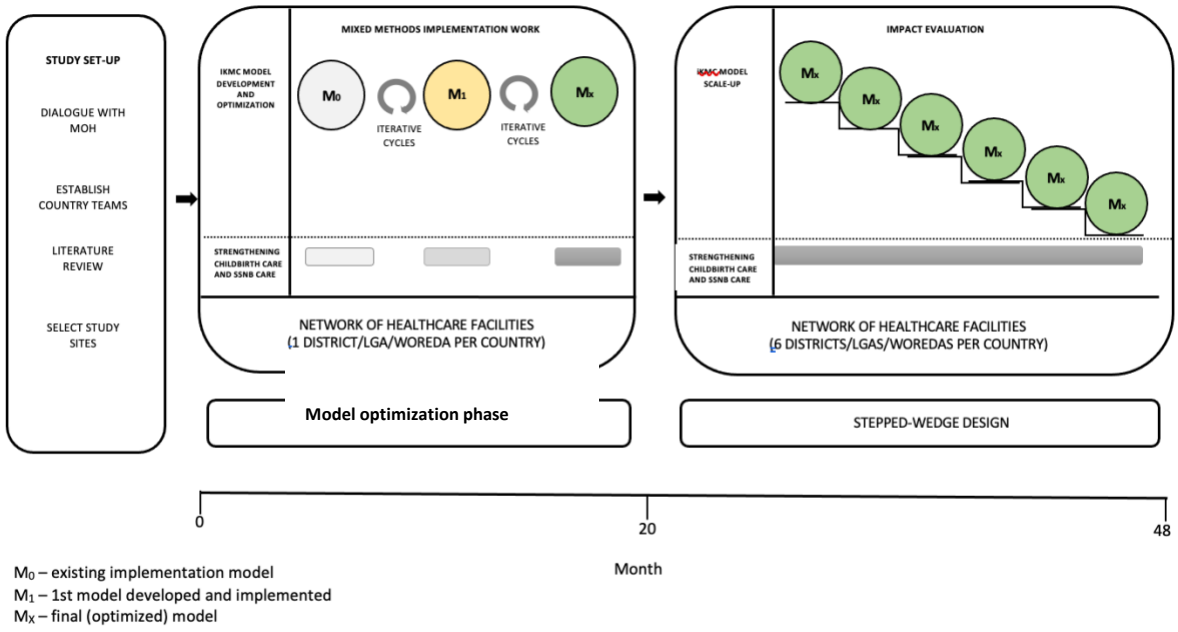
Additionally, the study will lay the foundations for research implementation platforms in each country that can assess other MNH interventions and care for preterm or LBW babies.

3. Methods

3.1 Overview of the study design

We propose a multi-country implementation research and effectiveness study. The study will be conducted in the context of improved care for preterm or LBW babies. The study will start with a model development and optimization phase. To develop and optimize the implementation model, we will use a mixed-methods design that applies both qualitative and quantitative research methodologies. Formative research will be used to identify barriers and facilitators for quality iKMC to design the initial implementation model. Concurrent programme learning using qualitative research and outcome measurement while implementing the model in routine care settings will be used to improve the model iteratively until high coverage of quality iKMC is achieved. The final (optimized) implementation model will be scaled up to six additional health administrative areas in each country using a stepped-wedge design to evaluate the impact of this scale up on neonatal mortality and other important outcomes.

Figure 3 – Overview of the study



We will align with the Every Newborn Action Plan (ENAP)[40] levels of care detailed in Annex 1, and include activities required to implement iKMC at level 1 (primary, essential newborn care), level 2 (secondary, special newborn care), and level 3 (tertiary care, intensive newborn care), where applicable.

3.2 Study setting and sites

The study will be conducted in six sites, two in Africa (Ethiopia and Nigeria) and four in South Asia (Bangladesh and India). These countries have a high burden of LBW and neonatal mortality; they contribute substantially to the global burden; and there is a strong commitment of the government to improving hospital-based care for preterm or LBW infants.

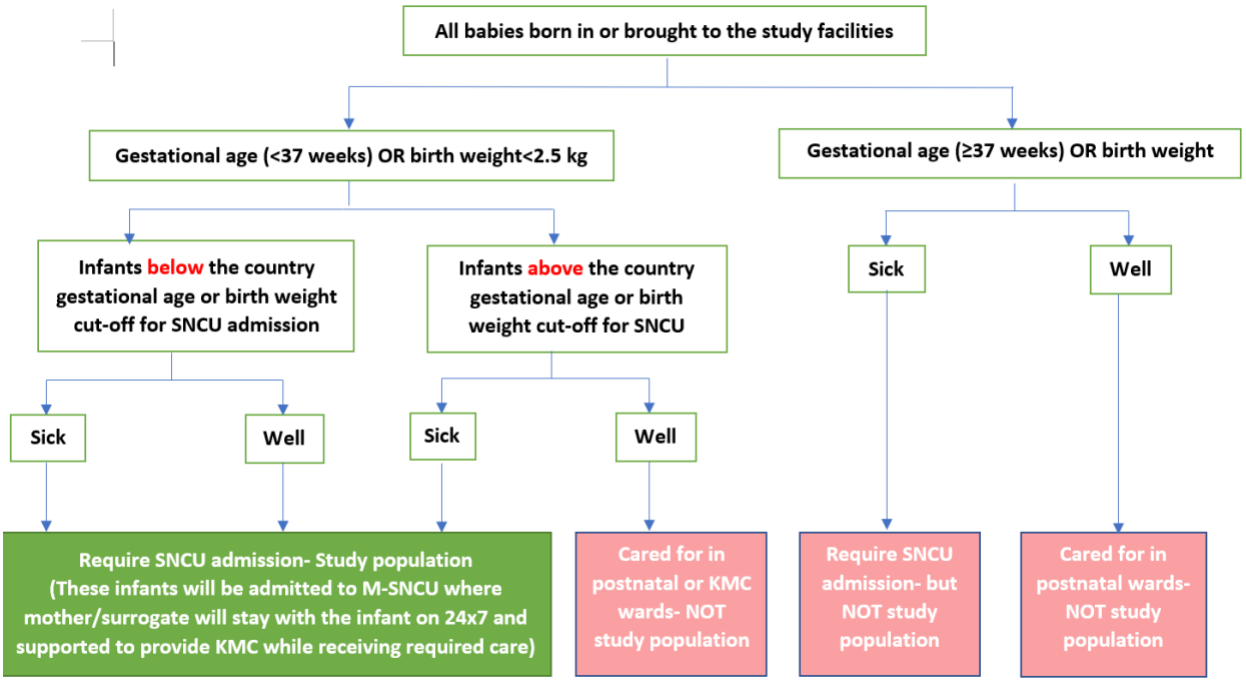
Each site has based their study in one or more health administrative areas (called 'district' in Bangladesh and India; 'woreda' in Ethiopia and 'local government area' in Nigeria). All sites will implement the study in areas that have: (i) population size of about 1-2 million in South Asia and half a million to a million in Africa; (ii) neonatal mortality and LBW rates which are the same or higher than national levels; (iii) institutional birth rates which are the same or higher than national levels (iv) quality of care consistent with local or national hospital standards; (v) at least one hospital with at least a SNCU ('level 2 unit') or a hospital where it is feasible to set up a SNCU ; and (vi) strong commitment of the facility and local government to sustain iKMC after the study has ended. Further details on the study sites can be found in Annex 2. The study districts have been selected jointly with the leadership of the ministries of health and their local subsidiaries.

3.3 Study population

Newborns: The study population is preterm or LBW newborns (gestational age <37 weeks or birthweight<2.5 kg) (requiring care in the SNCU, i.e., who are below the country cut-off point for birthweight or gestational age for SNCU admission, or those preterm or LBW newborns who are above the cut-off but are sick and need SNCU admission. See Figure 4 below.

WHO guidelines now include a recommendation for KMC for **all** preterm or LBW infants starting immediately after birth unless the newborn is critically sick.[39] Therefore, KMC provision for all preterm or LBW infants will be strengthened at all levels of care. However, the purpose of the study is to implement and scale up iKMC for preterm or LBW infants who are at high risk of being separated from the mother, i.e., those preterm or LBW infants who require SNCU care, either because they are too small or sick. Hence, while the study will promote and strengthen immediate KMC for all preterm or LBW infants, the study population will only comprise preterm or LBW infants who require SNCU admission after birth as depicted in Figure 4. During the intervention period, these infants will be admitted to M-SNCUs where their mother/surrogate will stay with them on a 24x7 basis and will be supported to provide KMC. During the control periods, these infants will be admitted to the normal/routine SNCU and KMC will be promoted and encouraged through existing mechanisms.

Figure 4 - Description of study population



The population eligible for outcome evaluation is described in Section 3.6.1

Health workers: Health workers (and managers) working at the participating sites will be the target of community-, facility- and provider-level components of the iKMC implementation models.

3.4 Study team

The national and provincial ministries of health are the most important partners in this implementation research effort. WHO will discuss and ensure that the national, provincial and district level programme managers are engaged in the design and implementation of the study. Another important stakeholder will be the local research group, which has the skills and experience to conduct the study. This research group has been jointly identified by the ministry of health and the WHO national office in each country.

The existing health workforce who are already part of the health system in the study site, programme managers and researchers will jointly make up the study team. The iKMC intervention will be delivered by the health workforce; the main role of the research team is to support the implementation of the intervention, and data collection for iterative programme improvements and programme evaluation.

The research team will consist of three small independent teams: (i) **programme learning team**, trained in interviewing techniques and qualitative methods will monitor activities for iKMC implementing facilities and hold discussions with key stakeholders to capture their perceptions of what is and what is not working. This team will be involved with formative research, programme learning, and process monitoring and will help formulate and improve the intervention.; ii) **implementation support team** will guide the health workforce and support the creation of an enabling environment to implement the intervention in iKMC implementing facilities; and (iii) **outcome measurement team,** will independently measure the outcomes in the study population. See Table 2 below.

Table 2. Description of study teams

	Government partners	**Research team**		
Overall role	Decision-making and implementation	Implementation, qualitative and quantitative research data collection and evaluation of the implemented programme		
Staff	Policy makers and health staff/health care providers	Formative research and programme learning team	Implementation team	Outcome evaluation team
Activities	Decide initial and subsequent implementation models Implement activities in the implementation model Responsible for all resources necessary Management and administrative support for implementation, training on standard protocol, Monitoring from national level Facilitate institutionalization for accountability, sustainability, and scalability	Formative research to develop the initial model. Continued programme learning data to help refine and optimize implementation model Monitor process outcomes Contribute to discussions to refine and optimize model	Support policy makers, programme managers, and health staff/health care to implement the model Ensure complete, valid documentation of service in the register Facilitate preparedness such as infrastructure, training, logistic arrangement including job aid, communication materials Contribute to refinement and optimization of the model	Collect quantitative data on outcomes including coverage of iKMC before, during, and after the development of optimized implementation model. Contribute to discussions to refine and optimize model

3.5 The iKMC implementation model

3.5.1 Key components of the iKMC implementation model

Based on learnings from the iKMC study coordinated by WHO, the iKMC (intervention) in this implementation study is defined as follows. A baby is considered to have received iKMC if:

- Skin-to-skin contact is initiated within 2 hours after birth if the baby is born within the iKMC implementing facility; if the baby is born outside, then within 2 hours of reaching the iKMC implementing facility (for those babies who reach the facility within 24 hours of birth)
- Continuous skin-to-skin contact is provided by a mother/surrogate for at least 8 hours per day during the stay in the level 2 M-SNCU (average hours per day for the overall M-SNCU stay)
- Support for early and exclusive breastmilk feeding is provided to the mother
- Required medical care for the mother and baby is provided without separation, as much as possible

The pre-requisite for the intervention is the transformation of the level-2 SNCU to level 2 M-SNCU by allowing the mother or surrogate to stay with the baby 24 hours/7 days.

Intervention characteristics including its design have been described by the WHO iKMC study[30], and the relative advantages and high-quality evidence of its efficacy in improving survival of preterm or LBW babies. In addition to the above, a minimum package of care for preterm and/or LBW babies requiring care in level 2 SNCUs will be provided (see Annex 1): (essential newborn care at birth, thermal control, KMC including continuous skin-to-skin contact for stable babies and exclusive breastmilk feeding, attention to hygiene and regular monitoring for all babies; and intravenous fluids, antibiotic therapy, and respiratory support including CPAP, if required). Core components of the intervention package include support to empower and enable the mother to take care of her baby and to ensure the appropriate care of the mother and baby, as described below:

- ***Promotion and support for continuous skin-to-skin contact, initiated as soon as possible after birth***

  As mentioned above, continuous skin-to-skin contact will be initiated within 2 hours of birth if born within the iKMC implementing facility and within 2 hours of reaching the iKMC implementing facility if born outside (who reach the facility within 24 hours of birth). Initiation of KMC will not have to wait for the baby to be clinically stable, aiming for at least 8 hours of skin-to-skin contact per day. This will be initiated by the mother or the surrogate within the birthing room or the operation theatre, continued during transfer and stay in the level 2 M-SNCU. Mother/surrogate and baby will be kept in the level 2 M-SNCU until the baby is stable enough to be transferred to the KMC ward and KMC will continue to be provided by the mother at the KMC ward until discharge from the hospital. At the time of discharge, the mother will be advised to continue KMC at home.

- ***Promotion and support for early and exclusive breastfeeding/breast milk feeding***

  Mothers will be encouraged and supported to put the baby to the breast and express milk when they are in the level 2 M-SNCU. Even if the baby is unable to feed from the breast, putting the baby to the breast provides the baby the opportunity to learn how to attach and suckle and stimulate milk production. Continuous skin-to-skin contact between mother and baby is likely to facilitate breastfeeding. Mothers and/or surrogates will receive counselling to promote and support exclusive breastfeeding. If the baby is unable to feed from the breast, breast milk feeding using a cup, or a tube will be supported. This breastfeeding support will continue through the length of stay in the hospital, including in the KMC ward. If a mother is deceased or unable to express breastmilk due to medical

reasons, the team will explore alternative feeding for the baby (e.g., donor milk or formula feed). At the time of discharge, the mother will be advised to continue exclusive breastfeeding at home.

- ***Health care for the mother and baby provided without separation and with respect***

The mother and baby will be provided health care without separation as much as possible. Mothers will be provided health care by midwives, nurses, and obstetricians while she is in the level 2 M-SNCU. If a mother has any complication for which she needs to stay in or be transferred to the adult intensive care unit or operation theatre, skin-to-skin contact will be initiated and/or continued with a surrogate. If the baby requires a procedure or treatment that is not possible during skin-to-skin contact, the baby will be shifted to an incubator or radiant warmer. Then, skin-to-skin contact will be temporarily interrupted for the period of the procedure or treatment and recommenced as soon as possible thereafter. Health workers will receive orientation and be supported to provide respectful care to mothers and/or surrogates and their newborns.

- ***Level 2 M-SNCU***

Converting the level 2 NICU into a level 2 M-SNCU, where the mothers can stay with their sick preterm or LBW newborns 24/7, is a key requirement to enable the provision of iKMC. The organization of services described below builds on the learnings from the iKMC RCT study.

All infrastructure, equipment, and staff required to provide high quality comprehensive care for the sick and small newborn, including respiratory support with CPAP, optimal nutrition with emphasis on mother's own milk feeding, adequate monitoring and protection of infants will be strengthened by government partners supported by the research team, before transforming it to a high-quality functioning level 2 M-SNCU (Figure 3.1). A conducive environment for mothers /surrogates to provide iKMC will be provided. These include beds and reclining chairs for mothers and surrogates, clothing that facilitates skin-to-skin contact and breastfeeding, food and dining area, shower, and toilet. In addition, an area to examine the mothers with privacy, a hand washing area and a pantry are desirable (Figure 3.2). A typical level 2 M-SNCU unit (space for one mother and her baby) will have a reclining adult bed and a reclining chair for the mother and surrogate, a warmer for the newborn, provision for intravenous fluids, oxygen, CPAP support and pulse oximeter for continuous monitoring. Concurrently, postnatal and KMC

wards in the iKMC implementing facility will be strengthened to enable the provision of KMC for preterm or LBW babies who do not require admission into the M-SNCU.

- ***Strengthening the linkages within the hospital across departments***

Any preterm or LBW newborns who are brought to the emergency ward, or to the paediatrics outpatient department (OPD), or accompanying the mother in the gynaecology/obstetric OPD for any postnatal problem, need to be assessed whether they require special care and directed to the M-SNCU or KMC ward accordingly. Staff at each of these contact points will be oriented and trained to identify eligible babies. To avoid delays due to admission processes, it may be beneficial to train the relevant staff so that they can initiate KMC wherever feasible.

- ***Strengthening the referral pathway and appropriate identification of newborns***

Birthing facilities without a level 2 SNCU will be crucial in achieving population level coverage. Care at these facilities will be strengthened, ensuring that babies are accurately weighed within one hour of birth, and babies below the country cut-off of gestational age or birthweight or above the country cut-off of gestational age or birthweight who are sick, are referred immediately to a hospital with a level 2 M-SNCU, based on national guidelines for referral. The staff will be trained and motivated to initiate KMC and ensure that babies are transported in skin-to-skin contact with the mother or surrogate. Strengthening the referral pathway would include facilitated decision making by the family, facilitated transport, addressing financial barriers through local government support, and increased readiness and preparedness of the level 2 M-SNCUs to receive the referrals. Sub-district and lower-level facilities will also be strengthened to provide KMC to preterm or LBW newborns who are stable and who do not meet the referral criteria based on each country's guideline. After discharge from the hospital, the mother and family will be linked to a community health worker (CHW) who can provide counselling and support for continued KMC at home.

Strengthening timely and appropriate identification and referral will be important for high coverage, particularly for babies born at home. Various strategies will need to be adopted, including but not limited to, social and Behavioral change communication activities to create awareness and generate demand; more frequent follow up of pregnant women who are at risk of giving birth to preterm or LBW babies as identified during antenatal visits; motivation of families and communities to inform CHWs when women go into labour or as soon as possible after birth; training of CHWs in appropriately weighing and identifying LBW newborns, and strengthening transport and referral for those preterm or LBW babies born at home.

3.5.2 Frameworks to guide the development and optimization of an iKMC implementation model

We will use the concepts of the *Generic Implementation Framework* [42] for the proposed study. This framework considers the non-linear and recursive nature of the implementation process as being foremost to implementation. At the centre of the framework is the innovation to be implemented, and surrounding the innovation are the contextual domains or levels of influence. Throughout the implementation process, we will consider factors, strategies, and outcomes that will influence the course of implementation. We strongly believe that adapting implementation based on process learning and the concurrent evaluation of coverage and quality is critical to achieving the optimal models, as demonstrated in the scale up KMC study.[42]

Specifically, we will use the *Consolidated Framework for Implementation Research* in the Generic Implementation Framework [42] to guide the development and process learning activities and include key concepts from the Dynamic Adaptation Process in implementation.[43] The Consolidated Framework for

Implementation Research is composed of the following five domains, with multiple constructs related to each domain:

1. ***Characteristics of individuals involved:*** This domain refers to characteristics of the individuals who would be key for implementation of the intervention, which include preterm or LBW newborns, mothers, parents and families, CHWs, midwives, nurse and doctors, facility managers, and programme managers at district, provincial and national levels. The study population are described in Section 3.4 above. The relevant constructs related to this domain include knowledge and beliefs about the intervention, self-efficacy, and individuals' motivation for change. These will all be explored during the formative research, and appropriate elements will be added to the implementation model. Finally, we will identify care-seeking practices for childbirth care including use of the private sector to determine how to strengthen care seeking and important stakeholders

2. ***Intervention definition and characteristics:*** This domain refers to characteristics of the intervention, which in this case will be iKMC. The intervention is described in detail in section 2.5 The specific barriers and facilitators to the implementation of the core elements of the intervention will be identified during formative research and the implementation model will be designed and adapted accordingly.

3. ***Outer setting or broader context:*** This domain refers to the economic, political, social, and cultural context which would influence implementation of iKMC. The relevant constructs related to this domain include resources for the care of preterm or LBW babies, relevant policies, political support, barriers, and enablers for efforts for newborn survival and KMC, societal norms and perceptions about care of the small infants and KMC. During formative research, we will review national, subnational and facility policies and standards to understand what policy changes need to be introduced to ensure implementation of iKMC. The cultural context that influences IKMC will also be explored

4. ***Inner setting or health system context:*** This domain refers to the health system, and health facility, and the context which would influence implementation of iKMC, including setting up M-SNCUs. The relevant constructs related to this domain include structural characteristics of the facilities, human resources and organization of care for preterm or LBW newborns, culture (overarching thinking about care of the small infants), implementation climate (need for change, compatibility with the intervention, relative priority, incentives, goals and feedback and learning climate), and readiness for implementation (leadership engagement, available resources, and access to information, knowledge and skills for implementing iKMC).

5. ***Process of implementation:*** This domain of the framework focuses on engaging the relevant stakeholders, executing, reflecting, and evaluating with the aim of optimizing the implementation model for iKMC. The process is described in detail in the sections below

3.5.3 Formative research

The first step in the study will be for the formative research team/ programme learning team to undertake an initial round of formative research to identify and understand barriers and enablers to implement iKMC in the specific local context. The overall aim of the formative research is to inform a user-centric

design of the intervention model, based on the needs, motivations and influencers of the mother-infant dyad and a clear understanding of supply issues (through the health system and health workers) (linked to the domains in the Consolidated Framework for Implementation Research namely the characteristics of individuals involved, the outer setting or broader context and the inner setting or health system context). We will use mixed-methods to understand how KMC and iKMC is currently implemented in the study sites, including in the private sector, and context-specific factors affecting implementation. We will capture how preterm or LBW babies are currently cared for, barriers and facilitators to implementation, and context-specific factors that will affect implementation of iKMC in each site, including the perspectives on care of preterm or LBW babies of key stakeholders. The formative research phase will directly inform the development of an optimal iKMC implementation model in participating sites.

The specific objectives of the formative research phase are:

1. To understand perceptions of women from varied backgrounds around care for preterm or LBW babies including care seeking practices and barriers and facilitators to reaching facilities, their perspective of care received in the health facilities, their perspectives on skin-to-skin care and breastfeeding, their concerns about caring for their baby and support they needed as well as acceptability of the intervention;
2. To explore family and community norms around support for care for preterm or LBW babies, community perceptions and values about care for preterm and LBW babies and KMC, and how to build family and community support for facility birth, referral to iKMC facilities and care for preterm or LBW babies in general and for iKMC implementation.
3. To explore health workers knowledge, norms and skills around care for the preterm or LBW babies and their perceptions about the feasibility and acceptability of different components of the iKMC implementation model;
4. To identify and understand factors affecting implementation and scale-up of iKMC, including existing policies and standards, the current practices to care for preterm or LBW babies, and explore the feasibility and acceptability of different components of the iKMC implementation model
5. To identify and agree with stakeholders the implementation strategies to barriers and enablers to effective implementation of the iKMC implementation model.

We propose the following activities in the formative phase:

1) Qualitative in-depth interviews (IDIs) with women who had preterm birth or LBW babies who were cared for in a study facility in the last month;

2) Focus group discussions (FGDs) with women in the community including those who gave birth in the last 12 months in a study facility or at home and female family members;

3) FGDs with men in the community including partners of women those who gave birth in the last 12 months in a study facility or at home

4) Small group (2-3 people) or individual interviews (depending on feasibility) with traditional birth attendants, women and community group leaders and other community stakeholders;

5) Small group (2-3 people) or individual interviews (depending on feasibility) health workers (CHWs, midwives, nurses, doctors, obstetricians, neonatologists, paediatricians and facility management);

6) Assessments of SNCUs to identify facility readiness for implementation of the WHO minimum package of care for small and sick newborn.

The qualitative study will take place in a sample of health facilities and community catchment areas across the six sites where iKMC interventions will be developed.

Additional details on the formative phase activities and programme learning, are included in Section 4 below.

In addition, An assessment will be conducted of existing SNCUs to assess the facility's readiness to provide a basic, minimum level of care to preterm or LBW infants, including KMC. It will include an evaluation of the availability of 1) adequate infrastructure (e.g., closed thermoneutral space with handwashing facility, private space for KMC), 2) human resources (number and type of staff, e.g., doctors and nurses trained in newborn care), 3) equipment and supplies (e.g., CPAP for respiratory support, pulse oximeters to ensure safe oxygen use), 4) standard operating procedures and protocols for newborn care (e.g., infection prevention and control including antibiotic administration, fluid management), 5) ability to support exclusive breastfeeding and assisted feeding for small newborns; and 6) detect and manage basic complications (e.g., hypoglycaemia and hypothermia)

3.5.4 Preparatory activities

The study team will conduct preparatory activities in selected districts, particularly in the selected hospitals where iKMC is to be implemented while formative research is being conducted. An important part of these preparatory activities will be to strengthen implementation of a minimum package of care for preterm or LBW babies requiring care in level 2 SNCUs (see Appendix 1).

The iKMC trial identified two key common gaps in care: the provision of appropriate respiratory support and periodic clinical monitoring of babies.[30] These gaps will be covered by ensuring that adequate number of safe CPAP machines and pulse oximeters are made available at all iKMC implementing facilities. In addition, standard operating procedures for the use of this equipment will be developed and introduced. To ensure high quality and coverage of KMC for stable babies, learnings from the scale up KMC study will be implemented.[42] The following activities will be done prior to the implementation of iKMC in level 2 M-SNCUs:

(1) Activities aimed at maximizing access of preterm or LBW babies to iKMC-implementing facilities including accurate birth weight recording and referral of preterm or LBW babies born at home or lower-level facilities that do not provide KMC including skin-to-skin contact,

(2) Activities aimed at initiating and maintaining KMC for stable preterm or LBW babies who were born in or referred to the facility in level 2 NICU through changes in infrastructure and training, motivation and support of facility staff. The level-2 NICU will be strengthened to provide effective interventions in the standard of care, including optimal use of CPAP, breastmilk feeding, prevention and treatment of infections, and monitoring,

(3) Activities aimed to promote birth at a health facility. In case of a home birth, CHWs will identify a preterm or LBW baby and promote immediate care seeking at iKMC implementing facility. Activities will be undertaken to strengthen referral and transport. Community level activities will also support continuation of KMC at home after discharge; these include telephone contact by hospital staff with CHWs and families and home visits by trained CHWs. This network of primary, secondary level facilities and community will transform the small and sick newborn care in the study implementation area.

3.5.5 Development of the initial iKMC implementation model

Based on findings of the formative research, an initial model (Model 0+ in figure 7 below) for implementation of iKMC will be developed for implementation within the existing health system. This will be done in co-design workshops which will be held in each country under the leadership of

national/provincial ministry of health, attended by the research group, district and hospital managers, doctor, nurse, and midwife leaders in participating hospitals, CHWs and women's and parents' groups representatives, and the WHO technical support team. We will facilitate group discussions to inform the implementation strategy using the APEASE criteria (Affordability, Practicability, Effectiveness, Acceptability, Safety, and Equity).[41] Similar methodology will be used during subsequent re-design workshops (see below).

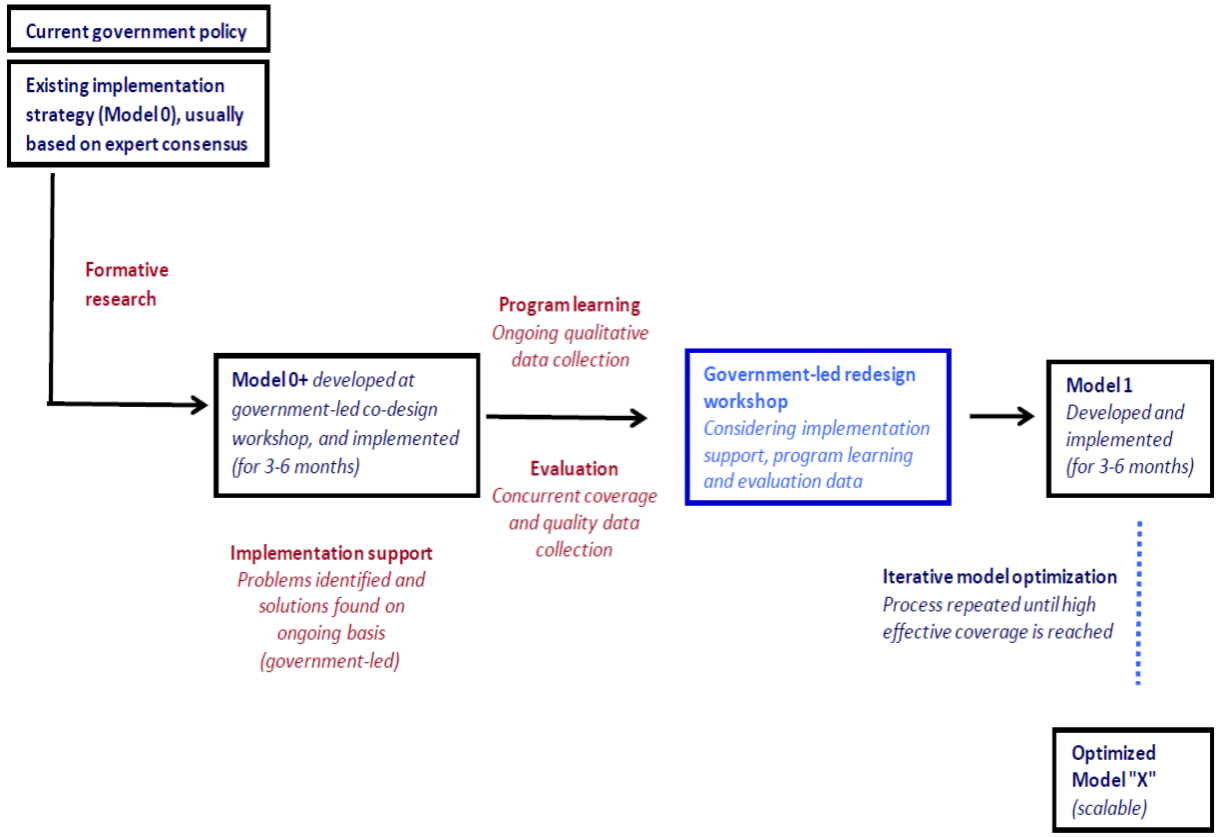
Implementation Model 0+ will be initiated with concurrent programme learning as well as quantitative data collection on coverage and quality outcomes. The quantitative coverage and quality data will be the parameter for optimization of the implementation model, while the qualitative programme learning data (through interactions with managers, health workers, CHWs and women and families to understand their perspective on implementation) will provide answers to why we are achieving or not achieving the desired outcomes.

As mentioned above, the implementors will be routine health system staff, and they will be supported by a small implementation support team. The two other teams, a programme learning team and an outcome measurement team, will respectively collect the above-mentioned qualitative and quantitative data. The programme learning team will frequently share data with the implementation and implementation support teams to continuously improve implementation.

After implementation of the initial model for 3-6 months, a re-design workshop led by the Ministry of Health will be organized. At this meeting, lessons from implementation and data from programme learning and coverage and quality measurement will be used to review and refine the implementation model. The aim of the re-design workshop would be to refine, improve and revise the implementation model to move towards a higher coverage of iKMC. A period of 3-6 months provides adequate volume and range of implementation experience with qualitative and quantitative data to support decisions on changes of the implementation model. However, this period will vary among the sites based on contextual needs.

The above process will be repeated every 3-6 months. We envisage at least three cycles during model design and optimization, until reaching a scalable model aiming for high coverage (aspirational for 80% coverage) and quality of iKMC. The WHO team will facilitate the sharing of learnings across different study sites to identify further opportunities to improve the implementation models. Experience from scale up of interventions such as KMC suggests that the development of the final (optimized) model may take about 12-18 months. Figure 7 summarizes this process of implementation model development and optimization.

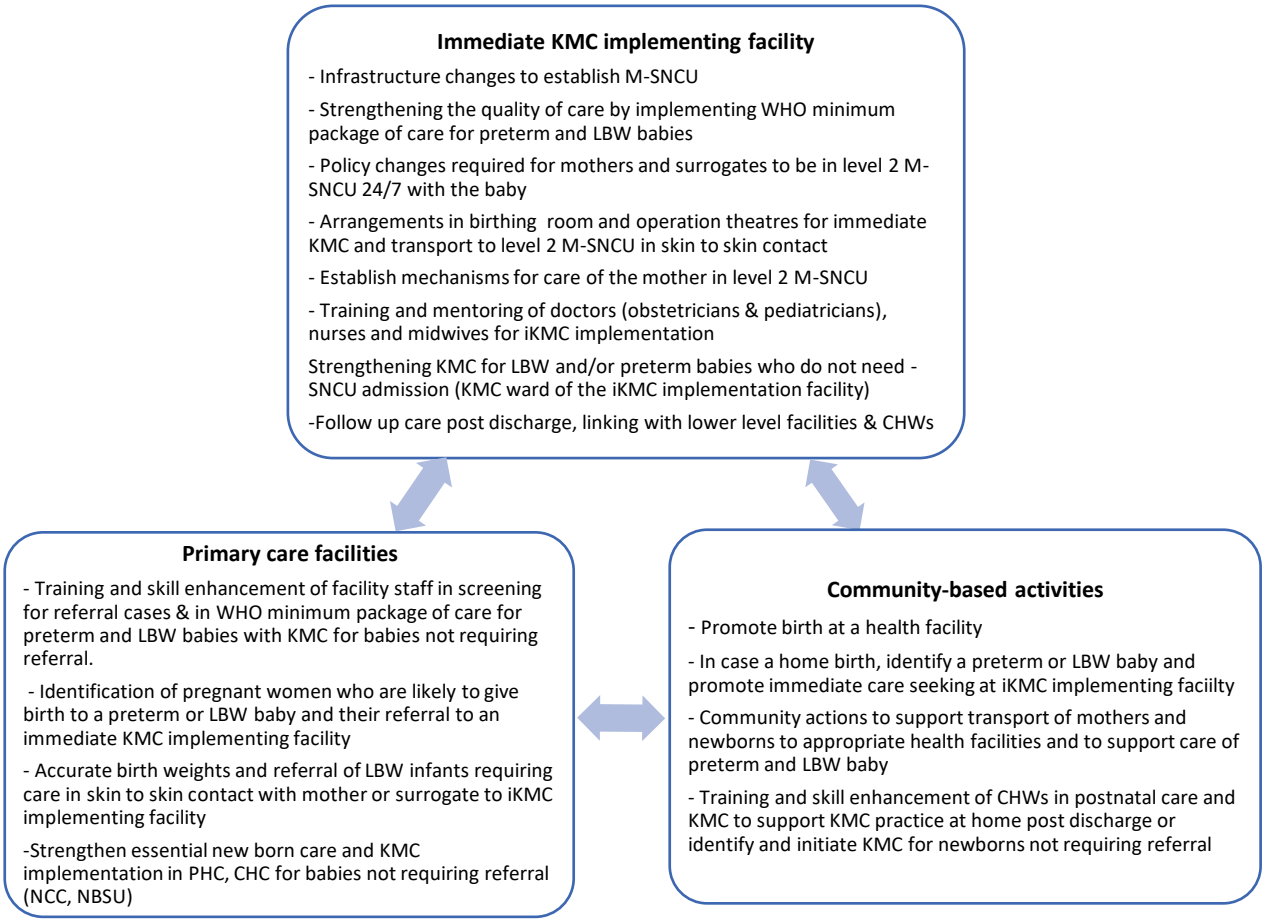
Figure 7 - Process of implementation model development and optimization



Source: reference 37

While the implementation model will largely focus on the hospitals where iKMC will be implemented, additional activities will be conducted in lower-level health facilities and communities in the study districts. A few examples of these activities are summarized in figure 8 below.

Figure 8. Activities expected in iKMC implementing facilities and communities in model optimization phase



3.5.6. Identification of questions related to scalability of the implementation

Prior to initiation of the scale up of the model and stepped-wedge evaluation, the research team will engage with the administration, government, and programme managers at national and subnational level to identify the questions of scalability of the model within the existing system. These questions could be related to the scale up pathway and approach, potential barriers, capacity required for scale up, and investments needed. Addressing these questions throughout the duration of the evaluation will help prepare for provincial and national scale up, which will include development of the scale up strategy, investment case and implementation roadmap.

3.5.7 Recap of the study strategy in the model optimization phase

The first step will be the engagement of key stakeholders in the selected study districts, as described in the sections above. Two concurrent activities will be conducted in the first 2-4 months of the project implementation: formative research and strengthening the quality of care by ensuring implementation of the WHO minimum package of care for the small and sick newborn[32]

The formative research team will conduct interviews and focus group discussions to explore the domains of the consolidated framework for implementation research as described above. The duration of formative

research will be relatively short, as this team will transition into the programme learning team and continue to collect relevant data throughout the model development and optimization period.

A rapid assessment of newborn care provided in the birthing room, operation theatre and level 2 NICU will also be conducted to identify gaps in implementation of the WHO minimum package of care for small and sick newborns. Based on the gaps identified, the study will support activities to address these gaps.

When the results of formative research are available, co-design workshops to develop the implementation model 0+ will be organized. This model will be implemented, with ongoing collection of qualitative and quantitative data for 3-6 months, and re-design workshops will revise the model as required. Two or three similar iterative cycles will continue to optimize the implementation model until the end of the model optimization stage.

3.6 Outcome evaluation in the model optimization phase

3.6.1 Study population for outcome evaluation

The study population for outcome evaluation is common across both phases of the study.

Inclusion criteria

Preterm or LBW newborns (gestational age <37 weeks or birthweight<2.5 kg) requiring care in the SNCU, i.e., who are below the country cut-off point for birthweight or gestational age for SNCU admission, or those preterm or LBW newborns who are above the cut-off but are sick and need SNCU admission.

Exclusion criteria*

Preterm or LBW newborns requiring SNCU care who are critically sick, for example:

- are unable to breathe spontaneously within the first hour after birth or
  have congenital malformations that interfere with the intervention, or the intervention interferes with the required care for the congenital malformation (e.g., anencephaly, congenital heart disease, gastroschisis, hydrocephaly, multiple malformations, omphalocele, tracheoesophageal fistula, abdominal detention. etc.)
- are in shock (in need of inotropes) or
  are receiving invasive mechanical ventilation in the first 2 hours of birth or admission to SNCU; or
- Liveborn who died in the first 2 hours of birth or first 2 hours of admission or were dead at the time of admission to the iKMC implementing facility

*These neonates (except deceased newborns) will be excluded from the study for outcome measurement purposes however all newborns will receive appropriate care in the iKMC implementing facility.

3.6.2 Outcomes for the model optimization phase

The main outcome of the design and optimization phase will be development of *the optimized implementation models* that achieves a high coverage and quality of iKMC and establish the norm of zero separation between the mother and her newborn in the four participating countries.

This will be measured through a primary coverage outcome in a tracer indicator that captures the skin-to-skin component of iKMC i.e., initiation and duration of skin-to-skin contact.

Primary coverage outcome**:** Proportion of preterm or LBW newborns requiring care in level 2 M-SNCUs) born in or brought to the iKMC implementing facility, within 24 hours of birth, who received iKMC. This will be captured through a tracer indicator on initiation and duration of skin-to-skin contact.

A baby is considered to have received iKMC if:

- Skin-to-skin contact is initiated within 2 hours after birth if the baby is born within the iKMC implementing facility, or within 2 hours of reaching the iKMC implementing facility if the baby is born outside the iKMC implementing facility (who reach the facility within 24 hours of birth) and
- Continuous skin-to-skin contact is provided by a mother/surrogate for at least 8 hours per day during the stay in the level 2 M-SNCU hospital (average hours per day for the overall M-SNCU stay)

Quality outcomes*:*

- Proportion of preterm or LBW infants who arrived to an iKMC implementing facility within 24 hours after birth among those born in a health facility who required referred at birth to an iKMC implementing facility
- Proportion of preterm or LBW infants on respiratory support (any oxygen or CPAP) who received skin-to-skin contact > 8 hours/day in the M-SNCU
- Proportion of preterm or LBW infants receiving KMC at discharge (8-24 hours of skin-to-skin contact and exclusively breastfed) in the 24 hours before discharge from the iKMC implementing facility
- Proportion of preterm or LBW infants who are exclusively breastfed at discharge
- Median age at putting the baby to the breast for the first-time during M-SNCU stay

Implementation outcomes:

In the model optimization phase, we will also monitor the following implementation outcomes, including experience of care by mothers/caregivers and newborns:

- ***Acceptability:*** iKMC including transport in skin-to-skin contact from birthing place to M-SNCU is acceptable to mothers (and/or surrogates). Mothers and caregivers are satisfied with the care received. iKMC is acceptable to health workers (facility and community).
- ***Adoption***: The challenges in adoption of iKMC by mothers, hospital managers and health providers (nurses, midwives, doctors) identified in programme learning are addressed.
- ***Adaptation***: Modifications to adapt the iKMC intervention to the social and health system context are implemented.

- ***Fidelity***: Quality iKMC care is provided to mothers and newborns in the level 2- M-SNCUs

Evaluation of the above outcomes and monitoring of the above implementation outcomes will increase our understanding of the challenges of scaling-up the intervention. The study will specifically provide us with experience of engaging multiple stakeholders, creating level 2 M-SNCUs and making them functional, fostering collaboration between obstetric and paediatric departments, and changing policies to allow iKMC implementation.

3.7 Scale up of the optimized implementation model in stepped-wedge trial phase

During this phase, the optimized iKMC implementation model will be implemented in a randomized stepped-wedge manner in 24 clusters (district/woreda/local government areas) across the four participating countries to evaluate its effectiveness on neonatal outcomes. These 24 clusters, i.e., six clusters (districts/woreda/ local government area) across the four countries to be included in the scale-up and effectiveness evaluation will be decided in consultation with the government in each country.

Each cluster would be one health administrative unit of district/woreda/ local government area with at least 1-2 health facilities having a functional level 2 SNCU. The characteristics of the study sites are described in section 3.2 and in Annex 2. The health facilities having a functional level 2 SNCU in all the six districts in a country will be supported to become iKMC implementing facilities by strengthening the quality of preterm and LBW newborn care to ensure a minimum package of care for small and sick newborns prior to their randomization for this effectiveness evaluation. Preparatory work for setting up M-SNCUs, including identification of space and organization of infrastructure, procurement of KMC supplies, and training of existing health workers will be done during this time. The process of institutionalizing monitoring and evaluation will also be started wherein process and outcome indicators will be incorporated in the Health Management Information System to be reviewed periodically by all stakeholders to ensure accountability, sustainability, and scalability.

3.7.1. Strengthening care for preterm or LBW babies in districts

Health facilities with level-2 SNCUs in the six identified districts/woredas/local government areas across all the four participating countries will be assessed for their ability to provide essential childbirth care for all newborns and WHO minimum package of care for small and sick newborns (see Annex 1). The identified gaps will be addressed by the study team in collaboration with the government and facility administration. Staff will be trained to provide quality routine intrapartum care, essential newborn, and preterm birth care (including care at birth, thermal care, KMC, feeding support, respiratory support including CPAP, and prevention and treatment of infection). Governments will ensure that all necessary supplies and equipment are available. During the time frame that the model is being developed and optimized in one study area per site, the activities to strengthen the SNCUs in the potential iKMC implementing facilities will be initiated in the other study areas. This will be done in the six districts/woredas/local government areas in each country and will be concluded before the scale-up effectiveness evaluation is launched and the optimized iKMC model is implemented.

3.7.2 Evaluating the impact of the scale-up: stepped-wedge cluster RCT design

The impact of the scale-up of the optimized model on neonatal mortality will be evaluated in a stepped-wedge, cluster-randomized trial design in 24 clusters (6 per country) over a 24-month duration divided

into eight 3-month periods (Table 3). The unit of randomization will be a cluster, i.e., a health administrative area like a district/woreda/local government area with 1-2 SNCUs that provide a minimum package of small and sick newborn care. Each cluster will be randomized sequentially to implement the optimized iKMC model. In India and Bangladesh, there will be 3 clusters per study site where each cluster is one district with 1-2 hospitals having functional level 2-SNCUs.

Table 3. Stepped-wedge cluster-randomized trial design, by country to evaluate the impact of iKMC-optimized model

		Y0	Y1-Q1 1-3 mo.	Y1-Q2 4-6 mo.	Y1-Q3 7-9 mo.	Y1-Q4 10-12 mo.	Y2-Q1 13-15 mo.	Y2-Q2 16-18 mo.	Y2-Q3 19-21 mo.	Y2-Q4 22-24 mo.
Bangladesh	Cluster 1	Minimum care package for small babies implemented	0*	T ¥	1‡	1	1	1	1	1
	Cluster 2		0	0	T	1	1	1	1	1
	Cluster 3		0	0	0	T	1	1	1	1
	Cluster 4		0	0	0	0	T	1	1	1
	Cluster 5		0	0	0	0	0	T	1	1
	Cluster 6		0	0	0	0	0	0	T	1
Ethiopia	Cluster 1	Minimum care package for small babies implemented	0*	T ¥	1‡	1	1	1	1	1
	Cluster 2		0	0	T	1	1	1	1	1
	Cluster 3		0	0	0	T	1	1	1	1
	Cluster 4		0	0	0	0	T	1	1	1
	Cluster 5		0	0	0	0	0	T	1	1
	Cluster 6		0	0	0	0	0	0	T	1
India	Cluster 1	Minimum care package for small babies implemented	0*	T ¥	1‡	1	1	1	1	1
	Cluster 2		0	0	T	1	1	1	1	1
	Cluster 3		0	0	0	T	1	1	1	1
	Cluster 4		0	0	0	0	T	1	1	1
	Cluster 5		0	0	0	0	0	T	1	1
	Cluster 6		0	0	0	0	0	0	T	1

		Y0	Y1-Q1 1-3 mo.	Y1-Q2 4-6 mo.	Y1-Q3 7-9 mo.	Y1-Q4 10-12 mo.	Y2-Q1 13-15 mo.	Y2-Q2 16-18 mo.	Y2-Q3 19-21 mo.	Y2-Q4 22-24 mo.
Nigeria	Cluster 1	Minimum care package for small babies implemented	0*	T ¥	1‡	1	1	1	1	1
	Cluster 2		0	0	T	1	1	1	1	1
	Cluster 3		0	0	0	T	1	1	1	1
	Cluster 4		0	0	0	0	T	1	1	1
	Cluster 5		0	0	0	0	0	T	1	1
	Cluster 6		0	0	0	0	0	0	T	1

** Refers to control period in which small or sick newborn care is strengthened.*

¥ Refers to transition period ***(no measurement)***

‡ Refers to intervention period in which the iKMC implementation model scaled up

In stepped-wedge design all clusters (i.e., district, woreda or local government area with at least 1-2 iKMC implementing facilities) start in the control phase (i.e., minimum package of care for small and sick newborns) and then move to the intervention phase (i.e., the optimized iKMC implementation model) at different timepoints, till all clusters have transitioned to the intervention condition. All six clusters within each country (i.e., all 24 clusters) will start with the control condition (see Table 3). At each of six cross-over times, equally spaced in 3-month blocks, one cluster in each country will be randomized to transition to the iKMC implementation model. By the sixth transition timepoint, all 24 clusters across all countries will have transitioned to the optimized model condition. A three-months transition period is included in each cluster to allow for the intervention to be implemented. All the implementation strategies which are part of the optimized model will be implemented during this period. Briefly, these will include infrastructural changes (e.g., M-SNCUs), supplies (e.g., KMC beds, chairs, and garments), staff training and supervision, monitoring and feedback in the iKMC implementing facilities, and strengthening of newborn care to ensure early identification and referral of eligible infants to the iKMC implementing facility in skin-to-skin contact with the mother or surrogate, and strengthening of referral pathways. There will be an additional 3-month period in which all clusters will be observed under the intervention condition. Once each cluster has crossed to the intervention, it will continue to be exposed to it for the remaining duration of the study. The study will run concurrently in all four participating countries and each country will follow the same design, but countries may run over slightly different calendar dates to allow for that the different trial set-up procedures and duration in each country. Different secular trends within each country will be incorporated into the analysis to allow for this. The impact outcomes, i.e., pre-discharge and neonatal mortality will be analysed globally for the 24 clusters, while the coverage outcomes will be analysed both by country and across sites.

The rationale for a stepped-wedge design in evaluating the effectiveness of the iKMC optimized implementation model is as follows:

- There are clear benefits to the use of iKMC for newborns. Therefore, it is important for the governments/ ministries /policymakers and the local healthcare providers involved in this

implementation research study to be assured that no districts/patients are denied improved access to iKMC because of being part of a research project. Through this design, they can participate in a randomized trial and all clusters can be guaranteed to receive the intervention.

- The optimized iKMC implementation model is a complex service delivery intervention. The stepped-wedge design takes advantage of the logistical needs of delivering a complex service delivery intervention, by rolling this out in a staggered fashion to all participating sites.

- The design ensures a randomized comparison group is available to generate high-quality evidence when time trends are considered.

3.7.3. Randomization

The study will run concurrently in the 24 clusters of the participating countries (6 clusters per country). The clusters will be the unit of randomization. In addition to the criteria for site selection described in section 3.2.1, the clusters should have made an in-principle commitment to implementing the iKMC optimized model components according to the schedule assigned by the randomized allocation scheme (i.e., stepped-wedge design).

Prior to trial commencement, all clusters will be randomly assigned to one of the sequences for the time from the control period to the intervention period, using a computer-generated list of random numbers (generated by the study statistician). Investigators and study teams will remain blinded to this allocation sequence. The next clusters to be randomized will only be revealed approximately 3 months prior to each cross-over timepoint, to provide adequate time for the preparation of iKMC model implementation.

3.7.4. Trial facilities and trial participants

The trial facilities will be facilities having a functional level 2 SNCU. There should be at least one such facility in each of the study clusters. The trial participants will be preterm or LBW infants requiring care in the SNCU of the trial facilities, either born alive or brought alive to the trial facilities within 24 hours of birth, as per the inclusion and exclusion criteria in section 3.6.1. While the study will promote and strengthen immediate KMC for all preterm or LBW infants, the study population will only comprise preterm or LBW infants who require SNCU admission after birth as depicted in Figure 4.

Intervention

The intervention would be the optimized iKMC implementation model in each site. Core component of the intervention is the conversion of level 2 SNCU to level 2 M-SNCU in trial facilities during the intervention period. Preterm or LBW infants who require SNCU admission after birth, as depicted in Figure 4, will be admitted to M-SNCU where mother/surrogate will stay with the newborn on 24x7 basis and supported to provide KMC.

Control

Usual care (minimum package of care for small and sick newborns including KMC) will be provided to preterm or LBW babies during the control period. Preterm or LBW infants requiring SNCU care will be admitted to the SNCU.

Both groups: In both intervention and control period, most preterm or LBW infants will go to the postnatal or KMC wards after discharge from the SNCU/M-SNCU and will continue KMC until discharge from the trial facilities.

3.7.5. Outcomes of the stepped-wedge trial phase

The primary and secondary outcomes for stepped-wedge trial phase are as below .

The study population for the evaluation of the outcomes are the same as the study population in the model optimization phase. See Section 3.6.1 above.

Primary outcome: Proportion of preterm or LBW infants who died during the first 28 days of life (among the trial participants). The primary outcome will be analysed globally in the 24 clusters.

Secondary outcomes (measured in both intervention and control periods)

- Breastfeeding:
    - Proportion of preterm or LBW infants who are exclusively breastfed at discharge from trial facilities
    - Median age at putting the baby to the breast for the first-time during M-SNCU/SNCU stay
    - Median age at initiation of breastmilk feeding during the M-SNCU/SNCU stay
- Proportion of preterm or LBW infants with clinical sepsis: As diagnosed by the attending physician either defined by clinical signs alone or presence of clinical signs with positive laboratory screening test while in M-SNCU/SNCU
- Proportion of preterm or LBW infants who has hypoglycaemia: Any blood glucose level of <45 mg per decilitre, measured when clinically indicated during M-SNCU/SNCU stay, as per the SNCU protocol of each study
- Proportion of preterm or LBW infants who has hypothermia: Any axillary temperature <36°C during M-SNCU/SNCU stay
- Proportion of preterm or LBW infants receiving KMC at discharge (8-24 hours of skin-to-skin contact and exclusively breastfed in the 24 hours before discharge) from the trial facility

The coverage, quality and implementation outcomes will be the same as in the model optimization phase, described in section 3.6.2 above. In the stepped-wedged trial the outcomes during the intervention exposure will be compared against the outcomes during control exposure.

The outcome measurement team will collect primary and secondary outcomes through routine health records and registers and/or through interviews with the mother/family.

Implementation outcomes:

During trial phase of the study, we will continue to collect the implementation outcomes monitored during the model optimization phase, and will also collect information related to costs:

- ***Acceptability:*** iKMC including transport in skin-to-skin contact from birthing place to M-SNCU is acceptable to mothers (and/or surrogates). Mothers and caregivers are satisfied with the care received. iKMC is acceptable to health workers (facility and community).
- ***Adoption***: The challenges in adoption of iKMC by mothers, hospital managers and health providers (nurses, midwives, doctors) identified in programme learning are addressed.

- ***Adaptation***: Modifications to adapt the iKMC intervention to the social and routine health system context are implemented.
- ***Cost***: what are the costs of implementing iKMC in routine health care settings?
- ***Fidelity***: Quality iKMC care is being provided to mothers and newborns in the level 2 M-SNCUs and KMC wards and to what extent the mothers are adhering to the recommended practices.

3.7.6 Measurement strategy

The independent outcome evaluation team will collect data on impact, coverage, and process outcomes:

- **Identification of preterm or LBW infants requiring SNCU care.** The evaluation team will collect data on all preterm or LBW infants admitted to the SNCUs in the study area (all inborn and outborns brought in the first 24 hours after birth). They will also record the date and time of birth as well as the date and time of admission to the SNCU.

- **Ascertainment of vital status*:*** The evaluation team will collect the data on the vital status of all preterm or LBW infants admitted to the SNCUs in trial facilities (i.e., all inborn and outborns brought in the first 24 hours after birth) till discharge and day 28 after birth. This will be done by daily visits to all SNCUs in the trial facilities in pre-discharge period and through telephonic contact on day 28 after birth. The evaluation team will make a home visit if the infant/family cannot be reached on the telephone. The cause of death will be recorded using a standard WHO death certificate for all in-hospital newborn deaths.

- **Ascertainment of secondary outcomes**. We will strengthen the existing clinical record keeping in the SNCUs and the use of a separate SNCU register wherein the routine SNCU staff will record the key secondary outcomes like breastfeeding, clinical sepsis, hypothermia, and hypoglycaemia. During the daily visits, the study evaluation team will cross-verify the entries in the SNCU register using the clinical records and healthcare provider and/or maternal interviews. The optimal strategy will be worked out during the preparatory phase. Documentation of iKMC will be the same as in the model optimization phase.

The coverage and process outcomes will be measured as described in section 3.6.2. The measurement strategy for the secondary outcomes will be refined based on the learnings from the model optimization phase of the study.

3.7.7. Statistical analysis of the stepped-wedge trial

Sample size and power calculations

The data on impact outcome (neonatal mortality by 28 days) will be pooled across all four countries. Due to the paucity of reliable preterm birth data, sample size calculations are based on LBW estimates. We estimated that an average of 500 LBW newborns (<2 kg) born in a cluster in an iKMC implementing facility(ies) or transferred to the hospital(s) before 24hr from birth per year will be required to ensure adequate sample size. This was calculated based on birth rate of 2% in Asia and 2.5% in Africa, resulting in estimated 20,000 livebirths in Asia and 18,750 livebirths in Africa. Of which, we assumed that yearly 5% of LBW newborns in Asia and 3.5% of LBW newborns in Africa would require care at SNCU (1000

LBW infants in Asia and 656 LBW infants in Africa a year: Average 656 a year). We then assumed that 60% of LBW newborns requiring care at SNCU would be inborn babies or transferred to SNCU within 24 hours after birth (approximately 500 LBW newborns). To allow for varying cluster sizes within countries, we have assumed a 0.75 variation coefficient. With 24 clusters across countries, the total sample size would be 21,000 LBW births during the 24 months study period.

Parameter	Estimates
District population Asia	1,000,000 (250,000 per quarter)
Districts population Africa	750,000 (187,500 per quarter)
No. of Livebirth Asia [a]	20,000/year (5,000 per quarter)
No. of Livebirth Africa [b]	18,750/year (4688/quarter)
No. of LBW requiring SNCU- Asia [c]	1,000/year (250/quarter)
No. of LBW requiring SNCU- Africa [d]	656/year (164/quarter)
Average no. of LBW requiring care in level-2 units (SNCU/M-SNCU)	828/year (207/quarter)
No. of LBW newborns requiring care in level-2 units born in facilities or transferred to facility within 24 hours after birth [e]	497/year (124/quarter) rounding off to 500/year (125/quarter)
Neonatal mortality in control exposure (based on the WHO iKMC trial)[30]	15%
Relative mortality reduction	20%
Intra-cluster correlation	0.01 (0.005 to 0.02)
Cluster auto-correlation coefficient	90%
Coefficient of variation of cluster size	0.75

[a] *Assuming a birth rate of 2% in Asia*
[b] *Assuming a birth rate of 2.5% in Africa*
[c] *Assuming 5% LBW infants will require SNCU care in Asia*
[d] *Assuming 3.5% LBW infants will require SNCU care in Africa*
[e] *Assuming 60% LBW infants requiring SNCU care would be inborn/transferred to SNCU within 24 hours after birth*

Statistical power calculations consider both the clustered and stepped-wedge nature of the design. To allow for clustering, it is necessary to have estimates of intra-cluster correlations (ICC). We have been guided by patterns and determinants of ICCs as per WHO Global Survey estimations.[44] For mortality outcome we have assumed an ICCs of 0.01 (considered sensitivity at 0.005 to 0.02). Considering the stepped-wedge design, we have allowed for temporal trends as fixed period effects, and additionally to allow for variation in temporal trends across countries (or clusters within countries) we have allowed for cluster-by-exposure random effects in addition to the cluster random effects. We have therefore

incorporated a two-period decay correlation structure with a cluster autocorrelation of 90% in addition to ICCs.

We will have 92% power at a 5% significance level to detect a 20% relative risk reduction in neonatal mortality from a baseline of 15% mortality to 12% mortality in the intervention exposure. All calculations were done based on a method proposed by Karla Hemming (University of Birmingham, UK) with the Shiny CRT calculator.[45]

Stepped-wedge trial analysis: All analyses will be by intention to treat, which means that clusters will be analysed according to their randomized allocation, i.e., time at which exposure status changed from control exposure to intervention exposure irrespective of whether this was achieved at the desired time. Newborn baseline characteristics will be summarized as means and standard deviations, medians and inter-quartile ranges, or numbers and percentages, as appropriate, grouped by exposure status. The CONSORT guidelines will be followed and a CONSORT trial diagram showing the outcome rate by cluster and by exposure status will be presented.[46]

Outcome (rates, proportions, mean/median, as appropriate) will be compared by exposure status (intervention and control). For the primary and secondary outcomes, a multilevel logistic regression model will be used to estimate the effect of the intervention. The binomial distribution and log link function will be considered. The relative risk and the 95% confidence interval will be reported as the effect size estimate. The statistical analysis will adjust for clustering in the data, calendar time, and varying treatment effect between clusters, countries, and with time. We will also consider including the length of the intervention period in the model as an effect modifier. All analyses will be carried out using STATA 16.0.

The main analysis will be carried out once all outcome data have been entered into the study database and validated as being ready for analysis. A comprehensive statistical analysis plan will be developed in discussion with the trial statistician. The statistical analysis plan will be written, approved, and finalized prior to the commencement of trial recruitment.

3.8 Promote and support the government to scale up iKMC at provincial and national level

The overarching aim of this project is not only to develop optimized models for iKMC, but to make these models available for scale up nationally and internationally to reduce newborn morbidity and mortality. The project will have established both the necessary evidence base for scaling up iKMC, as well as the necessary resources, tools, materials, and strategies to do so. Assuming effectiveness, this will become the established international standard by which iKMC can be adopted and optimized across all settings. We would also have addressed questions of scalability related to scale up approach, capacity, and investment. Above all, the government would already have had the experience of implementing iKMC in multiple districts as well as observed its benefits.

In this process, WHO and the research teams will work closely with the provincial and national governments to develop a scale up strategy, investment case and implementation roadmap based on learning from the two phases of the study. In addition to supporting appropriate policies, strategies, and plans, WHO will help convene donors and partners to achieve scale up, under the leadership of the national government. The districts for model optimization and scale up will serve as demonstrable models for other districts and provinces to learn from, and the research team will be transformed to a technical support unit. WHO will also support the government to apply for grants and potential international development loans. The implementation research grant would thus initiate a sequence of actions that eventually result in national scale up of an effective intervention that has the power of revolutionizing care of preterm or LBW infants.

We expect substantial policy and practice implications of this project directly in the countries where the project will be done, as well as indirectly in other countries. Within the study countries, not only will the scale up of iKMC help achieve the ENAP target[40] related to KMC coverage, but the approach of will simultaneously strengthen other essential interventions in level 2 M-SNCUs, such as CPAP and infection prevention and management. This will also set the foundation of adding other interventions such as antenatal corticosteroids and other interventions for women at risk of preterm birth. A substantial reduction in neonatal mortality would be the expected and most desirable result.

WHO will disseminate the impact and learnings from the study to all countries and engage with the governments to introduce and scale up iKMC as part of the care of the sick and small newborn. WHO will also involve the STAGE-MNCAH&N-KMC Working Group, which is a multi-partner group in these efforts.

3.9 Cost and cost effectiveness

Evaluation of cost and cost-effectiveness of the optimized implementation model is essential to provide the economic evidence required by policymakers to adopt the model. Specifically:

- **Affordability**: Estimates of the total additional annual cost of including the model into the country level health systems, including cost per child to receive intervention in the M-SNCU, societal cost, provider, and beneficiary cost.
- **Cost-effectiveness**: The cost-effectiveness of the iKMC intervention will be compared in a selected cluster between the control and intervention period.
- **Sensitivity analysis**: Identification of key cost and epidemiological inputs that have the greatest influence on total cost and cost-effectiveness.

Costs will firstly be categorized as: research-related, programmatic, or shared research/programme costs. We will use programmatic costs only wherever possible. Programmatic cost of start-up and recurrent cost will be collected throughout the stepped-wedge trial phase: (i) preparation phase, such as establishing necessary infrastructure; and (ii) implementation phase, such as capital and recurrent costs including initial training costs and refresher training costs, running costs, salaries, procurement and maintenance costs, other training costs, quality assurance procedures, installation of equipment; and monitoring including technical support, IT equipment and resolving unexpected obstacles, cost of institutionalization; incremental costs for incorporating in HMIS, establishing dash board and periodic review meetings with all stakeholders.

The exact items to be costed will depend on the final composition of the optimized implementation model and will be identified in consultation with local stakeholders and health economics experts. We will use standard methods in consultation with health economics experts including the WHO CHOICE tool.[48]

3.10 Laying the foundation for a platform that enables introduction of additional MNH and small and sick Newborn interventions

The focus of this implementation research study is iKMC, however, the platform created can be used to introduce other small and sick newborn interventions, and other maternal and newborn health interventions. The study will build capacity of local research teams and programme implementers to conduct large-scale implementation research and will demonstrate the value of the research to a wider audience. We anticipate that the increased understanding, uptake, and 'institutionalization' of implementation science in health programmes in the participating country health system will result in important benefits.

4. Recruitment of participants, study data collection and management

4.1 Recruitment of participants

4.1.1 For the formative research and programme learning

See section 3.5.3 on formative research above. As mentioned, formative research will take place in a purposive sample of health facilities and community catchment areas across the sites where iKMC interventions will be developed. The health facilities to be included as sites in the qualitative study will be selected to ensure location, representativeness of facility characteristics eligible for implementation, and other key variables. The purpose of the formative research is to contribute to a first round of formative data collection, thus pragmatic actions are planned to ensure contextual information and perspectives from different stakeholders are obtained and synthesized to be used for model development. Ongoing programme learning throughout the model optimization phase will provide additional insights to further develop and refine the model.

Participants for formative research will be identified for the different activities planned as below. :

1) IDIs with women who had preterm birth or LBW babies who were cared for in a study facility in the last month - will be identified by research assistants from the facility registry

2) Focus group discussions (FGDs) with women in the community including those who gave birth in the last 12 months in a study facility or at home and women family members – will be identified by research assistants through community health networks.

3) FGDs with men in the community including partners of women those who gave birth in the last 12 months in a study facility or at home – will be identified by research assistants through community health networks.

4) Small group (2-3 people) or individual interviews (depending on feasibility) with traditional birth attendants, women and community group leaders and other community stakeholders; – will be identified by research assistants through community health networks.

5) Small group (2-3 people) or individual interviews (depending on feasibility) with health workers (community health workers, midwives, nurses, doctors, obstetricians, neonatologists, paediatricians and facility management) – will be identified in the different health facilities.

Maximum variation sampling will be used to encourage the recruitment and sampling to reach research participants with diverse characteristics. For example, women who had preterm or LBW babies to be interviewed should include women of different ages, geographic zones, parity and ethnicities. As data will be analyzed in parallel with data collection, we will look for thematic data saturation and adjust the sample size as necessary (e.g., discontinuing further interviews if saturation is deemed achieved, or conducting additional interviews as needed until saturation is deemed achieved).

The research teams will facilitate contact with potentially eligible participants. Each individual will be provided with an information sheet about the study, invited to participate by the research team, and if they agree, asked to provide consent.

During the model optimization phase, the programme learning team will conduct individual or small group interviews with mothers, fathers and community members, health workers, CHWs, and other stakeholders to redesign and refine the iKMC delivery model to improve its ability reach effective and quality KMC coverage. Users' and implementers' perspective on the iKMC intervention will be explored. In total, there are seven groups of participants to consider for interview: 1) mothers who do iKMC well, 2) mothers who do iKMC but not well, 3) mothers who do not do iKMC, 4) fathers, family and community members, 5) health workers who provide iKMC in the facility, 6) CHWs who identify home births, who refer newborns born at home eligible for iKMC and/or who follow-up preterm or LBW newborns after discharge, and 7) other stakeholders. These participants will be identified through the same networks as mentioned for the formative research.

4.1.2 For the outcome evaluation in the model optimization phase and the stepped-wedge trial phase

Recruitment strategy of participants for the evaluation of the primary outcome in the model optimization phase and the stepped-wedge trial phase will be the same.

Recruitment of participants involves the following activities in the community, primary-care facility, and iKMC implementing facilities. Community-based activities aim to improve identification of eligible babies that are born outside the study facility. The primary care facilities, staff/ health workers will be oriented, sensitized and trained to identify pregnant women who are likely to give birth to a preterm or LBW baby. They will be trained to 1) refer pregnant women with risk of preterm birth or LBW babies to an iKMC implementing facility 2) measure birth weights immediately and accurately after birth and refer LBW requiring SNCU care in skin-to-skin contact with mother or surrogates to the iKMC implementing facility. At the iKMC implementing facility, physicians will identify eligible mothers and babies in the labour room and operation theatre for those born in the facility; or in the emergency, OPD, SNCU or KMC ward, where babies will be referred. For babies who are referred, triaging will be done to categorize babies i) who need to be referred to a tertiary care hospital, ii) those who can be admitted to KMC ward and do not need SNCU care and iii) those who will need to be admitted in the M-SNCU. All staff in the study will receive extensive training in the WHO minimum package of care for preterm and LBW babies and iKMC. A register will be created and will have names of all preterm or LBW babies in all facilities. The research assistant will have access to this register to ensure that all eligible mothers and babies are enrolled in the study.

4.2 Data collection and data management for model optimization phase

4.2.1 Formative research and programme learning

Information on the different data collection activities during the formative research is outlined above. Instruments, or semi-structured discussion guides, for the different activities will be developed guided by barriers and facilitators learned from the iKMC trial[30] and the scale-up KMC study[42]. We will also explore the feasibility of proposed activities. All instruments will be reviewed and adapted by the study teams in each site and translated and tested prior to data collection, as part of training of the research teams.

Women who had a preterm or LBW baby in a study facility will be interviewed to understand personal journeys, and barriers and facilitators to receiving care for their babies, particularly for KMC and for

starting KMC immediately after birth, their experience of the care received during their stay in the facility as well as support needed after discharge from the facility to care for their baby. We will use a gender and intersectionality analysis approach to understand how gender relations and power dynamics within the household, community and encounters with health workers influence a woman's decisions about care and her experience of receiving care for a preterm or LBW baby's birth and the support she needs to continue providing care in the home. This will provide us with a holistic understanding of an individual woman's care pathway from the home, through different levels of facility-based care, and potential power dynamics that may need to be addressed in the implementation strategy.

We expect about 20-30 women will be interviewed only once and the interview will take no longer than one hour. In addition, the standard operating procedures will recommend interviewers to offer pauses for mothers during the interview. Privacy will be ensured.

Some of the specific questions to be addressed are:

- From woman's perspective: how do women feel about providing skin-to-skin care, starting immediately after birth? How do women feel about the extended stay in the facility and what support is available to ensure there is support in the home?
- From a community perspective: What support can they provide to the mother for the care of the baby? Who can serve as an appropriate surrogate to mothers for providing iKMC in each site according to their culture and how their availability at the time of birth can be ensured?
- From system perspective: how can the women be given appropriate care and comfort while they are in the hospital to provide KMC to their infants and to ensure their satisfaction with the care provided? How can space to accommodate mothers and infants remaining together be ensured in the M-SNCUs?
- What skills do health workers need to support mothers to provide iKMC?
- Where KMC has been practiced already, what are the challenges that the mothers face in providing continuous skin-to-skin contact and exclusive breastfeeding to their babies and how can they be resolved?
- If not being practiced, from the providers' perspectives what could be the anticipated challenges in implementation.

Discussions with other household members including men will be conducted to determine their perspectives and experience with the care of the preterm or LBW infant and the support they can provide to the mother. This will aid in the choice of surrogates and steps needed to ensure presence of surrogates at the time of birth and to ensure continued KMC in the home. This will help us to optimize health system strategies addressing women, families, and communities. Separate FGDs will be held with women and with men.

Compensation for participants involved in the formative research will be provided based on the local norms and standards in each setting. These participants may also be provided with light refreshment (such as a cold beverage and snack).

Interviews with health managers and health workers of different cadres (nurses, midwives, doctors, CHWs) across the networks of care (primary health centre, first level facility, second level and higher-level facility) to understand factors affecting the implementation of iKMC and continued KMC. This will

help us to understand the current provision of early newborn care for preterm or LBW babies and explore the feasibility and acceptability of different components of the iKMC implementation model. Given that caring for women and babies born preterm or LBW requires a team-based approach across multiple cadres (CHWs, nurses, midwives, obstetricians, paediatricians), we will explore how hierarchies and gendered relations between cadres may influence care for both women and babies.

At the start of the interviews and group discussions, participants will be asked to confirm that they have received the information sheet and signed the consent form. IDIs are expected to last approximately 60 minutes, focus group discussions are expected to last approximately 90 minutes.

Both IDIs and group discussions will be conducted by researchers with experience in qualitative methods and in maternal and newborn health programmes.

As mentioned, data will be analyzed in parallel with data collection, monitoring for thematic data saturation. Interviews and discussions will be digitally recorded, and notes of each session will be taken, including descriptive and reflective information. All notes will be anonymized to ensure privacy and confidentiality of participants. Participants and sites will be given identifying numbers for reference. All data will be stored and backed up on secured password- protected system and will not be accessed nor shared with a third party without prior permission. See Section 4.3 for additional information.

The team will identify key themes emerging from the notes of the different activities and will report extracts to provide examples of specific issues. Themes identified will be mapped to the different domains of the Consolidated Framework for Implementation Research and to key areas related to iKMC intervention implementation, identifying key barriers and facilitators for iKMC implementation.

As mentioned, for programme learning activities discussions will be organized with different stakeholder groups to receive input on what is working and not working well in iKMC implementation. Instruments and processes will be adapted from the formative research. Assuming consensus in each of the population groups mentioned, we estimate five participants from each group to be interviewed for a total of up to 40 interviews during each 3-4 months cycle. The final number of interviews might vary according to consensus levels. At the start of the interviews, participants will be asked to confirm that they have received the information sheet and signed the consent form.

4.2.2 Model optimization outcome measurement

Birth weight of live births in iKMC implementing facilities, primary level birthing facilities and at homes: the evaluation team will collect birth weight data of live births in all health facilities in the district through periodic visits to these facilities. The number of preterm or LBW babies requiring admission to the level 2 M-SNCU will be documented based on the admission criteria for that unit (e.g., <1.8 kg). They will also record the date and time of birth for such LBW babies born in iKMC implementing facilities, as well as date and time of birth and of admission for babies born at lower-level facilities and at home.

The outcome measurement team will collect the data on the time of initiation of iKMC and who initiated iKMC through daily visits to newborn care units in iKMC implementing facilities in the district. For babies born at home or in a primary level facility and brought to iKMC implementing facility, information on the time of initiation of KMC will be ascertained from the mother or another caregiver and data will also be taken from the register in the primary level facility. Daily information on the hours of skin-to-skin contact will be collected by the evaluation team (by asking the mothers) while the baby is in the level 2 M-SNCU. Staff at the iKMC implementing facilities will record the time of initiation and duration of KMC in hospital records.

Detailed information on definitions, numerators, and denominators for each outcome in the model optimization phase is described in Table 4.

Study team will train and supervise staff at the iKMC implementing facilities to record above mentioned information in the register accurately. Spot checks will be conducted by the study team to ensure quality of data collected in the iKMC implementing facilities. Ongoing monitoring and discussions by the WHO team will also include regular review of data.

Table 4. Definitions, numerators, and denominators of outcomes in model optimization phase

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
Primary coverage outcomes				
Proportion of preterm or LBW newborns requiring care in the M-SNCU born in or brought to the iKMC implementing facility, within 24 hours of birth, who received iKMC.	Numerator: Number of preterm or LBW newborns who received iKMC (in an iKMC implementing facility) Denominator: Number of preterm or LBW newborns admitted in the M-SNCU born in or brought to the iKMC implementing facility, within 24 hours of birth (Expressed as a percentage)	A baby is considered to have received iKMC if: 1. Skin-to-skin contact is initiated within 2 hours after birth if the baby is born within the iKMC implementing facility, or if the baby is born outside the iKMC implementing facility, within 2 hours of reaching the iKMC implementing facility (who reach the facility within 24 hours of birth) and 2.Skin-to-skin contact is provided by a mother/surrogate for at least 8 hours per day during the stay in the level 2 M-SNCU hospital (average hours per day for the overall M-SNCU stay)	Outcome measurement team	By checking M-SNCU register / clinical records filled by routine staff in M-SNCU and interviews with mothers at M-SNCU
Other outcomes				

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
Proportion of preterm or LBW infants who are transported to an iKMC implementing facility within 24 hours after birth among those referred to an iKMC implementing facility	Numerator: Number of preterm or LBW infants who are transported to an iKMC implementing facility within 24 hours after birth Denominator: Number of preterm or LBW infants* requiring referral to an iKMC implementing facility *Infants requiring referral born in birthing facilities or at home whose birth weight is known		Outcome measurement team	By checking M-SNCU register / clinical records filled by routine staff in M-SNCU At iKMC implementing facility when the baby is admitted Birth weight and or gestational age data will be collected from all birthing facilities for the denominator
Proportion of preterm or LBW infants on respiratory support (any oxygen or CPAP) who received skin-to-skin contact > 8 hours/day in the M-SNCU	Numerator: Newborn who received skin-to-skin contact > 8 hours/day in the M-SNCU Denominator: Preterm or LBW infants on respiratory support in the level 2 M-SNCU (Expressed as a percentage)		Outcome measurement team	By checking M-SNCU register / clinical records filled by routine staff in M-SNCU and interviews with mothers At M-SNCU
Proportion of preterm or LBW infants receiving KMC (8-24 hours of skin-to-skin contact and exclusively breastfed) in the 24 hours before discharge from the iKMC implementing facility	Numerator: Number of preterm or LBW infants receiving 8-24 hours of skin-to-skin contact and exclusively breastfed in the 24 hours before discharge Denominator: Number of preterm or LBW infants who admitted in the M-SNCU in the iKMC implementing facilities who are discharged alive (Expressed as a percentage)		Outcome measurement team	By checking hospital register / clinical records filled by routine staff i ward and interviews with mothers At iKMC implementing facility

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
Proportion of preterm or LBW infants exclusively breastfed at discharge	Numerator: Infants who are exclusively breastfed Denominator: Preterm or LBW infants requiring M-SNCU care born alive in or brought alive to the iKMC implementing facility i		Outcome measurement team	By checking hospital register / clinical records filled by routine staff i and interviews with mothers at iKMC implementing facility (discharge area)
Median age at putting the baby to breast for the first-time during M-SNCU stay (Expressed in median hours/days)	Median age in hours/days when a preterm or LBW infants is first put to mother's breast during M-SNCU stay		Outcome measurement team may cross-verify the information using the clinical records.	By registering data on all preterm or LBW infants admitted to M-SNCUs in CRF At iKMC implementing facility when the baby is admitted and interviews with mothers

We will use the standards for reporting implementation studies (StaRI)[47] statement to report on the design and development of the optimized implementation model development.

4.2.3 Stepped-wedge trial phase

During the stepped-wedge design trial phase, an independent outcome evaluation team will collect data on impact, coverage, and process outcomes as described under section 3.3.4. The evaluation team will collect data on all preterm or LBW infants admitted to the SNCUs in the study area (all inborn and outborns brought in the first 24 hours after birth). They will also record the date and time of birth as well as the date and time of admission to the SNCU. The evaluation team will collect the data on the vital status of all preterm or LBW infants admitted to the SNCUs in trial facilities (i.e., all inborn and outborns brought in the first 24 hours after birth) till discharge and day 29 after birth. This will be done by daily visits to all SNCUs in the trial facilities in pre-discharge period and through telephonic contact on day 29 after birth. The evaluation team will make a home visit if the infant/family cannot be reached on the telephone. The cause of death will be recorded using a standard WHO death certificate for all in-hospital newborn deaths.

All mothers whose preterm or LBW infants have required SNCU care in the trial facilities in both the intervention and control period will be approached for permission to follow up on day 29 to determine the vital status of the baby at the end of the neonatal period. The follow up on day 29 for ascertaining the vital status at the end of the neonatal period will be done by the evaluation team. The research assistant will have access to the facility birth register that are routinely maintained in the birth facility which will have the names of all women who have given birth in that facility. Facility birth register will be used to check again the record of completed interview to help ensure that all women and babies who should have been enrolled will be enrolled and therefore will help ensure that all newborns are followed up.

We will strengthen the existing clinical record keeping in the SNCUs and the use of a separate SNCU register wherein the routine SNCU staff will record the key secondary outcomes like breastfeeding clinical sepsis, hypothermia, and hypoglycaemia. During the daily visits, the study evaluation team will cross-verify the entries in the SNCU register using the clinical records and healthcare provider and/or maternal interviews. The optimal strategy will be worked out during the preparatory phase. For documentation of continued KMC post-discharge, the outcome evaluation team will administer a pre-tested questionnaire to the mother telephonically on day 29. Documentation of iKMC implementation will be similar as in the model optimization phase.

Detailed information on definitions, numerator, and denominator for each outcome in the model optimization phase is described in the Table 5, however it is important to note that the measurement strategy for the secondary outcomes will be refined based on the learnings from the model optimisation phase.

Table 5. Definitions, numerators, and denominators of outcomes in stepped-wedge trial phase

	Numerator and denominator	**Specific notes to the indicator**	**Data collected by**	
			Who	**How and where**
Primary outcome to be measured in both intervention and control periods for each study cluster				
Proportion of preterm or LBW infants who died during the first 28 days of life (among trial participants)	Numerator: Number of neonatal deaths by 28 days of age Denominator: Number of preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities (Expressed as percentage or rate per 1000 livebirths)		Outcome evaluation team	By daily visits to M-SNCU/SNCU until discharge, and through telephone contact on day 29 of age post-discharge
Secondary outcomes to be measured in both intervention and control periods for each study cluster (the measurement strategy will be refined based on learnings from phase 1)				
Breastfeeding outcomes: 1. Proportion of preterm or LBW infants who are exclusively breastfed at discharge from trial facilities	Numerator: Number of preterm or LBW infants who are exclusively breastfed Denominator: Number of preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities who are born alive in or brought alive to the trial facilities.		First outcome will be measured by the outcome evaluation team Second and third outcomes will be measured using routine M-SNCU/SNCU staff records and maternal interviews. Outcome	Using hospital registers and maternal interviews

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	**How and where**
2. Median age at putting the baby to breast for the first time in the M-SNCU/SNCU stay (Expressed in median hours/days) 3. Median age at initiation of breastmilk feeding during the M-SNCU/SNCU stay (Expressed in median hours/days)	Age in hours/days when a preterm or LBW infants is first put to mother's breast during M-SNCU/SNCU stay in the trial facilities. Age in hours/days when a preterm or LBW infant receives first breastfeeding or breastmilk feeding during facility stay Both these outcomes would be measured in preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities		evaluation team may cross-verify the information using the clinical records. The optimal strategy will be worked out during the preparatory phase.	
Proportion of preterm or LBW infants with clinical sepsis	Numerator: Number of preterm or LBW infants who are diagnosed to have clinical sepsis by the attending physician during M-SNCU/SNCU stay Denominator: Preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities (Expressed as percentage)	As diagnosed by the attending physician either defined by clinical signs alone or presence of clinical signs with positive laboratory screening test while in M-SNCU/SNCU		
Proportion of preterm or LBW infants who has hypothermia	Numerator: Number of preterm or LBW infants with any instance of axillary temperature <36°C, during M-SNCU/SNCU stay Denominator: Number of preterm or LBW infants	Temperature measurement schedule may be site-specific (M-SNCU/SNCU based protocol)		

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
	admitted in the M-SNCU/SNCU in the trial facilities (Expressed as percentage)			
Proportion of preterm or LBW infants who has hypoglycaemia	Numerator: Number of preterm or LBW infants with any measure of blood glucose < 45mg/dl (2.6mmol/l) during M-SNCU/SNCU stay Denominator Number of preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities (Expressed as percentage)	Blood glucose measurement schedule may be site-specific		
Proportion of preterm or LBW infants receiving KMC (8-24 hours of skin-to-skin contact and exclusively breastfed) in the 24 hours before discharge from the iKMC implementing facility	Numerator: Number of preterm or LBW infants receiving 8-24 hours of skin-to-skin contact and exclusively breastfed in the 24 hours before discharge Denominator: Number of preterm or LBW infants admitted in the M-SNCU/SNCU in the trial facilities who are discharged alive (Expressed as a percentage)		Outcome evaluation team	By checking hospital register / clinical records filled by routine staff i ward and interviews with mothers

Data collection and management for stepped-wedge design trial phase, process and outcome data described in the section 4 will be captured using a tablet device or in net-book computers. The front-end component of the data collection module will have range, logical, consistency check inbuilt into the programme ensuring data integrity and data quality. Data in the back end will be stored either in MySQL, an open-source relational database management system, or a Structure Query Language server relational database management system. A two-way data synchronization will be done daily to ensure the server and the data collector's machine have updated data to implement data integrity checks. A data monitoring module will have features such as to produce data outputs for regular data quality check, generation of the visit schedules and data completeness checks and analyzable data set

In partnership with local research institutions, a dedicated common data management platform will be developed and implemented across all sites, for both the model development phase (formative phase) and

the stepped-wedge trial phase. Each team will be responsible for data management for its site. A standardized database across all sites will be created where each site can adapt the system according to their own needs. A standardized database for the study will be created using open-source platform. The questions, response options, variable names and data structure will be identical for all sites. Each site will have a data manager who will be responsible for performing data quality checks, managing local query, and ensuring correctness and completeness of information in CRFs. Any discrepancies will be immediately addressed. All effort will be made to minimize missing data.

4.3 Data management and confidentiality

The following measures will be taken to ensure participant confidentiality:

- Study data for each participant will be identified by a unique anonymous ID number.
- The local study register linking personal information and trial ID numbers, and all personal information of participants, will be kept separate from the CRFs
- Study documents will be kept securely under lock and key in the research offices and will not be accessible, other than to the researchers
- Data will be entered by study ID number in the password-protected data management system to which only study staff will have access
- The study report will not contain the names of any participants
- After completion of the study all study documents, including audio recordings, will be archived in accordance with institutional and national rules for clinical research archiving for a minimum period of 10 years.
- The data will be digitally archived for permanent storage.

A good clinical practice -compliant data management system will be used to protect data in every aspect of data management from data collection to data analysis. Data will be linked to participant identification numbers and each site will have a data manager responsible for ensuring data quality. To facilitate harmonization of data and ensure data quality, we will use a standard set of case report forms (CRFs); core variable tables; and data collection processes. Data will be password protected and stored in a local server of each site. An automated database backup module will be used to take the database backup daily. One copy of the database will be stored in an encrypted form in another computer in the network and one copy will be maintained outside the office premise under the strict supervision of the data manager.

Data quality improvement: Imbedded range and consistency checks in electronic CRF (online real-time checks) will be put in place at the time of data collection. A scheduled, two-layer data quality check for completeness and accuracy will be implemented both at the site and at the WHO Data Coordination Centre. Data is owned by each study site. The study site will share cleaned de-identified cumulative dataset (with participant ID) with WHO for review and feedback through secure password protected systems. Monthly data monitoring reports will be shared with study sites and WHO study coordination team to monitor progress and quality of data. Random spot checks and data validation will be coupled with independent audits.

5. Ethical considerations

All project activities will be conducted in accordance with international norms and standards on ethical research practice, including the Declaration of Helsinki and the Council for International Organizations of Medical Sciences International Ethical Guidelines for Health-related Research Involving Humans.[49,50,51] Ethical approval for this project will be sought from WHO and relevant Institutional Review Boards

(IRBs) in participating countries/sites. Country leads will facilitate any study-related monitoring, regulatory inspections, audits, and ethical review at their site as required. Scientific approvals will be obtained at the local, national, and international levels.

Current evidence showed the study intervention itself has proven to be safe and efficacious. As per the recently-released WHO recommendations[39], provision of KMC immediate after birth to all preterm or LBW babies will be considered the standard of care); therefore, initiation of iKMC will not require a consent from participants. For formative research, programme learning and outcome measurements that includes direct data collection from mothers, caregivers, health workers, health managers, and stepped-wedge design (ascertainment of vital status at day 29), a written consent will be requested. As described in 4.2.1, all mothers who have received the intervention will be approached for permission to follow up on day 29 to determine the vital status of the baby at the end of the neonatal period. A verbal confirmation for follow up will be obtained by the research assistant at discharge.

Mothers who are minors will be eligible for enrolment in this study. Assent from the mother will be obtained before recruitment but the consent form will be signed by the minor mother's guardian (parent). A legally acceptable representative can be either of the parents or the guardian of infant in the absence of parents. When explaining the details in the information sheet, the study team member will ask if the parent or guardian has any questions and if there are any, will answer the questions.

The consent forms will be translated into a local language that facilitate the consent process. For illiterate participants the consent form will be read by the research staff in presence of a literate witness.

Additionally checking questions will be asked to assess the participants understanding about the study. Once the team is satisfied that the study procedures are well understood, consent will be documented. A copy of the signed consent form will be returned to the participants.

In the consent process, participants will be briefed that the mother and baby will continue to receive standard care as per hospital policy in case of refusal to participate in the study or withdrawal of consent. Mothers will be made aware that even after providing consent, they will be free to withdraw from the study at any stage and in case they withdraw later, they and their babies will continue to receive the same quality of care as required by any other patient with the same condition. At the time of withdrawal of consent, the mothers will be free to decide about use of collected data.

Approach to informed consent for each of the study activities is summarized in Table 6.

Table 6. Consenting of study participants

Activity **(What is the consent for?)**	**Participant**	**How to identify the participant?**	**Type of informed consent**	**Who will administer the consent?**	**Timing of the request for informed consent**	**Consent form**
Consent for participation in formative research and programme learning	Mothers and families of preterm or low-birth-weight babies Representatives of community groups and leaders Health workers at community and facility level and health facility managers	Facility registers and stakeholder networks	Written informed consent	Research assistant	Upon the interview or group discussion for formative research	ICF_Mother_formative_research ICF_community stakeholders_formative_research ICF_health workers_formative_research
Consent for granting access to clinical data for research purpose (for model optimization and stepped-wedge trial phases)	All mothers whose newborn baby (ies) are eligible for care at M-SNCU/SNCU	Facility registers	Verbal informed consent	Treating health care provider	Upon admission to the M-SNCU/SNCU	4_ICF_Verbal_consent_data_sharing
Consent for participating in outcome evaluation in model optimization phase and stepped-wedge trial phase	All mothers whose newborn baby (ies) are eligible for care at M-SNCU/SNCU	Facility registers and physicians	Written informed consent	Research assistant	Upon admission to the iKMC implementing facility M-SNCU/SNCU	5.1_ICF_Written_consent_Mother_model_optimization_phase 5.2_ICF_Written_assent_Mother_model_optimization_phase 5.3_ICF_Written_consent_Mother_trial_phase

Activity (What is the consent for?)	Participant	How to identify the participant?	Type of informed consent	Who will administer the consent?	Timing of the request for informed consent	Consent form
						5.4_ICF_Written_assent_Mother_trial_phase

* During the stepped-wedge trial phase, mothers will be informed about the study throughout the control and intervention periods (informed consent starts with the control phase).

5.1 Benefit

There are a few well documented benefits of intervention. The biggest benefit of this study may be that the iKMC may lower the mortality and morbidity rates in preterm or LBW neonates who takes part in the study. Since the mother and baby will be in close contact from birth during iKMC, the baby will be more likely to be colonized by the mother's protective microbiome and more likely to receive early breastfeeding. There will be also less handling of the baby by other persons, thus reducing the risk of infection. The iKMC will also increase mother-baby bonding and potentially reduce mother's anxiety. Implementing institution will be benefited with updated equipment in SNCU and with trained staff and health care providers to provide KMC immediately after birth. Implementing country will be benefited from materials which will be made available during the study, including, but not limited to, national guideline for M-SNCU, Standard operating procedure (SOP) for role clarification of the health workers in SNCU, labour and birthing room, postnatal ward, and triage, update national guideline and training manual of KMC with provision of iKMC.

5.2 Risk

There might be a risk of poor outcome of a baby if s/he is preterm or LBW babies and unstable, however there will be well-equipped establishment of M-SNCU run by thoroughly trained staff, with continuous monitoring system, hence risk will be mitigated.

The unavailability of mothers/caregivers willing to provide consent might be a recruitment barrier due to maternal illness or post-caesarean section and the absence of other family members at the hospital during the early admission period. The health workers will be well trained in counselling of the family member for providing the iKMC in the absence of mother. Hence this risk will be mitigated. Community engagement will also help mitigate this risk by creating awareness regarding iKMC and the potential need for surrogates.

There might be a risk of being overloaded of preterm or LBW newborns in the iKMC implementing facility because of efforts to strengthen the referral system. We will strengthen the capacity of the iKMC implement facility to provide the WHO minimum care package for preterm or LBW newborns.

6. Study governance

6.1 WHO oversight

In advance of the start of implementation, all sites will be visited by WHO to ensure that all arrangements are in place and to support teams in any challenges being faced. The initial visit will also aim to be an

opportunity to strengthen collaboration of the project with health authorities. The Principal Investigator from each site will be required to submit a brief project status report every three months to WHO. A formal progress report on designated WHO forms will be submitted by each site every year and this will be shared with the study Steering Committee. WHO technical staff will conduct at least one monitoring visit to each site every twelve months. There will be a detailed structured review of study implementation at each visit

6.2 Steering Committee

WHO will establish a Steering Committee (SC) and be responsible for organizing its meetings. Meetings will take place prior to study implementation, every 9-12 months and at the end of the study. The Steering Committee will be the technical body responsible for the design and implementation of the study. The committee will be convened by WHO that will also be its Secretariat. It would be comprised of each of the PIs, the study coordinators from WHO, a representative of the Ministries of Health of the four countries and 2-3 experts. The SC will also have the responsibility for coordinating activities in the various sites, supervising the implementation, and reporting of the progress of the study, and for the planning and review of the analyses and presentation of the study results.

6.3 Data Safety Monitoring Board

A data safety monitoring board (DSMB) will be appointed by the WHO before initiation of the stepped-wedge trial. The roles and responsibilities of the DSMB in this trial include:

- To safeguard the interests of the study participants, potential participants, investigators, and sponsors
- To assess the safety and efficacy of the study intervention according to data available at a predefined schedule. This schedule will be fixed in advance by the DSMB
- To monitor the study's overall conduct and quality, and protect its validity and credibility
- To make recommendations to the trial steering committee concerning continuation or termination of study or any other modification necessary based on the observed effects of the intervention

The DSMB will be composed of qualified professionals who are completely uninvolved in the running of the study. Names and qualifications of the DSMB members will be provided to WHO Ethics Committee prior to commencement of the trial. It is planned that the DSMB will be composed of five members, including an independent Chair, a statistician, and three technical experts familiar with the intervention, maternal and newborn health care, and the study methodology. DSMB members should be independent and constructively critical of the ongoing trial, but also supportive of aims and methods of the trials.

Serious adverse events of neonatal mortality will be reported to the DSMB quarterly. No formal interim analysis is planned for either efficacy or futility. However, in the scale- up cluster RCT, the DSMB will closely monitor trends of neonatal mortality for safety reasons. Closed reports of neonatal mortality at the 24 networks of care will be reported to the DSMB at the end of each period. The reports will be blind to the exposure (control or intervention) through which each care network is passing. Though the intervention is proven to be efficacious in research settings, integrating the intervention to routine care settings will likely meet challenges and encounter associated risks (section 6.2). If the DSMB interpreted that the trend in neonatal mortality was concerning, unblinding of the exposure would be done by the trial statistician to assess the potential association with the intervention. All DSMB members will review the protocol before agreeing to join the Board. DSMB will discuss and formulate the DSMB charter which includes triggers set for data review or analyses, definition of a quorum, format used in the reports and guidelines for monitoring the study. Guidelines should also address stopping the study for safety concerns.

7. Research capacity strengthening

To promote and strengthen knowledge sharing across sites, a visit to a M-SNCU (established as part of the IKMC trial) will be organized for all the sites to observe and learn about the benefits and feasibility of M-SNCUs in real time.

This study provides an important opportunity to enhance research capacity in the countries. Activities will be planned to target young researchers and mentor them along with senior and mid-level local researchers involved in the study, such as

- Emphasis on local research ownership with support from international / WHO team
- Training on methods, data collection & analysis
- Leading the local workshops with the ministries.
- Embedding of postgraduate research projects in project activities
- Special sessions, concrete smaller responsibilities, for young researchers
- Support for young researchers to attend WHO meetings, proposal development workshops, country presentations and paper writing workshops

As part of efforts to implement the above activities, we will establish linkages between institutions with strong implementation science training programmes and local research groups to support implementation research capacity building before and during the study. Additional support will be provided through workshops, webinar series, online discussion boards and ongoing communication and coaching calls throughout the project.

8. Project Timeline

Phase one: 21 months

1. Initial organization of teams and site identification – 3 months
2. Formative research, implementation of Minimum package of care and initial model development – 6 months
3. Model optimization – 12 months

Phase two: 27 months

1. Scale up and stepped-wedge evaluation of model – 24 months
2. Phase 3 activities – 3 months

Overall project duration: 48 months

9. How this project will contribute to ENAP goals and targets

The scale up of interventions included in this project will contribute to the following ENAP targets:

- Reduction of neonatal mortality in all countries to <12/1000 live births: About three quarters of all neonatal deaths occur in preterm or LBW infants. The most effective interventions to reduce this mortality are KMC, antenatal corticosteroids, respiratory support including CPAP and prevention and management of infections. This project will substantially reduce these deaths not only because of scale up of iKMC, but also of the other interventions at level 2 special newborn care units (please see table below in which we have highlighted the interventions that will be strengthened at level 1 and level 2.

- Improvement in ENAP coverage targets for KMC and for treatment of serious newborn infections.

- Service readiness target, 80% of districts in every country have at least one *functional* inpatient level 2 special newborn care unit.

Evidence-based interventions for inpatient care for small and sick newborns at the ENAP health systems level of care are described in Annex 1. The interventions which will be strengthened in this study, in addition to scaling up iKMC, are highlighted in blue. These interventions which will be strengthened in this project are also summarized below:

9.1 Level 1 primary care facility

- referral of women who are a high risk of delivering a preterm or LBW infant to a higher-level hospital for childbirth (not mentioned in the ENAP table)

- accurate recording of birth weight of the baby

- referral of babies below the birth weight cut-off for special newborn care in skin-to-skin contact with the mother or a surrogate.

9.2 Level 2 special newborn care

- Thermal care

- Kangaroo mother care, including follow up

- Assisted feeding for optimal nutrition (cup feeding and nasogastric feeding)

- Safe administration of oxygen

- Prevention of apnoea

- Detection and management of neonatal infection

- Detection and management of hypoglycaemias

- Safe administration of intravenous fluids

- Continuous positive airway pressure
- Comfort and pain management

10. COVID-19 related risks and potential mitigation

The COVID-19 pandemic is likely to pose challenges and have potential risks to this project. These include lockdowns and restrictions which make it difficult to achieve high coverage of interventions, with both supply side and demand side problems. WHO has been working for the past months with these countries on mitigation of indirect effects of the pandemic on maternal and child health. The lessons learned and shared across countries will be used to keep maternal and newborn health in the focus of health programmes. Surges of cases may cause delays in the project, which we will build into the implementation strategy and minimize the financial implications of any delays on the project. Another challenge restrictions on international and domestic travel which may complicate planned activities such as in-person workshops, technical support, and site monitoring visits. If necessary, many of these activities will be conducted remotely over a series of participatory webinars, virtual tours, or other remote methods that we have learnt in the past 18 months. We do not anticipate that these remote activities will increase the costs beyond available travel budget.

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12. Annexes

Annex 1. Every newborn action plan (ENAP) health system level for newborn care organizing services by level of care (Inpatient care for small and sick newborns: requirements for care at different health system levels)

The interventions we will focus on within this study's scope are highlighted either in yellow (part of ENAP interventions) or pink (part of our project).

Level	Type of care provided	Health system requirements		Standards of care & evidence-based interventions
PRIMARY	Essential newborn care	Place	• Space for childbirth, with specific areas and for postnatal care for mother and baby to stay together • Infrastructure for handwashing • Outpatient facility for routine postnatal care and management of newborn problems	• Immediate newborn care (thorough drying, skin-to-skin contact of the newborn with the mother, delayed cord clamping, hygienic cord care) • Neonatal resuscitation (for those who need it) • Early initiation and support for exclusive breastfeeding • Routine care (Vitamin K, eye care and vaccinations, weighing and clinical examinations) Prevention of mother to child transmission of HIV • Assessment, management, and referral of: o bacterial infections including treatment of Possible Severe Bacterial Infection (PSBI) where referral not possible* o jaundice and diarrhoea o feeding problems o birth defects and other problems • Pre-discharge advice on mother and baby care and follow up • Referral of women who are at high risk of delivering a preterm or LBW baby to a higher-level hospital for childbirth • Skin to skin contact with the mother or surrogate
		People	• Skilled attendance 24/7 (e.g., midwifery and nursing staff +/- doctors) • Support staff for cleaning	
		Health technologies	Linen/towels for drying and wrapping • Bag and mask resuscitation • Radiant heater, warmth source • Thermometer • Equipment for clean cord care • Vitamin K, eye ointment • Weighing digital scale, tape • Immunization commodities • Antibiotics • Oxygen • Pulse oximeter	
		Support system	• Water, sanitation, and hygiene (WASH) and infection prevention and control • Communication and functional referral system • Newborn patient record and facility register • Written policy on zero separation • Easy access to fathers/caregivers	

Level	Type of care provided	Health system requirements		Standards of care & evidence-based interventions
SECONDARY	Special newborn care	Place	• A dedicated warm space of a facility, with specific areas for resuscitation, stabilization, and care • Dedicated area for KMC • Accommodation for mothers (space for mother to room in and stay with their baby) • Electricity supply (e.g., generator back-up) • Infrastructure for storage of human milk	• Thermal care • Comfort and pain management • Kangaroo mother care, including follow up* • Assisted feeding for optimal nutrition (cup feeding and nasogastric feeding) • Safe administration of oxygen • Prevention of apnoea • Detection and management of neonatal infection • Detection and management of hypoglycaemia • Detection and management of jaundice • Detection and management of anaemia including blood transfusion • Detection and management of neonatal encephalopathy • Seizure management • Safe administration of intravenous fluids • Detection and referral management of birth defects • Immediate Kangaroo Mother Care *Transition to intensive care* • Continuous positive airway pressure** • Exchange transfusion** • Detection and management of necrotizing enterocolitis (NEC)** • Specialized follow up of high-risk infants (including preterm)
		People	• Specialized nursing and midwifery staff 24/7 • Doctor with neonatal skills on call • Support staff (nursing auxiliary and cleaning staff)	
		Health technologies	• Syringe pump and accessories (e.g., neonatal cannula) • • Feeding equipment (nasogastric tubes and cups/spoons) • Basic diagnostics (e.g., glucometer, urine dipsticks) and micro-methods • Medicines (e.g., antibiotics, caffeine, IV fluids, phenobarbital) • Mobile X-ray system • Warmers and cots • Effective phototherapy equipment (e.g., LED) • Continuous positive airway pressure	
		Support system	• 24/7 access to the facility for mothers and caregivers • Facilities for bathing, laundry, and cooking/food • Clinical charts and facility register	
TERTIARY	Intensive newborn care	Place	• Designated intensive care ward • 24/7 uninterrupted electricity • Space for mother to room in and stay close to their baby	• Advanced feeding support (e.g., parenteral nutrition) • Mechanical/assisted ventilation, including intubation • Screening and treatment for retinopathy of prematurity • Surfactant treatment • Investigation and management of birth defects • Paediatric surgery • Genetic services
		People	• Nurses with specialized competencies in neonatal care 24/7 • Doctors with specialized competencies in neonatal care 24/7 • Neonatologist on call • Other specialist doctors with competencies in neonatal care (anaesthetics, surgery, radiology, cardiology, neurology, ophthalmology • Allied health professional (physiotherapy, nutrition, speech therapy, occupational therapy, audiology, etc.)	
		Health technologies	*In addition to special care equipment and commodities* • Intermittent positive-pressure ventilation, high flow oxygen via nasal cannula • Monitoring equipment • Surfactant therapy • Advanced medicines • Supplies for advanced nutrition support (e.g., total parenteral nutrition) • Specialist equipment and accessories	
		Support system	• 24/7 advanced laboratory support other diagnostics including medical imaging • Transport and safe referral if needed • Hospital information management system	

** Outpatient care.*

***The interventions listed under special care mark a transition to intensive care. Hospitals providing special care should introduce these interventions before upgrading to intensive care.*

Annex 2. Site specific information

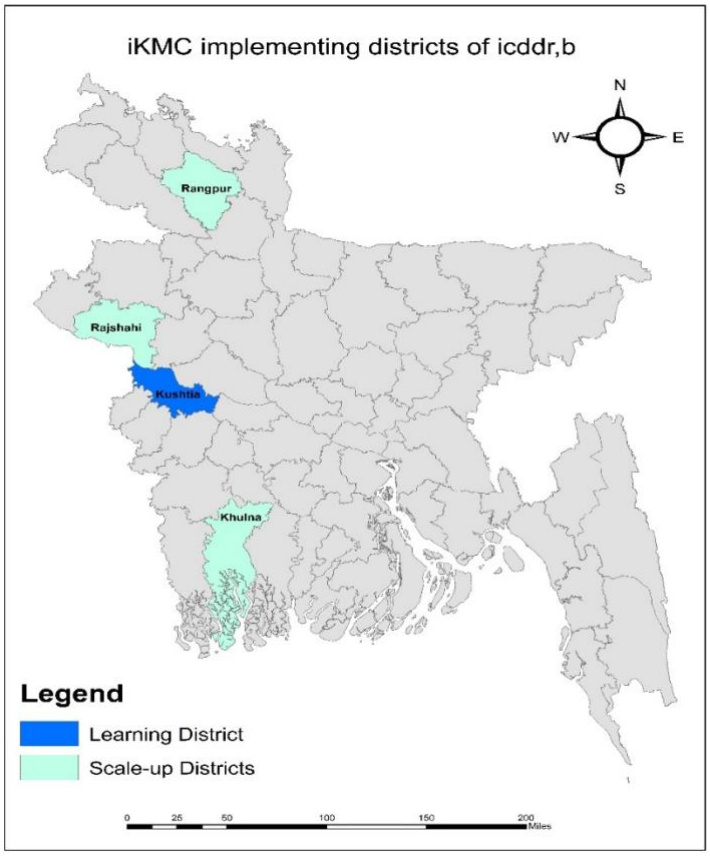
Site name: Bangladesh – Kushtia District (icddr,b)

1. **Description of study area (briefly describe the criteria that justifies selection of the site):**

1.1 **Learning district: Kushtia** district

The first phase of the study will be conducted in **Kushtia** district (Figure 1), north-western part of Bangladesh. The total area of the district is 1,601 km^2 with a population density of 1,207 people per km^2. There are **six sub-districts** (Table 1), 4 municipalities, 39 wards, 70 mahalas, 61 union parishads, 710 mouzas, and 978 villages in this district [1]. The enumerated population of Kushtia district is around 2.2 million [1].

Figure 1: Map for iKMC implementing districts of icddr,b



We propose to design and optimise the iKMC implementing model in Kushtia **250-bedded General Hospital**. Kushtia 250-bedded General Hospital is a secondary-level public hospital situated in Sadar sub-district, Kushtia town. It offers sick child outpatient and inpatient care services and has a labor and delivery unit, a **20-bedded paediatric inpatient ward** with **10 beds** dedicated for newborn care, a **12-bedded Special Care Newborn Unit (SCANU)**, and a **3-bedded KMC corner**. It is the sub-district

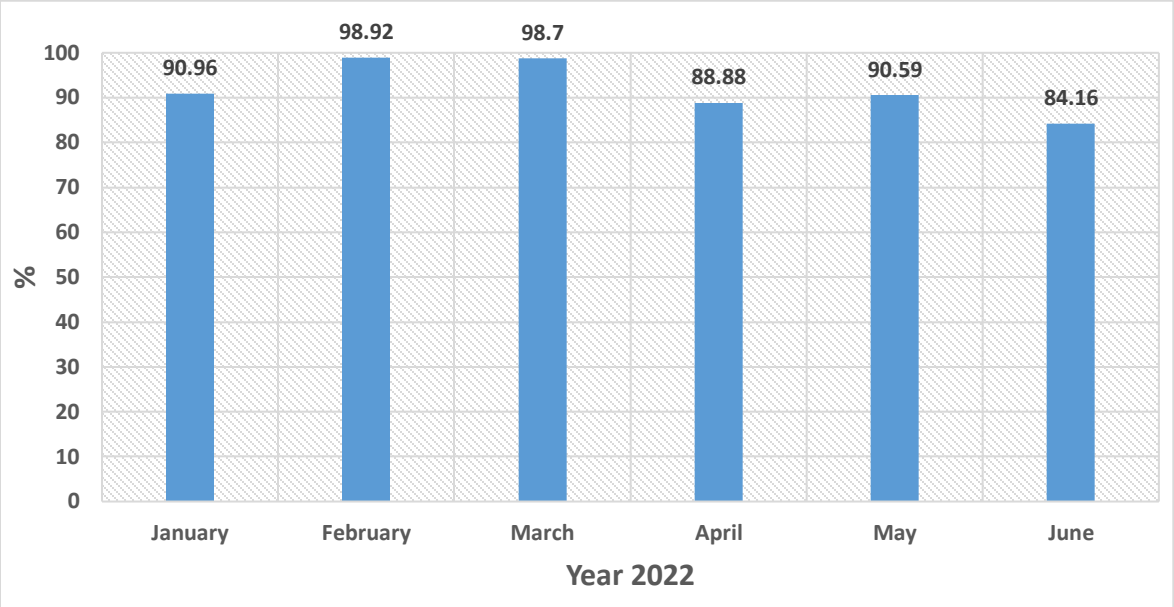
hospitals' referral facility, and all services are free of cost. Nationally, in terms of delivery, KMC, and SCANU utilisation in 2021, Kushtia General Hospital has placed 8th, 4th, and 28th respectively.

Table 1: Facility mapping of Kushtia district

	▪ SUB-DISTRICT NAME						
TYPE OF HEALTH FACILITY	**Kushtia Sadar**	**Bheramara**	**Daulatpur**	**Khoksha**	**Kumarkhali**	**Mirpur**	**Total**
District Hospital (secondary level referral)	1	0	0	0	0	0	1
Upazila Health Complex (primary level referral)	0	1	1	1	1	1	5
Union Health and Family Welfare Centre (health centre)	13	5	13	5	12	12	60
Community Clinic (health outpost centre)	37	18	43	17	56	37	208

From January-June, 2022, **903 normal deliveries** and **921 caesarean sections** were conducted in Kushtia General Hospital resulting in **1,756 livebirths** and 112 stillbirths. In the same time period, **356 babies admitted** in the **SCANU**- among them **115 were in-born**, and **241 were out-born**. Among the admitted newborn, **203** newborn had a birth weight of >2000gms, **22** had 1800-1999 g, **49** had 1500-1799 g, and **82** had <1500 g respectively. The number of deaths occurred in SCANU was 81. The most cited complication for SCANU admission was **low-birth-weight (LBW) (n=188)** (Table 2). The other frequently cited complications were respiratory distress/perinatal asphyxia (n=145), sepsis (n=62), and **prematurity (n=28)**. The **average duration** of SCANU stay was **5.1 days**. The average bed occupancy rate for SCANU was **92%** during Jan-Jun' 2022 and the highest was 99% in February'22 (Figure 2). The size of the SCANU is 785 sq ft. There is a team of 19 members dedicatedly are working in SCANU including **two senior paediatric consultants**, **three medical officers**, **12 nurses**, and two support staff (Table 3). Among the nurses, **seven** are trained in kangaroo mother care.

Figure 2: Bed occupancy rate at SCANU, Kushtia General Hospital (Jan-Jun, 2022)



In first 6 months of 2022, **111 babies received KMC** in the hospital – among them **46** were in-born and **65** were out-born. The majority (77.5%) of these babies were discharged on request. Only 34 babies received 1st follow-up after discharge, and 19 of them received 2nd follow-up after the discharge. The **average duration** of stay in the **KMC corner** was **5** days. There were no reported deaths in the KMC corner in the hospital in the mentioned time period.

Table 2: Distribution of newborn admitted in the KMC and SCANU at Kushtia General Hospital during Jan-Jun 2022

	January'22	**February'22**	**March'22**	**April'22**	**May'22**	**June'22**	**Total**
# of live births	325	277	290	287	276	301	1756
# of babies born LBW (≤2000gms)	6	11	7	10	11	7	52
# of in-born babies received KMC	7	11	7	10	4	7	46
# of out-born babies received KMC	12	7	14	7	13	12	65
# of total babies received KMC	19	18	21	17	17	19	111
# of babies admitted to SCANU	54	51	64	59	65	63	356
Complaints of SCANU admission							

	January'22	February'22	March'22	April'22	May'22	June'22	Total
Prematurity	19	23	26	30	22	18	138
LBW	32	32	30	38	30	31	193
Respiratory Distress	27	26	11	40	34	19	182
Jaundice	2	4	3	2	3	2	16

Table 3: Human resource and logistic arrangement in SCANU, Kushtia General Hospital

Human Resource	
# of Paediatric Consultant	2
# of Medical Officer	3
# of Nurses	12
# of Support Staff	2
Logistic Arrangement	
# of Bed	12
# of Radiant Warmer	8
# of CPAP	0
# of Pulse Oximeter	3
Provision of Oxygen support	Present
Provision of IV fluid	Present
Provision of KMC	Absent
Space (sq ft)	785

Kushtia General Hospital also serves as the first referral point for the other five sub-districts. Each of the five sub-districts has one primary-level hospital (Upazila Health Complex/UHC) with **50 inpatient beds**. On average, they serve catchment populations of around 300,000. Each offers outpatient IMCI services and has a labour and delivery ward and a KMC corner. In Jan-Jun 2022, an average of **167 deliveries** were conducted in these five UHCs. On average, **20 LBW babies** (<2000gms) were born in each UHC in the first half of 2022. The utilisation of KMC services in these UHCs is low - an average of **10 babies received KMC** in these UHCs. We will establish a functional referral linkage among these UHCs with Kushtia General Hospital during phase-1 of this study.

One advantage of Kushtia for phase-1 of this study is that it has a reasonably well-functioning health system. Nationally around 48% of births occur in health facilities, which is 69% in Kushtia. Similarly, the coverage of 4+ ANC is also higher in Kushtia than that of the national average. Another advantage is that Kushtia was the district learning laboratory for designing, developing, demonstrating, and testing the comprehensive newborn care package (CNCP), including KMC during 2015 -2017. icddr,b was responsible for conducting the assessments and evaluation. KMC services were introduced in the General Hospital and a few of the sub-district hospitals, one of the first among public hospitals in Bangladesh. Learning from this implementation research in Kushtia helped Government of Bangladesh (GoB) to identify the gaps and operational challenges and finalise the national KMC implementation package for national scale-up. Moreover, Kushtia was also the demonstration site for introducing the outpatient-based management of "Possible Serious Bacterial Infection" where referral is not possible in Bangladesh. Learning from the implementation research helped to finalise the implementation package and make evidence-based decisions for national scale-up. The feasibility of introducing pulse oximetry in routine IMCI services was assessed very recently through an implementation research study in Kushtia. Based on the demonstration learnings and key findings, GoB has decided to introduce pulse oximetry in IMCI services throughout Bangladesh. Hence, selecting Kushtia will help us in two ways: Firstly, the newborn

services in Kushtia are reasonably functioning, and the General Hospital-based KMC service is reasonably good in terms of caseload, adherence, duration, and follow-up; Secondly, the health managers of Kushtia are sensitised to the concept of co-designing newborn interventions and implementation research, which may contribute in optimise iKMC model and successfully implement the intervention package.

1.2 Other Districts that study will be scaled-up:

The other three districts that we have selected to scale-up iKMC intervention are **Khulna, Rajshahi, and Rangpur** (Figure 1). The implementing sites will be public Medical College Hospitals of each districts. Medical College Hospitals are the tertiary-level service providers and serve as the highest level of the referral system.

Khulna is a divisional city with **9 sub-districts**, 1 city corporation, 74 unions, and 1,119 villages in its vicinity. It is an area of 4,389 km^2. The population density per km^2 is 710 and there is a total of approximately 3.0 million inhabitants are currently residing in this very district [1]. Khulna Medical College Hospital (KMCH) is the highest referral point for all the healthcare facilities in the district.

In the first half of the year 2022, in total, almost **2,953 deliveries** were conducted which resulted in **2,808 live birth** and **141** stillbirths in KMCH. It had provided KMC to **229** intra-mural and extra-mural newborns in its **14-bedded KMC corner**. It also has a **44-bedded** well-functioning neonatal intensive care unit (**NICU**). The total size of the NICU is **5,000 sqft**. Neonates with hypoxemia, prematurity-related complications, and LBW mostly admitted in the NICU. From January-June 2022, a total of **1,149 neonates** with hypoxemia, **839** with prematurity-related complications, and **687** with LBW (<2000gms) were admitted in NICU (Table 4). Other commonly cited complications for NICU admission were: respiratory distress, sepsis, and jaundice, etc. The human resource of the NICU is supported by **2 paediatric consultants**, **2 medical officers**, **19 nurses**, and 9 support staff (Table 5).

Table 4: Distribution of newborn admitted in the KMC and SCANU at Khulna Medical College Hospital during Jan-Jun 2022

	January'22	**February'22**	**March'22**	**April'22**	**May'22**	**June'22**	**Total**
# of Live Births	490	448	520	530	297	523	2808
# of babies born LBW (≤2000gms)	-	-	110	101	91	140	442
# of In-born babies received KMC	-	-	36	25	27	19	107
# of Out-born babies received KMC	-	-	39	22	30	31	122
# of total babies received KMC	-	-	75	47	57	50	229
# of babies admitted to SCANU	338	285	324	310	297	323	1877
Complaints of NICU Admission							
Prematurity	137	128	148	158	132	136	839
LBW	124	131	134	160	77	185	687
Hypoxemia	219	198	139	200	180	213	1149
Respiratory Distress	137	104	113	88	91	136	669
Jaundice	15	12	22	20	17	11	97
Sepsis	31	31	32	23	27	25	169

Table 5: Human resource and logistic arrangement of NICU, Rajshahi Medical College Hospital

Human Resource	
# of Paediatric Consultant	2
# of Medical Officer	2
# of Nurses	19
# of Support Staff	9
Logistic Arrangement	
# of Bed	44
# of Radiant Warmer	10
# of CPAP	2
# of Pulse Oximeter	3
Provision of Oxygen support	Present
Provision of IV fluid	Present
Provision of KMC	Absent
Space (sqft)	5000

In Khulna district, there is one district-level hospital and **nine UHCs**. In January-June 2022, **105 vaginal deliveries** and **158 caesarean sections** took place in the DH and an average of 111 vaginal deliveries took place in the UHCs. Among the live birth outcomes, **13 babies and 115 babies** were delivered with LBW (<2000gms) in the DH and UHCs respectively. The reported KMC uptake in **DH was 264** and in **UHCs was 10** for the first half of the year. Most of these critical cases of these facilities are often referred to KMCH, therefore, it also gives us an opportunity to bring a large number of out-born iKMC eligible neonates to enrol in the study.

Our 2nd implementing site for scale-up is Rajshahi Medical College Hospital (RMCH). Rajshahi district has **9 sub-districts**, 1 city corporation, 71 unions, and 1,853 villages. It is 2,407 km^2 in size and home to 2.6 million people with a population density of 1,100 per km^2 [1].

On average **714** facility births take place in RMCH each month and **100 in-born** and **out-born** newborn get treatment in its NICU. Therefore, the NICU of RMCH besides managing about 50 in-born patients, also serves about same number of out-born neonates each month. It has a **6,600 sqft** NICU with **40 beds**. Most of the newborns admit in the NICU with the complaints of LBW (<2000gms) and prematurity-related complications (Table 6). Besides, it also serves a large number of neonates with sepsis, jaundice, congenital anomalies etc. The NICU is managed by **2 Assistant Professors**, **6 Medical Officers**, **23 nurses,** and 8 support staff (Table 7).

Table 6: Distribution of newborn admitted in the KMC and SCANU at Rajshahi Medical College Hospital during Jan-Jun 2022

	January'22	**February'22**	**March'22**	**April'22**	**May'22**	**June'22**	**Total**
# of Live Births	826	1031	800	-	869	759	4285
# of babies born LBW (≤2000gms)	40	29	48	-	15	-	132
# of In-born babies received KMC	11	1	3	10	4	7	36
# of Out-born babies received KMC	0	0	0	0	0	0	0
# of total babies received KMC	11	1	3	10	4	7	36
# of babies admitted to SCANU	123	57	81	93	79	98	531
Complaints of NICU Admission							
Prematurity	94	42	56	73	42	32	339
LBW	94	42	56	62	42	32	328
Hypoxemia	72	51	50	21	56	30	280
Respiratory Distress	60	20	35	65	48	34	180
Jaundice	5	0	5	2	2	4	18
Sepsis	15	35	17	17	22	32	138

Table 7: Human resource and logistic arrangement of NICU, Rajshahi Medical College Hospital

Human Resource	
# of Paediatric Consultant	-
# of Medical Officer	6
# of Nurses	23
# of Support Staff	8
Logistic Arrangement	
# of Bed	40
# of Radiant Warmer	30
# of CPAP	4
# of Pulse Oximeter	9
Provision of Oxygen support	Present
Provision of IV fluid	Present
Provision of KMC	Absent
Space (sqft)	660

RMCH serves as the highest referral point for a **10 UHCs**. In January-June 2022, number of vaginal deliveries took place for UHCs from Jan-Jun 2022 was **1,245**. Among the live birth outcomes, **52 babies** were delivered with LBW in UHCs. The reported **KMC uptake** in UHCs was **22** (on average) for the first half of the year. Implementing iKMC in RMCH will avail us to serve a large range of neonates with different health conditions and test iKMC' s role in improving their quality of health status.

Our 3rd implementing site for this phase is Rangpur Medical College Hospital (Rangpur MCH). Rangpur MCH is the highest referral point for **eight sub-districts**, 1 city corporation, 83 unions and 1,435 villages. Almost 3.0 million people reside in Rangpur district with a population density of 1,320 km^2 [1].

A total of **1,575 live births** took place at RMCH from January to June 2022. Among them, births with low weight (**<2,000 gm**) account for approximately **200 cases**. Rangpur MCH has a **36-bedded NICU** where on average **288 newborn** receive treatment each month. The ratio of in-born patients and out-born patients served in NICU was **8:2** in the first 6 months of 2022. Alike KMCH and RMCH, the most cited complaints for NICU admission in Rangpur MCH were LBW and prematurity-related complications (Table 8). However, a large number of neonates with hypoxemia, respiratory distress, and jaundice also took admission at NICU. There are **3 paediatric consultants**, **23 nurses,** and 9 support staff working in NICU to support the treatment of the patients admitted (Table 9).

Table 8: Distribution of newborn admitted in the KMC and SCANU at Rangpur Medical College Hospital during Jan-Jun 2022

	January'22	**February'22**	**March'22**	**April'22**	**May'22**	**June'22**	**Total**
# of Live Births	295	283	283	265	225	224	1575
# of babies born LBW (≤2000gms)	45	27	32	55	35	0	194
# of In-born babies received KMC	16	10	13	16	11	7	73

	January'22	February'22	March'22	April'22	May'22	June'22	Total
# of Out-born babies received KMC	24	18	24	27	13	28	134
# of total babies received KMC	40	28	37	43	24	35	207
# of babies admitted to SCANU	277	304	306	280	263	301	1731
Complaints of NICU Admission							
Prematurity	70	60	60	126	124	143	583
LBW	63	95	95	147	147	140	687
Hypoxemia	42	60	60	71	68	82	383
Respiratory Distress	86	143	143	120	95	47	634
Jaundice	41	64	64	80	77	97	423
Sepsis	36	30	30	14	7	14	131

Table 9: Human resource and logistic arrangement of NICU, Rangpur Medical College Hospital

Human Resource	
# of Paediatric Consultant	03
# of Medical Officer	-
# of Nurses	23
# of Support Staff	9
Logistic Arrangement	
# of Bed	36
# of Radiant Warmer	14
# of CPAP	4
# of Pulse Oximeter	15
Provision of Oxygen support	Present
Provision of IV fluid	Present
Provision of KMC	Present
Space (sqft)	-

In Rangpur, the number of UHCs is **eight**. In January-June, 2022, an average of **218 vaginal deliveries** took place in the UHCs. Among the live birth outcomes, **43 babies** (on average) were delivered with LBW in UHCs. The reported KMC uptake in UHCs was **25** for the first half of 2022.

In terms of facility delivery, approximately 61%, 53%, and 47% of births take place in the facilities in Khulna, Rajshahi, and Rangpur respectively whereas national average is 48%. So, an advantage of choosing these three districts is, that it allows us to measure the impact of iKMC in reasonably better performing and average performing districts both. Another point we considered while selecting these three districts are the size of NICUs have in their MCHs are relatively spacious, therefore, the establishment of M-NICU will be easier to implement. The last point we considered is that the M-NICU

established in those MCHs can serve as references and learning points for the next-level national scale-up for M-SCANU and M-NICU.

2. The linkages that were established with the local institutions (government, health system, etc)

Bangladesh health system is a centrally governed health system. The different programmes and departments such as Maternal, Newborn, Child, and Adolescent Health, Hospital Services Management, and Upazila Health Care etc. work together under Directorate General of Health Services (DGHS) of Ministry of Health and Family Welfare. to deliver quality health services. To implement the iKMC, we have established communications with Director, Line Directors, Programme Managers, and Deputy Programme Managers of relevant departments, and programmes.

We collaborated with government led National Newborn Health Programme (NNHP) & Integrated Management of Childhood Illness (IMCI) under Maternal, Newborn, Child, and Adolescent Health Programme (MNC&AH) as primary implementers for iKMC study. The representatives from these programmes during proposal submission followed by protocol development workshops had been ensured in different capacity. Deputy Programme Manager (DPM) of NNHP is engaged in the study as one of the co-investigators in the global protocol and presence of Line Director, Programme Manager and five other DPMs of NNHP had been ensured during several formal and informal sensitization and protocol development workshops respectively. The PM and two of the DPMs of NNHP are also the co-investigators of the Icddr,b's iKMC country protocol. icddr,b and NNHP had implemented several projects together earlier and few highlights from those are IMCI pulse oximetry implementation study, preterm birth prevention and management study, newborn signal function study, IMCI training module and chart booklet update according to WHO guideline and study related to possible severe bacterial infection. NNHP will again lead the co-design workshop of the iKMC model development with other government stakeholders, professional bodies, and development partners on behalf the icddr,b team.

In addition to that we also collaborated with Hospital Services Management, Hospitals and Clinics Services, Upazila Health Care of the DGHS to implement the iKMC model in the designated healthcare facilities. Previously icddr,b implemented studies such as oxygen survey, IPC due to Covid-19 with the collaboration of Hospitals and Clinics Services and better health district model study with Upazila Health Care. Maintaining the continuity, the presence of the Line Director, Deputy Director, and Programme Manager of these departments had been ensured during the proposal development, sensitization and protocol development workshops in the capacity of co-investigators and implementers. Being the policy makers, their role in developing and managing the referral system among the implementing facility, community and primary healthcare facilities and providing intervention in the iKMC implementing facilities are instrumental. They will not only guide us to develop a strong referral system, however they will be the focal implementers to establish and maintain the referral ecosystem during the implementation and national scale-up.

We also have ensured presence of various professional bodies and development partners such as Bangladesh Perinatal Society, Bangladesh Neonatal Forum, and Bangladesh Midwifery Society. We also linked with the prominent neonatologists and Obs&Gyn experts from Dhaka Children's hospital and the country's only medical university Bangabandhu Sheikh Mujib Medical University. WHO, Bangladesh and Save the Children have substantial contribution in ensuring the wellbeing of the newborn and preterm babies in Bangladesh, hence we will also establish communication and collaboration with WHO country office and Save the Children, Bangladesh for their technical support. Through the collaboration and professional linkage, we will ensure the presence of government stakeholders, professional bodies, expert practitioners and development partners pivotal role in implementing new interventions like iKMC through taking part in advocacy, providing technical support, and expert consultation.

Besides, Since Kushtia had been the implementing site for several studies of icddr,b, icddr,b's investment in creating the professional linkage with the health system officials of different position and ranking is phenomenal in Kushtia. icddr,b maintains a good professional understanding with the Civil Surgeon, Superintendent of the General Hospital and Upazila Health and Family Planning Officers of UHCs. Thus, we have received the due support from them in our previous studies conducted in Kushtia. This goodwill and networking will be wielded to ensure the successful implementation in this study.

Finally, as M-SCANU needs infrastructural changes, thus we plan to collaborate with the Health Engineering Department, Local Government Engineering Department, and Public Works Department to redesign and renovate the SCANU and NICU to M-SCANU and M-NICU respectively.

3. Description of the process that will be followed to identify participants to the study at the site:

The population of interest will be preterm (i.e., <37 weeks of gestation) and low birth weight (<2000gms) newborns in the entire network of health care facilities in the study area, irrespective of their residence. To identify the potential participants, firstly, we will organize i) advocacy and sensitization meeting with key stakeholders, public and private, engaging MOHFW in the lead ii) capacity building of clinical providers at iKMC providing facilities; iii) coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births.

Training sessions for the healthcare providers at the implementing health facilities will be organized so that they can identify the women with a high likelihood of preterm birth (PTB) at <37 weeks of gestation or low birth weight (LBW) baby during routine clinical care. We will also train the providers at the primary/lower-level health facilities of both the public and private sectors on in the study area on accurate birth weight measurement, the study interventions, including diagnosis of women with a high probability of preterm birth so that they can identify the women with the likelihood of preterm delivery and identification of LBW babies. A pool of master trainers (MT) of the district will be developed by national level core trainers. MTs will training the clinical providers of the districts. They will also contribute technical supervision to ensure quality of care.

4. Complete description of consent (and assent process): as described in the generic protocol.

5. Given the country context, the risk/benefit assessment for all participating groups (e.g., children, families, institutions, countries, etc.).

Benefit

- The biggest benefit of this study may be that the iKMC may lower the mortality and morbidity rates in preterm or LBW neonates who takes part in the study.
- Since the mother and baby will be in close contact from birth during iKMC, the baby will be more likely to be colonized by the mother's protective microbiome and more likely to receive early breastfeeding.
- There will be also less handling of the baby by other persons, thus reducing the risk of infection.
- The iKMC will be a useful method that can be useful for improving the mental health of mothers.
- The institution will be benefited with updated equipment in SCANU and with trained staff on iKMC.

- Country will be benefited with updated SoP/National guideline for mother-SCANU, developed SoP for role clarification of the HCWs in SCANU, labour room, postnatal ward and triage, update national guideline and training manual of KMC with provision of iKMC.

Risk

- There might be a risk of poor outcome of the baby as all of the participants will be LBW and/or preterm or unstable. There will be well-equipped establishment of Mother-SCANU & well-trained HCPs with 24/7 continuous monitoring system, hence this risk will be mitigated.
- The unavailability of caregivers willing to consent and provide the iKMC services within 2 h after birth might be a major recruitment barrier due to high rates of maternal illness or post-caesarean section and absence of other family members at the hospital during the early admission period. The healthcare providers will be well trained in counselling of the family member before the delivery for providing the iKMC in the absence of mother. Hence this risk will be mitigated.
- There might be a risk of being overloaded of LBW neonates in the iKMC implementing facility because of establishing functional referral system. We will strengthen the capacity of the iKMC implement facility to provide standard minimum care package for the LBW neonate.
- The Covid-19 pandemic might pose challenges and have potential risks to this project. These include lockdowns and restrictions, which make it difficult to achieve high coverage of interventions, with both supply side and demand side problems. Another challenge might be the restrictions on international and domestic travel, which may complicate planned activities such as in-person workshops, technical support and site monitoring visits. If necessary, many of these activities will be conducted remotely over a series of participatory webinars, virtual tours or other remote methods.

6. Types of services/interventions that will be offered by referral, and the linkages that will be established with such institutions/services, in order to ensure the smooth referral.

The following activities will be done in order to ensure the smooth referral to iKMC

Policy change advocacy required for iKMC

- Advocacy meetings with policymakers of Ministry of Health & Family Welfare
- Update national guideline and SOP for M-SCANU and M-NICU
- Update national guideline and training manual of KMC with provision of iKMC
- Iterative sensitization workshops for establishing "zero separation" norm and early initiation and exclusive breastfeeding

6.1 Intramural birth

6.1a Arrangements in labour room and operation theatres for smooth transfer of mother and neonate to M-SCANU from labor room or operation theatre

- Establish cross-collaboration of Obs&Gyn and neonatology departments
- Provision of waiting space for surrogates
- Ensure logistic support such as KMC sling and hygiene products
- Provide wheelchairs to carry the skin-to-skin contact providing mothers and surrogates

6.1b Training and mentoring of doctors, nurses, and midwives for iKMC implementation

- Support the arrangement of the trainings for the HCWs of SCANU, labour room, postnatal ward and triage on WHO minimum package of care for preterm and LBW babies and iKMC

- Series of workshop will be conducted among the healthcare providers working in the pediatric word in the iKMC implementing facility to strengthening their capacity to appropriately identify the LBW neonate to iKMC.
- Series of workshop will be conducted among the healthcare providers working in the pediatric word in the iKMC implementing facility to strengthening their capacity to refer the LBW neonate to iKMC.
- We will check the BEmONC register regularly to ensure the effective referral procedure for the LBW neonates.

6.2 Extramural birth

The study primary care facilities are aimed at maximizing access of LBW babies to iKMC-implementing facilities as-

6.2a Identification of pregnant women who are likely to give birth to a preterm or LBW infant and their referral to an iKMC implementing facility

- Implement the WHO screening tool to identify the pregnant women with preterm/LBW risk babies.
- We will conduct training followed by refresher training on WHO screening tool among health care provider in UHCs and UHFWCs.
- Establish strong referral linkage between the primary-level and iKMC facilities by stakeholders and local government consultation

6.2b Accurate birth weights and referral of LBW infants with mother or surrogate to iKMC implementing facility

- Ensure high quality birth weighing machines availability at the primary-level facilities
- Support training on birth weight and gestational age measurement among the HCWs in primary-level facilities
- We will conduct sensitization workshop, training followed by refresher training, follow-up and reviewing among healthcare providers in UHCs and UHFWCs in iKMC implementing districts to strengthening their capacity to refer the LBW neonate to iKMC facility.

Private facility-based activities are aimed at supporting some private families where high-volume deliveries occur.

6.2c Sensitisation

- Authority and healthcare providers from the private health care facility will be sensitised about the iKMC.
- We will conduct training followed by refresher training on WHO screening tool, birth weighing, and appropriate referral among healthcare providers in private facility.

6.2d *Follow-up and review*

- We will conduct follow-up meeting at 3-monthly and will review their performance on referral.

Community-based activities are aimed at supporting initiation of iKMC at the facilities as-

6.2e Promote birth at a health facility

- Sensitisation of the Community Support Groups (CSG), and Community group (CG) about the iKMC
- Arrange community awareness campaign by involving CSG, CG, CHCP and local government
- Engage FWAs, CSBAs, and HAs to counsel pregnant mothers and families

6.2f In case a home birth, identify a preterm or small baby and promote immediate care seeking at iKMC implementing facility

- Create family awareness by campaign through "MA Shova (mothers meeting)" by CHCP to bring sick small newborn to iKMC implementing facility
- Initiate a Hotline number to inform the iKMC facility about the birth of sick newborn.

6.2g Community actions to ensure transport of mothers and newborns to appropriate health facilities and to support care of preterm or LBW baby

- Engage community support groups and local government to develop 'Mom-van' to transport mothers and newborns to iKMC facilities

6.3 Referred to higher level facility are aimed at referring very sick newborn to higher level facility-
6.3a Referred from the iKMC facility

- We will refer the very sick child from Khustia General Hospital to Bangabandhu Sheikh Mujib Medical College Hospital (BSMMCH) in Faridpur, formerly known as Faridpur Medical College Hospital, if required. This hospital has SCANU with highly experienced and efficient doctors and other staff. The SCANU has 14 incubators and 12 beds for the stable children and 2 KMC corners.

7. **Data Management: The data management will be as described in the** master protocol. Further detail will be written once overall data management strategy is decided.

8. **Data Analysis:** The analysis will be conducted jointly in accordance with the master protocol

9. **Sample Size:**

For stepped wedge design phase, sample size will be calculated. During model optimisation, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. **Dissemination Strategy (**How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.

This dissemination of the study findings will be done through the presentation in different in-house, national, international seminars, and conferences for local and international audiences. National-level audiences will be government programme implementers, professional bodies and non-governmental organizations at national and sub-national levels. As government officials are engaged in this study, site visits will be performed by them regularly throughout the study. Periodically research team will share the findings with national and sub-national level stakeholders. We are planning to share the formative research findings with stakeholders through series of consultative workshops and meeting. So that the stakeholders are aware of the findings and can give their input where necessary. It will also enable the implementation of the intervention, and scalability by sharing expert ideas and views of the stakeholders. During the implementation and scale-up phase shared results will help stakeholders to adopt and learn. Through the dissemination meetings, the key research findings will be shared with the participants of the study. The study findings will also share with international stakeholders such as India, Ethiopia, Nigeria, and funding organization.

The important findings of this research will be shared with the communities in the study area through counselling and community meeting. It is expected that sharing this result with the community will increase the facility birth and promote immediate care seeking for preterm or LBW babies. These meetings will be arranged with the help of CHWs, district health staff, and other community stakeholders such as community leaders or community health committees, if present. Queries of the community will be responded by the study team and local stakeholders.

Moreover, we will be focusing on different international conferences related to newborn health to share our findings. We anticipate disseminating this study result in form of publications such as internal bulletin, peer-reviewed journals, and policy brief. The local research team and the personnel from the health ministries will be the lead authors of the publication.

11. Additional ethical considerations at the study site:

We do not anticipate any additional ethical concerns other than what is written in the master protocol.

12. Translated consent forms: forms have been shared with the IRB.

13. Local Ethical Approval or proof of submission: please refer to the table of IRB submission.

14. The CVs of the investigators: CVs have been submitted with the Master Protocol.

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Site name: Bangladesh –Manikganj District (Projahnmo)

1. Description of study area (briefly describe the criteria that justifies the selection of the site):

1.1 Learning district: ***Manikganj***

Manikganj district will be the learning district for the iKMC study. The district is situated in the Dhaka division. The district is comprised of seven Upazilas (subdistrict), each with an average population of 200,000. Compared to most of the districts in Bangladesh, this district has relatively higher antenatal care (ANC) coverage by a medically trained professional (85%) and an institutional delivery rate (~70%)-conditions amenable to implementation of iKMC. However, Bangladesh's Multiple Indicator Cluster Survey 2019 estimated that the neonatal mortality rate (NMR) in the district is 32 per 1000 live births, which is comparatively higher than the national NMR (26 per 1000 live births).

The district has one district hospital, six upazila health complexes, and a network of public health facilities below the subdistrict level providing primary health care operated by the Ministry of Health and Family Welfare (MOHFW) of the Government of Bangladesh (GoB). In addition, there are about >30 private-for-profit and NGO health facilities providing varying levels of care, including delivery care.

The 'District Hospital' in Manikganj is a 250-bedded secondary level health facility operated by DGHS/MOHFW. It serves as the referral center for other primary-level health facilities in the district. The hospital has the provision of Comprehensive Emergency Obstetric and Newborn Care (CEmONC) including a well-functioning Special Care Newborn Unit (SCANU) and a dedicated KMC ward to provide minimum care for preterm and low birth weight newborns (e.g., care at birth, respiratory support, feeding support, infection prevention management). The 15 bedded-SCANU is equipped with lifesaving equipment and supplies (e.g., radiant warmer, safe oxygen use, pulse oximeter, CPAP, phototherapy machine.) to treat small and sick newborns. The hospital is staffed with obstetricians, pediatricians, anaesthesiologists, medical officers, and nurses, however the number of staff are not sufficient especially pediatrician and nurse in SCANU. The staff working in the pediatric department (physicians and nurses) are trained in Comprehensive Newborn Care Package (CNCP), KMC, Emergency Triage Assessment and Treatment (ETAT), and Sick Newborn Care. The SCANU provides 24/7 services for both inborn and out-born newborns within the district.

The Monno Medical College Hospital is a 500 bedded private tertiary care facility. It is situated in the Ghior subdistrict of Manikganj district. This hospital has 10 bedded SCANU and provides care to PTB and LBW babies for both inborn and out-born newborns within the district.

1.2 Other Districts that study will be scaled up: ***Tangail, Gopalganj, and Sylhet****.*

Tangail and Gopalganj districts are in the Dhaka division and Sylhet district is in the Sylhet division. Since the icddr,b team plans to work in Khulna and Rajshahi divisions, these districts are selected to ensure a general representation of the country and meet the site selection criteria. There is a 250-bedded secondary level "District Hospital" in each district, operated by DGHS of the MOHFW. The district hospital is generally located in the Sadar subdistrict (district headquarter) and serves as a referral center for other health facilities located in the district. The district hospitals in these three selected districts have SCANU and KMC wards but need to modify to convert Mother-SCANU and need to deploy more pediatricians and nurses. The hospitals provide Comprehensive Emergency Obstetric and Newborn Care (CEmONC), including care at birth, resuscitation, respiratory support, feeding support, and infection

prevention management for preterm and low birth weight neonates. The district hospitals are linked with a wide network of primary health care centers and birthing health facilities operated by MOFHW, private for-profit and NGO hospitals, and maternity clinics.

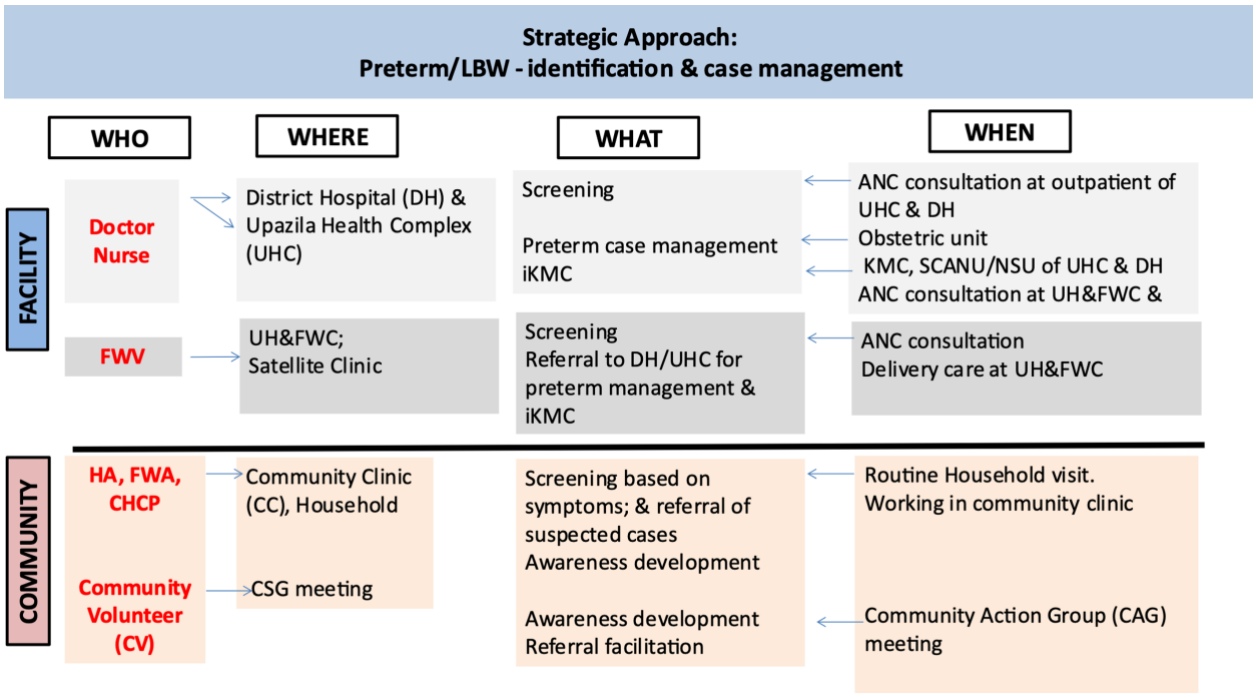
2. The linkages that were established with the local institutions (government, health system, etc)

The implementation of iKMC will be within the existing health system. To support the implementation of the study activities, the study team includes directors and programme managers of the government health services at all levels, including health managers from national, subnational, and local levels. At the central level, the Line Director of Maternal, Newborn, Child & Adolescent Health, Programme Manager of National Newborn Health Programme, Line Director of Hospital Services and Management of DGHS serve as investigators. In addition, we have engaged the district and sub-district (Upazila) health managers, including hospital administrators and physicians (neonatology/pediatrics and OBGYN) to ensure their active engagement and participation. Furthermore, the study team continuously liaises with the managers/administrators of the private health facilities. To ensure adequate implementation, the study team also includes the neonatology department of Bangabandhu Sheikh Mujib Medical University (BSMMU) and the Obstetrical and Gynaecological Society of Bangladesh (OGSB). Additionally, we have involved relevant professional bodies (e.g., Bangladesh Neonatal Forum) and legislative body of newborn health (National Technical Working Committee for Newborn Health) represented by the chairperson of the body in this team. The neonatologist and obstetrician in the team will be responsible for providing necessary technical support to MOHFW/DGHS, including training, strategic direction to implementation, and other technical support during both the optimization and scale-up phases. The team at Projahnmo Research Foundation will be responsible for monitoring and supervising study activities and evaluation activities.

3. Description of the process that will be followed to identify participants to the study at the site:

The population of interest will be preterm (i.e., <37 weeks of gestation) or low birth weight (<2000gms) newborns in the entire network of health care facilities in the study area, irrespective of their residence. To identify the potential participants, firstly, we will organize i) advocacy and sensitization meeting with key stakeholders, public and private, engaging MOHFW in the lead ii) capacity building of clinical providers at iKMC providing facilities; iii) coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births.

Training sessions for the healthcare providers at the implementing health facilities will be organized so that they can identify the women with a high likelihood of preterm birth (PTB) at <37 weeks of gestation or low birth weight (LBW) baby during routine clinical care. We will also train the providers at the primary/lower-level health facilities of both the public and private sectors on in the study area on accurate birth weight measurement, the study interventions, including diagnosis of women with a high probability of preterm birth so that they can identify the women with the likelihood of preterm delivery and identification of LBW babies. A pool of master trainers (MT) of the district will be developed by national level core trainers. MTs will training the clinical providers of the districts. They will also contribute technical supervision to ensure quality of care. In addition, we will establish functional referral linkage which is mentioned below.



4. **Complete description of consent (and assent process):** as described in the generic protocol.

5. **Given the country context, the risk/benefit assessment for all participating groups (e.g., children, families, institutions, countries, etc.).**

Bangladesh is among the top five countries globally, having the highest number of preterm births with an estimated 600,000 PTB annually. The National Low Birth-weight Survey, Bangladesh, estimated that about 22.6% of infants are LBW. Annually approximately 15,000 children under 5 years of age die in Bangladesh due to complications related to PTB and LBW making them the second leading cause of neonatal deaths. Given the intensity of the burden of PTB and LBW in the country, it is a priority of the Government of Bangladesh to adopt effective interventions and strategies to reduce neonatal mortality related to PTB/LBW. As stated in the background section in the protocol, the efficacy of iKMC in reducing neonatal mortality is well-proven. As this study aims to develop and scale up an optimized implementation model of iKMC within the functional health system, this study would be of immense importance to the country to tackle the problem. It would benefit the children and families by reducing PTB/LBW-related complications and their related healthcare costs and improving the health and well-being of newborns. Furthermore, the institutions would be strengthened and benefited through capacity building of the healthcare providers, logistical support, and infrastructural changes to establish M-SCANU.

6. **Types of services/interventions that will be offered by referral, and the linkages that will be established with such institutions/services, in order to ensure the smooth referral.**

We will establish referral linkages between the iKMC implementing health facilities and all other health facilities to ensure timely referral of LBW and preterm babies, including pregnant women with a high likelihood of PTB. We will also coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births. Firstly, we will identify gaps in referral systems in the study area. The focus will include both on referral of outborn cases and also on inborn cases which are sometime not transferred from OBGYN unit to KMC/SCANU of same

facility. Based on the gaps and needs we will establish referral linkages between the iKMC implementing facilities and other health facilities to ensure timely referral of all pregnant women with a high probability of preterm birth and PTB/LBW babies to iKMC-implementing hospitals. We will develop and provide a uniform referral template to all health facilities within the implementing district. we will orient the health care providers across all health facilities on the study interventions and activities to ensure smooth referral. Family Welfare Visitors (FWV), the designated pregnancy care provider at Union level will be linked with the referral system to identify and refer appropriate cases during ANC consultation and delivery care at Union Health and Family Welfare Center (UH&FWC). At the community level, we will engage local CHWs of MOHFW and NGOs (e.g., Family Welfare Assistants, Health Assistants, Community Health Care Providers) and community support groups (e.g., MOHFW's Community Clinic support group) to strengthen the referral linkages with the iKMC facilities. In addition, we intend to maintain a pool of privately owned local vehicles to ensure timely and smooth referral of mothers and babies from the community/rural areas to the iKMC facilities. The community health care workers will assist the families to arrange the vehicles and transport mothers and babies.

7. **Data Management: The data management will be as described in the** master protocol. Further detail will be written once overall data management strategy is decided.

8. **Data Analysis:** The analysis will be conducted jointly in accordance with the master protocol.

9. **Sample Size:** For stepped wedge design phase, sample size will be calculated. During model optimisation, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. **Dissemination Strategy (**How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.)

    Two key approaches of dissemination will include scientific dissemination through publication in peer reviewed journals and the policy and programmatic dissemination. The findings of the implementation research will be disseminated at ground level with the community, local health authorities, professional organizations within the country and internationally through community meetings conducted locally, national and international seminars, workshops and conferences.

11. **Additional ethical considerations at the study site:**

We do not anticipate any additional ethical concerns other than what is written in the master protocol.

12. **Translated consent forms:** forms have been shared with the IRB.
13. **Local Ethical Approval or proof of submission:** please refer to the table of IRB submission.
14. **The CVs of the investigators:** CVs have been submitted with the Master Protocol.

Site name: Ethiopia – Oromia Region

1. Description of study area (briefly describe the criteria that justifies the selection of the site):

1.1 Learning district: The first phase of the iKMC Implementation Research (IR) will be implemented in a network of hospitals with a total estimated catchment population of 893,465 and annual expected birth of 31,004. Shashemene referral hospital, Gambo and Arsi Negele primary hospitals serving populations in Shashemene town, Shashemene Zuria Woreda, and Arsi Negele Woreda; two adjacent Woredas in West Arsi Zone, Oromia region.

Table 1. Networks of hospitals in the first phase iKMC IR, Oromia region, Ethiopia

	Zones	Woreda	Site	Name of hospitals	Catchment population	Expected # of Delivery	Network population
1	West Arsi	Shashemene Town	Site 1	Shashemene RH, Mekla Odda GH	188,926	6,556	
2	West Arsi	Shashemene Zuria	Site 1	Gambo PH	331,896	11,517	
3	West Arsi	Arsi Negele	Site 1	Arsi Negel PH	372,643	12,931	893,465
					893,465	31,004	893,465

1.2 Other Districts that study will be scaled up:

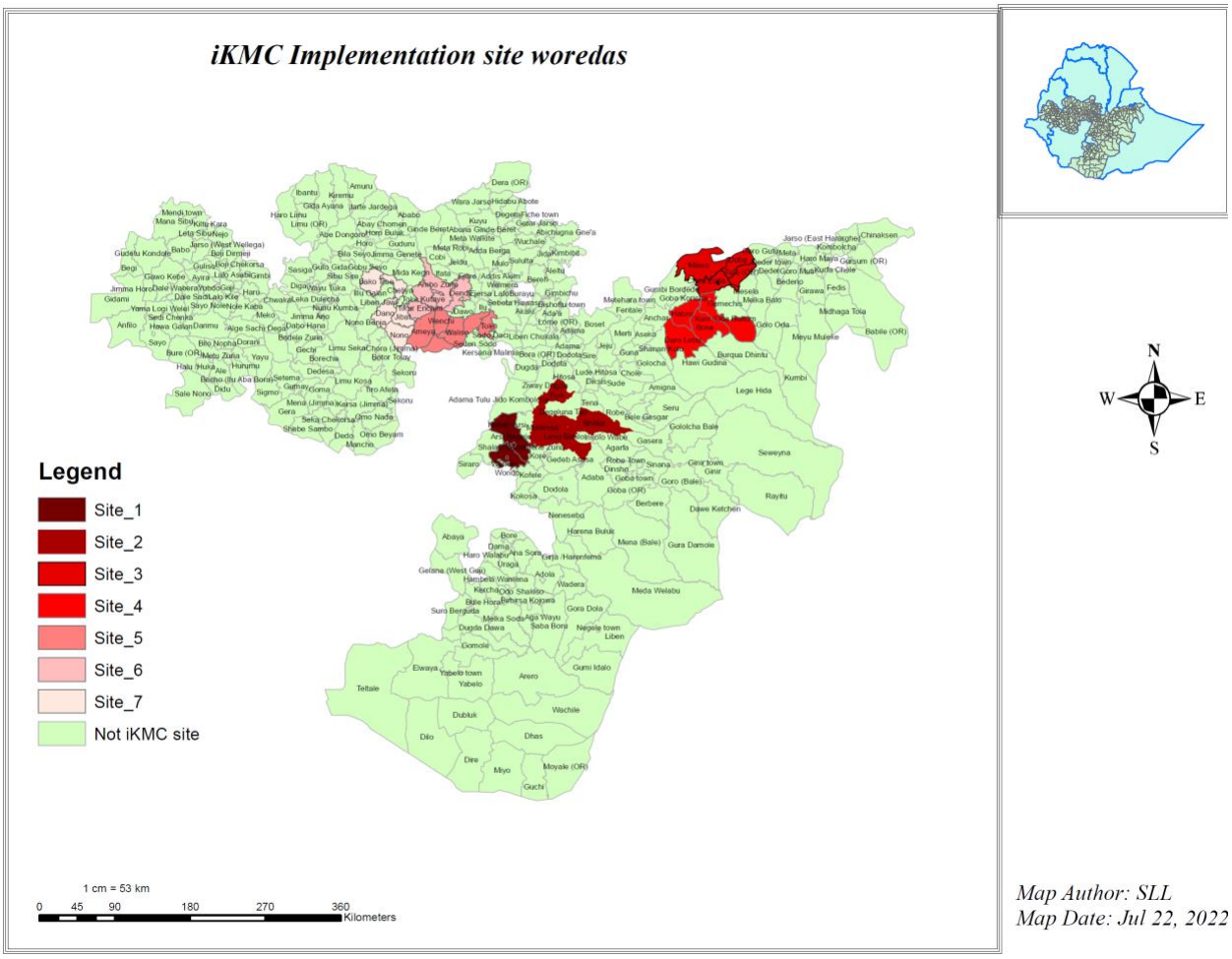
During the second phase, we will scale up the interventions across 21 hospitals located in Arsi, West Hararghe, South West Shoa, and West Shoa Zones of Oromia Region. Although the hospitals cater larger geographical areas and population, we will use as denominator the population of the Woredas where the hospitals are located. The estimated annual births attended by these facilities in the four zones are 174,574. Adjustment to the second phase sites could be made in consultation with the Ministry of Health and Oromia Regional Health Bureau and based on the implementation learnings from the first phase. (Table 2)

The hospitals are located within 300 km distance from Addis Ababa - a reasonable distance for frequent supervision by research investigators and Oromia Regional Health Bureau and Ministry of Health staff. All of the hospitals are being supported by the Saving Little Lives (SLL) project. The support, among others, includes strengthening of the neonatal care at labour and delivery, NICU, and KMC units through provision of essential equipment and supplies (such as digital weighing scale, fetal heart monitor, CPAP, KMC chairs, refrigerator, KMC wrap etc.) and continued clinical mentorship.

Table 2. Networks of hospitals in the second phase iKMC IR, Oromia region, Ethiopia

	Zones	Woreda	Site	Name of hospitals	Catchment population	Expected # of Delivery	Network population
4	Arsi	Limuna Bilbilo	Site 2	Bokoji PH	251,879	8,740	
5	Arsi	Shirka	Site 2	Gobessa PH	223,527	7,756	
6	Arsi	Munessa	Site 2	Kersa PH	228,592	7,932	
7	Arsi	Tiyo	Site 2	NA	118,357	4,107	
8	Arsi	Assela Town	Site 2	Assela SH	126,518	4,390	948,873
9	West Hararghe	Mieso	Site 3	Asebot PH	187,030	6,490	
10	West Hararghe	Chiro Zuria	Site 3	NA	224,699	7,797	
11	West Hararghe	Doba	Site 3	NA	178,940	6,209	
12	West Hararghe	Tulo	Site 3	Hirna PH	202,575	7,029	
13	West Hararghe	Chiro Town	Site 3	Chiro GH	63,281	2,196	856,525
14	West Hararghe	Habro	Site 4	Galamso GH	265,942	9,228	
15	West Hararghe	Boke	Site 4	NA	203,604	7,065	
16	West Hararghe	Daro Labu	Site 4	Daro Labu PH	271,356	9,416	
17	West Hararghe	Kuni	Site 4	NA	209,319	7,263	950,221
18	South West Shoa	Woliso Town	Site 5	St. Luke GH	71,246	2,472	
19	South West Shoa	Woliso	Site 5	Woliso PH	190,998	6,628	
20	South West Shoa	Ameya	Site 5	Ameya PH	164,869	5,721	
21	South West Shoa	Wenchi	Site 5	NA	124,831	4,332	
22	South West Shoa	Goro	Site 5	Gindo PH	62,216	2,159	
23	South West Shoa	Becho	Site 5	Tulo Bulo GH	105,958	3,677	
24	South West Shoa	Tole	Site 5	BanItu PH	84,773	2,942	804,891
25	West Shoa	Ambo Zuria	Site 6	NA	143,792	4,990	
26	West Shoa	Ambo Town	Site 6	Ambo RH, Ambo GH	90,584	3,143	
27	West Shoa	Toke Kutaye	Site 6	Guder PH	167,554	5,814	
28	West Shoa	Dendi	Site 6	Ginchi PH	233,369	8,098	
29	West Shoa	Tikur Enchini	Site 6	NA	96,831	3,360	732,130
30	West Shoa	Cheliya	Site 7	Gedo GH	220,182	7,640	
31	West Shoa	Bako Tibe	Site 7	Bako PH	175,363	6,085	
32	West Shoa	Dano	Site 7	NA	131,936	4,578	
33	West Shoa	Jibat	Site 7	NA	97,468	3,382	
34	West Shoa	Nono	Site 7	NA	113,409	3,935	738,358
					5,030,998	174,574	5,030,998

Figure: iKMS implementation site woredas



2. The linkages that were established with the local institutions (government, health system, etc)

Addis Ababa University has a strong partnership with the ministry of health and Oromia regional health bureau. In addition to using some of the Woredas for its undergraduate programme rural health practices the Addis Ababa University implements several collaborative research and programmes in the region. Between 2016 – 2019 with the leadership of the regional health bureau we successfully conducted the sKMC implementation research. Building on the sKMC implementation research we are working with the region to scale-up the Saving Little Lives (SLL) project in 108 hospitals in the region. The iKMC implementation research will be conducted in the subset of the SLL sites where we have an existing partnership.

3. **Description of the process that will be followed to identify participants to the study at the site:**

The population of interest will be preterm (i.e., <37 weeks of gestation) and low birth weight (<2000gms) newborns in the entire network of health care facilities in the study area, irrespective of their residence. To

identify the potential participants, firstly, we will organize i) advocacy and sensitization meeting with key stakeholders, public and private, engaging MOHFW in the lead ii) capacity building of clinical providers at iKMC providing facilities; iii) coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births.

Training sessions for the healthcare providers at the implementing health facilities will be organized so that they can identify the women with a high likelihood of preterm birth (PTB) at <37 weeks of gestation or low birth weight (LBW) baby during routine clinical care. We will also train the providers at the primary/lower-level health facilities of both the public and private sectors on in the study area on accurate birth weight measurement, the study interventions, including diagnosis of women with a high probability of preterm birth so that they can identify the women with the likelihood of preterm delivery and identification of LBW babies. A pool of master trainers (MT) of the district will be developed by national level core trainers. MTs will training the clinical providers of the districts. They will also contribute technical supervision to ensure quality of care.

4. **Complete description of consent (and assent process)**: as described in the generic protocol.

5. **Given the country context, the risk/benefit assessment for all participating groups (e.g., children, families, institutions, countries, etc.).**

The Ethics Review Committee (ERC) of the organization will be responsible to evaluate the risk/benefit analysis. Considering the nature of the intervention and the multi-country RCT recently published, iKMC as the core strategy within the WHO minimum care package for preterm and LBW babies, is the standard of care for these babies.

The risk will fall under the category of minimal risk which is defined as “the probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely”.

The RCT has shown to reduce neonatal mortality by 25% compared to the conventional care, therefore the anticipated benefits outweigh the risks.

IKMC is the best intervention available for preterm and LBW babies. The risk will be inherent to the babies due to preterm birth or low birth weight and not due to the intervention. There is no anticipated adverse event due to the intervention. The intervention will be provided in the hospital under strict supervision and close monitoring. There will be no extra costs to the participants as the intervention will be provided through the government health systems, which is free of cost in India. However, the final decision will be taken in a full committee review by the ERC.

6. **Types of services/interventions that will be offered by referral, and the linkages that will be established with such institutions/services, in order to ensure the smooth referral.**

We will establish referral linkages between the iKMC implementing health facilities and all other health facilities to ensure timely referral of LBW and preterm babies, including pregnant women with a high likelihood of PTB. We will also coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births. Firstly, we will

identify gaps in referral systems in the study area. The focus will include both on referral of outborn cases and also on inborn cases which are sometime not transferred from OBGYN unit to KMC/SNCU of same facility. Based on the gaps and needs we will establish referral linkages between the iKMC implementing facilities and other health facilities to ensure timely referral of all pregnant women with a high probability of preterm birth and PTB/LBW babies to iKMC-implementing hospitals. We will develop and provide a uniform referral template to all health facilities within the implementing district. we will orient the health care providers across all health facilities on the study interventions and activities to ensure smooth referral. Family Welfare Visitors (FWV), the designated pregnancy care provider at Union level will be linked with the referral system to identify and refer appropriate cases during ANC consultation and delivery care at Union Health and Family Welfare Center (UH&FWC). At the community level, we will engage local CHWs of MOHFW and NGOs (e.g., Family Welfare Assistants, Health Assistants, Community Health Care Providers) and community support groups (e.g., MOHFW's Community Clinic support group) to strengthen the referral linkages with the iKMC facilities. In addition, we intend to maintain a pool of privately owned local vehicles to ensure timely and smooth referral of mothers and babies from the community/rural areas to the iKMC facilities. The community health care workers will assist the families to arrange the vehicles and transport mothers and babies.

7. **Data Management**: The data management will be as described in the master protocol. Further detail will be written once overall data management strategy is decided.

8. **Data Analysis**: The analysis will be conducted jointly in accordance with the master protocol.

9. **Sample Size**: For stepped wedge design phase, sample size will be calculated. During model optimisation, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. **Dissemination Strategy (How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.)**

    Two key approaches of dissemination will include scientific dissemination through publication in peer reviewed journals and the policy and programmatic dissemination. The findings of the implementation research will be disseminated at ground level with the community, local health authorities, professional organizations within the country and internationally through community meetings conducted locally, national and international seminars, workshops and conferences.

11. **Additional ethical considerations at the study site:**

    We do not anticipate any additional ethical concerns other than what is written in the master protocol.

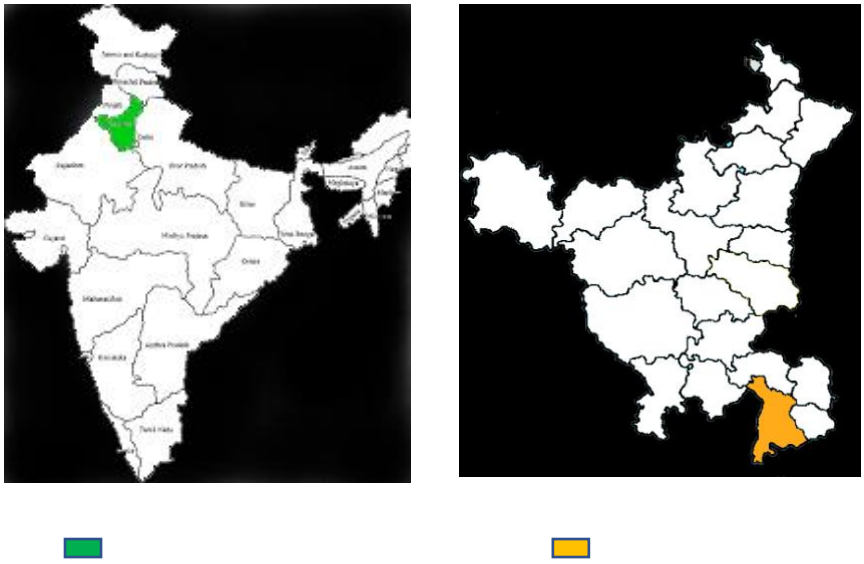
12. **Translated consent forms:** forms have been shared with the IRB.
13. **Local Ethical Approval or proof of submission:** please refer to the table of IRB submission.
14. **The CVs of the investigators:** CVs have been submitted with the Master Protocol.

Site name: India – Haryana State

1. Description of study area (briefly describe the criteria that justifies the selection of the site):

1.1 Learning district: Nuh (Mewat)

Location of the Study district (aspirational district)



Nuh District, one of the 22 districts in the Indian state of Haryana, is the proposed site for the implementation research. The district is spread over 1507 square kilometres (582 square m) having 5 blocks, 443 villages and 5 small towns with 10,89,406 (~1 million) population. Most of the population lives in rural areas (88.6%). The predominant religion is Muslim (79.2%), 20.4% are Hindu. Literacy rate is 41.8%. The average annual per capita income in the district is 45934 INR (638 USD) (Ref. Census 2011). The public health care facilities include 138 sub centres, 22 Primary Health Centres (PHC), 4 Community Health Centres (CHC), One District Hospital and One Medical College in the district.

During the year 2019-20, there were 40865 births in the district out of which 70% were institutional deliveries, with 60% deliveries in public facilities. Based on this, the birth rate is 38/1000 population. Most of babies (95.6%) were weighed at birth and 10.4% babies were low birth weight. (Ref. HMIS). According to the NFHS 5 data, 28.7% of the women aged between 20-24 years are married before 18 years of age; only 45.9% had 4 ANCs, and 18% women consumed iron folic acid tablets in pregnancy for 100 days.

There seems to be some discrepancies based on the different data sources. During the year 2021-22 (July-June), 1872 deliveries took place in the facility with 12.6% caesarean sections: 11% (197) preterm births and 41.9% (765) Low Birth Weight (LBW) babies were born in the facility.

Below are the SNCU indicators from the proposed district hospital: July 2021-June 22

Table: SNCU indicators from the proposed district hospital: July 2021-June 22

Sr No	Indicators	Number (%)
1	Number of Admissions	763
2	Inborn Admission	196 (25.7)
3	Outborn Admission	567 (74.3)
4	Admission < 2.5 KG	505 (66.2)
5	Admission < 2000gms	311 (40.8)
6	LBW babies requiring level 2 care < 1.8 KG	251 (32.9)
7	Pre-Discharge neonatal Mortality	17 (2.2)
8	Preterm Admission	524 (68.7)
9	KMC Initiated	150 (19.7)
10	Average Stay in SNCU	5.8 days
11	Cases referred	169 (22.1)

Nuh is one of the “aspirational” and worst performing districts in the country and the government of Haryana therefore wants the scale up to start from the district of Nuh. The government has also proposed the district hospital, Nuh as the study facility to scale up iKMC. It is a 100 bedded hospital providing secondary level health care services. It is a referral hospital and caters to the cases referred from the lower-level health care facilities in the district. Emergency obstetric services are available in the facility, with a 14 bedded Special Newborn Care Unit (SNCU) and a 6 bedded KMC ward.

While there are multiple challenges in selecting this district for the study, several advantages justify the rationale for selection of this district as the study learning district. Being an aspirational district, the government commitment will be high, with the political will for improvement. The tertiary facility for referral is available within the district and well functional. It is 30 km from the district hospital. There are very few private hospitals, which will enable high coverage. The KMC ward is in place and sufficient space is available to establish the M-SNCU.

1.2 Other Districts that study will be scaled up:

Other districts will be decided in consultation with the government partners.

2. The linkages that were established with the local institutions (government, health system, etc):

The study will be led by the Haryana government at the state and local district levels. Under the leadership of Dr. Sonia Trikha, the Director General of Health Services, Haryana, the health officers at the district hospital will be primarily responsible for conducting the project activities. The district hospital is closely linked with the lower level government hospitals, that is primary health centres, community health centres from where patients are referred to the district hospital. The district hospital is also linked with the higher tertiary level facility, that is the medical college hospital.

The Centre for Health Research and Development, Society for Applied Studies (CHRD, SAS), will be the implementing partners, with technical support provided by the team from Safdarjung Hospital (SJH) and Translational Health Science and Technology Institute THSTI, that led the randomised controlled trial of iKMC in India. A Scientific Advisory Committee (SAC) will be constituted (Dr. Harish Chellani, the PI of the WHO-coordinated multi-country trial to evaluate the impact of continuous KMC initiated immediately after birth; Dr. Rani Gera, head of the department of pediatrics, SJH, Dr. Shinjini Bhatnagar, professor of Eminence, THSTI, Dr. Nita Bhandari, senior scientist, CHRD SAS and Dr. Jose Martines, Scientific Coordinator, Centre for Intervention Science in Maternal and Child Health, Centre for International Health, University of Bergen, Bergen, Norway). The SAC will ensure scientific standard of the research, scientific relevance of the research question, review the appropriateness of study protocol, methods, tools, data management and analysis and conduct periodic review of study progress.

3. Description of the process that will be followed to identify participants to the study at the site:

The study participants will include the preterm or low birth weight babies, who are born in the facility (initiated within 2 hours of birth) or out-born babies, that is, those babies who are born in other facilities or at home within the study district and referred to the study facility (who reach the KMC facility within 24 hours of birth).

- In this study the activities conducted at pre-facility and facility levels will enable identification and referral of eligible babies.

- The **pre-facility activities** will aim to improve identification of eligible babies that are born outside the study facility. All the relevant staff in the lower-level government delivery facilities will be oriented, sensitized and trained in the iKMC programme objectives, clinical assessment of babies to screen for eligibility, appropriate techniques to measure birth weights and provision of functional weighing scales and in the WHO minimum package of care for preterm and LBW babies.

- Social behavioral change communication activities will be conducted in the community to create awareness and generate demand. Community level health workers, ASHAs and ANMs will be trained in the objectives of the iKMC programme, HBPNC including KMC. At antenatal clinics, high risk pregnant women who are at the risk of giving birth to LBW or preterm babies will be flagged for more frequent follow up to identify births as soon as possible. Contact numbers of ASHAs and ANMs will be provided to families to inform when women go into labour. For LBW and pre-term babies who do not require admission to M-SNCU, KMC will be initiated at the lower-level facilities or at home. Referral system will be streamlined through strengthened transportation (ambulance) services, referral slips, increased accountability and follow up. Transportation will be promoted through mobilization of local resources at village level and involving the village administrative body.

- At **facility level**, eligible babies for KMC will be identified in the labour room and OT for those born in the facility; or in the emergency, OPD, SNCU or KMC ward, where babies will be referred. For babies who are referred, triaging will be done to categorize babies who need to be referred to NICU at tertiary care hospital, those who can be admitted to KMC ward and do not need SNCU care and those who will need to be admitted in the M-SNCU. All staff in the study will receive extensive training in the WHO minimum package of care for preterm and LBW babies and iKMC.

4. Complete description of consent (and assent process):

Since this is implementation research and iKMC has proven to be efficacious, individual written informed consent will not be needed from mothers or families to start the KMC intervention. KMC will be provided by the government as standard of care for preterm and LBW babies.

Individual written informed consent will however be requested from mothers, caregivers and health workers for the collection of research data, during formative research, programme learning activities and for outcome measurements.

The informed consents will be translated into simple Hindi language that can be easily read and understood. If the participant is literate, the worker will allow him/her to read the consent. For those non literate, the consent form will be read aloud by the worker obtaining consent in the presence of an impartial literate witness. If the participant is literate, he/she will sign on the consent form. For those who are non-literate, a thumb imprint will be taken which will be witnessed (counter signed) by an impartial literate witness. A copy of the signed consent form will be given to the participant. Legally acceptable representative can be either of the parents or the caregiver/guardian of infant in the absence of parents. When explaining the details in the information sheet, the study team member will ask if the parent or guardian has any questions and if there are any, will answer the questions. Additionally checking questions will be asked to assess the caregivers understanding about the study. Once the team is satisfied that the study procedures are well understood, consent will be documented.
In our study population, assent will not be needed as all women will be 18 years of age or above.

5. Given the country context, the risk/benefit assessment for all participating groups (e.g., children, families, institutions, countries, etc.).

The Ethics Review Committee (ERC) of the site organization will be responsible to evaluate the risk/benefit analysis. Considering the nature of the intervention and the multi-country RCT recently published, iKMC as the core strategy within the WHO minimum care package for preterm and LBW babies, is the standard of care for these babies.

The risk will fall under the category of minimal risk which is defined as "the probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely".

The RCT has shown to reduce neonatal mortality by 25% compared to the conventional care, therefore the anticipated benefits outweigh the risks.

IKMC is the best intervention available for preterm and LBW babies. The risk will be inherent to the babies due to preterm birth or low birth weight and not due to the intervention. There is no anticipated adverse event due to the intervention. The intervention will be provided in the hospital under strict supervision and close monitoring. There will be no extra costs to the participants as the intervention will be provided through the government health systems, which is free of cost in India.

6. **Types of services/interventions that will be offered by referral, and the linkages that will be established with such institutions/services, to ensure the smooth referral.**

Newborns requiring referral will be sent to the tertiary level facility, which is the Shaheed Hassan Khan Mewati Government Medical College (SHKMGMC), Nallhar. It is a 652 bedded medical college hospital having a 6 bedded NICU with ventilator support and 6 bedded KMC Unit.

Government operated ambulances are available in the district for referral transport. With consultation to the government partners the referral transport system will be strengthened in the district to support the referral cases from the lower-level facilities to the district hospital and further to the medical college. KMC during transit will be ensured.

7. **Data Management: The data management will be as described in the** master protocol. Further detail will be written once overall data management strategy is decided.

8. **Data Analysis:** The analysis will be conducted jointly in accordance with the master protocol.

9. **Sample Size:** For stepped-wedge design sample size will be calculated. During model optimization, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. **Dissemination Strategy (**How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.)

Two key approaches of dissemination will include scientific dissemination through publication in peer reviewed journals and the policy and programmatic dissemination. The findings of the implementation research will be disseminated at ground level with the community, local health authorities, professional organizations within the country and internationally through community meetings conducted locally, national and international seminars, workshops and conferences.

11. **Additional ethical considerations at the study site:**

We do not anticipate any additional ethical concerns other than what is written in the master protocol.

12. **Translated consent forms:** forms have been shared with the IRB.

13. **Local Ethical Approval or proof of submission:** please refer to the table of IRB submission.
14. **The CVs of the investigators:** CVs have been submitted with the Master Protocol.

Site name: India - Uttar Pradesh State

1. Description of study area (briefly describe the criteria that justifies selection of the site):

1.1 **<u>Learning district</u>:** Kanpur Nagar district (to be confirmed in consultation with local ministry)

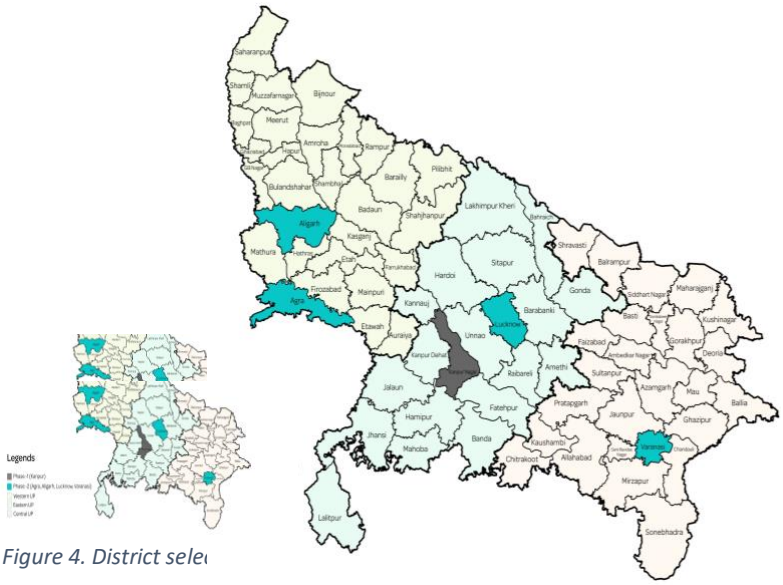


Figure 4. District sele

The study will be conducted in two phases. In phase I, the implementation model will be developed through an iterative co-development process with involvement of key stakeholders in chosen facilities in one district. In phase II, the implementation model will be scaled up across 3 additional districts in UP, and the impact on neonatal mortality and other important outcomes will be evaluated. We will choose the Phase I district in alignment with the high level strategy from central UP.

Figure 4. District selection for the study

1.2 <u>Other Districts that study will be scaled-up</u>:

The Phase II districts will be chosen to ensure regional representation across UP, and therefore one district each will be chosen from western, central and eastern UP (see Figure 4). Objective criteria for choosing the study districts include: (i) admission rate of <1800 gram infants in NICU-SNCU combination of >= 45 per month, (ii) overall NMR in <1800 gram infants of >= 15%.

2. The linkages that were established with the local institutions (government, health system, etc)

The first step would be engagement of key stakeholders in the selected study districts, as described in the sections above. Two concurrent activities will be conducted in the next 2-4 months, formative research and strengthening the quality of care by ensuring implementation of the WHO minimum package of care for the small newborn.

The formative research team will conduct interviews and focus group discussions to explore the five domains of the consolidated framework for implementation research as described above. The

duration of formative research will be relatively short, as this team will transition into the programme learning team and continue to collect relevant data throughout the study.

A rapid assessment of the quality of newborn care provided in the delivery room, operation theatre and level 2 NICU will be conducted to identify gaps in implementation of the WHO minimum package of care for small babies. Based on the specific gaps identified, the study will support activities to address these gaps. The iKMC trial identified two key common gaps in care: the provision of appropriate respiratory support and periodic clinical monitoring of babies. These gaps will be covered by ensuring that adequate number of safe CPAP machines and pulse oximeters are made available at all hospitals, and having standard operating procedures for the use of this equipment. To ensure high quality and coverage of KMC for stable babies, learnings from the scale up KMC study will be implemented. The following activities will be done prior to the implementation of iKMC in level 2 M-NICUs: (1) Primary level activities are aimed at maximizing access of LBW babies to KMC-implementing facilities; these activities included accurate birth weight recording and referral of LBW infants born at home or lower level facilities that do not provide KMC in skin to skin contact, (2) Secondary Level activities aimed at initiating and maintaining KMC for stable LBW babies who were born in or referred to the facility in level-2 special newborn care units through changes in infrastructure and training, motivation and support of facility staff. The level-2 NICU will be strengthened to provide effective interventions in the standard of care, including optimal use of CPAP, breastmilk feeding, prevention and treatment of infections, and monitoring (3) Community level activities aimed at supporting continuation of KMC at home after discharge; these include telephonic contact of hospital staff with families and home visits by CHWs. This network of primary, secondary level facilities and community will transform the small and sick newborn care in the area.

When results of formative research are available, co-design workshops to develop implementation model 0+ will be organized. This model will be implemented, with concurrent collection of qualitative and quantitative data, for 3-6 months, and a re-design workshop will revise the model as required. Two or three similar iterative cycles will continue to optimize the implementation model until the end of model optimisation.

3. Description of the process that will be followed to identify participants to the study at the site:

The study participants are LBW/ preterm infants born in an iKMC implementing facility or out-born babies from the catchment/referral area admitted to the study facilities who reach the iKMC implementing facility within 24 hours of birth).

Recruitment of participants involves the following activities in the community, primary-care facilities and iKMC implementing facilities. Community based activities aim to improve identification of eligible babies that are born outside the study facility. The primary care facilities, staff/ health care providers will be oriented, sensitized and trained to identify pregnant women who are likely to give birth to a preterm or LBW baby. They will be trained to 1) refer pregnant women with risk of preterm birth or LBW babies to an iKMC implementing facility 2) measure birth weights immediately and accurately after birth and refer LBW requiring SNCU care in skin-to-skin contact with mother or surrogates to the iKMC implementing facility. At the iKMC implementing facility, physicians will identify eligible babies in the labour room and operation theatre for those born in the facility; or in the emergency, OPD, SNCU or KMC ward, where babies will be referred. For babies who are referred, triaging will be done to categorize babies I) who need to be referred to NICU at tertiary care hospital, ii) those who can be admitted to KMC ward and do not need SNCU care and iii) those who will need to be admitted in the

M-SNCU. All staff in the study will receive extensive training in the WHO minimum package of care for preterm and LBW babies and iKMC. A register will be created and will have names of all preterm and LBW babies in all facilities. The research assistant will have access to this register to ensure that all eligible babies are enrolled in the study.

4. Complete description of consent (and assent process):

Evidence showed Study intervention itself has proven to be safe and efficacious. As per the new WHO guideline, provision of KMC immediate after birth to all preterm and LBW babies will be considered the standard of care; therefore, initiation of iKMC will not require a consent from participants. For formative research and programme learning that includes direct data collection from mothers, caregivers, health workers, health managers, and stepped wedge design phase (ascertainment of vital status at day 29), an individual written consent form will be used to obtain consent. The consent form will be translated into a local language that facilitate the consent process. For illiterate participants the consent form will be read by the research staff in presence of a literate witness. A copy of signed consent form will be returned to the participants. Legally acceptable representative can be either of the parents or the guardian of infant in the absence of parents. When explaining the details in the information sheet, the study team member will ask if the parent or guardian has any questions and if there are any, will answer the questions. Additionally checking questions will be asked to assess the caregivers understanding about the study. Once the team is satisfied that the study procedures are well understood, consent will be documented.

In the consent process, participants will be briefed that the mother and baby will continue to receive standard care as per hospital policy in case of refusal to participate in the study or withdrawal of consent. Mothers will be made aware that even after providing consent, they will be free to withdraw from the study at any phase, and in case they withdraw later, they and their babies will continue to receive the same quality of care as required by any other patient with the same condition. At the time of withdrawal of consent, the mothers will be free to decide about use of collected data.

5. Given the country context, the risk/benefit assessment for all participating groups (e.g., children, families, institutions, countries, etc.).

Benefit

There are a few well documented benefits of intervention. The biggest benefit of this study may be that the iKMC may lower the mortality and morbidity rates in preterm and LBW neonates who takes part in the study. Since the mother and baby will be in close contact from birth during iKMC, the baby will be more likely to be colonized by the mother's protective microbiome and more likely to receive early breastfeeding. There will be also less handling of the baby by other persons, thus reducing the risk of infection. The iKMC will be useful for improving the mental health of mothers. Implementing institution will be benefited with updated equipment in SNCU and with trained staff and health care providers to provide KMC immediately after birth. Implementing country will be benefited from materials which will be made available during the study, including, but not limited to, national guideline for mother-SNCU, SoP for role clarification of the HCWs in SNCU, labour room, postnatal ward and triage, update national guideline and training manual of KMC with provision of iKMC.

Risk

There might be a risk of poor outcome of the baby as all the participants will be LBW/ preterm and potentially unstable, however there will be well-equipped establishment of M-SNCU run by thoroughly trained staff, with continuous monitoring system, hence risk will be mitigated.

The unavailability of caregivers willing to consent and provide the iKMC services within 2 hrs after birth might be a major recruitment barrier due to high rates of maternal illness or post-caesarean section and absence of other family members at the hospital during the early admission period. The healthcare providers will be well trained in counselling of the family member before the delivery for providing the iKMC in the absence of mother. Hence this risk will be mitigated.

There might be a risk of being overloaded of LBW neonates in the iKMC implementing facility because of establishing functional referral system. We will strengthen the capacity of the iKMC implement facility to provide WHO minimum care package for LBW neonates.

6. **Types of services/interventions that will be offered by referral, and the linkages that will be established with such institutions/services, in order to ensure the smooth referral.**

The model development phase is proposed be conducted in Kanpur Nagar district in central UP (Figure above), although the final district will be chosen in close consultation with stakeholders in the health system and participating institutions. The district covers the entire spectrum of rural, peri-urban and urban population and therefore provides a rich spectrum of scenarios for model development. Two-thirds of its population of about 5 million resides in Kanpur city and the rest is spread across 10 rural blocks. Kanpur has 3 district-level facilities with functional SNCUs, one of which (Hallet Hospital) is run by a medical college. Each of the 10 rural blocks has a community health center (CHC), three of which have been designated as newborn stabilization units (NBSUs). The district hospitals other than Hallet and one NBSU have pre-existing KMC Lounges. We plan to set up the first iKMC facility in Hallet Hospital, which receives direct referrals from CHCs as well as from the other district hospitals. UP has a roadmap to establish medical colleges in each of its 75 districts, and 15 medical colleges have recently been established in addition to 23 pre-existing medical institutions with ongoing further expansion. Thus, the healthcare system in Kanpur Nagar reflects the emerging system in other districts of UP. The district and some of its health facilities, including Hallet Hospital are the site for another ongoing WHO-collaborative trial and an implementation research study on possible serious bacterial infections, whose goals are harmonized with the proposed study. The study team has established close research and implementation partnerships with stakeholders at the district, block and facility levels.

7. **Data Management: The data management will be as described in the** master protocol. Further detail will be written once overall data management strategy is decided.

8. **Data Analysis:** The analysis will be conducted jointly in accordance with the master protocol

9. **Sample Size:** For stepped-wedge design phase, sample size will be calculated. During model optimisation, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. Dissemination Strategy (How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.

We will choose districts that have a combination of a well-established medical college with a fully functional NICU along with a district hospital with a reasonably well-performing SNCU, and pediatric and obstetric teams that have the eagerness and capacity to institutionalize KMC within their facilities. After the study, these districts will serve as dissemination and training centers for iKMC integration for other districts in their region.

11. **Additional ethical considerations at the study site:**

We do not anticipate any additional ethical concerns other than what is written in the master protocol.

12. **Translated consent forms:** forms will be shared with the IRB.
13. **Local Ethical Approval or proof of submission:** please refer to the table of IRB submission.
14. **The CVs of the investigators:** CVs have been submitted with the Master Protocol.

Site name: Nigeria – Osun State

1. Description of study area (briefly describe the criteria that justifies the selection of the site):

1.1 Learning district:

The learning facility is State Specialist Hospital Asubiaro, a secondary health care centre in Osun Central Senatorial district, Osun State. The state is located in South west zone, Nigeria with a total population (projected) of 5.1 million people. About 96.2% of women in the state had skilled care at delivery while 6.8% of babies had skin to skin contact within one hour of birth. The neonatal mortality rate for Osun state is 32 per 1000 live births (NDHS 2018). Osun State was selected for the study because it is peaceful and has hosted a number of previous multi-country studies in the past and co-operation/support was readily obtained from the State and Local Government Authorities. It is also the state of residence of the study investigators which will enhance close monitoring and supervision.

There are three senatorial districts in the state, each with three secondary health facilities, several Primary Healthcare Centres (PHCs), as well as private and faith-based facilities. The State Specialist Hospital, Asubiaro is located in the state capital, Osogbo. It receives referrals from faith Based and PHCs within its catchment areas.

The Obstetric Unit of the hospital is manned by two consultant Obstetricians, two Medical Officers and two-house officers. There are about 200 deliveries per month with a Caesarean section rate of 30% in the facility and about 10 deliveries are for late preterm births (early preterm labours are promptly referred). The neonatal unit comprises 4 rooms, located about 10 meters from the obstetric unit and is currently not in use. Women at risk of early preterm deliveries are therefore referred to the nearby tertiary health facilities. Kangaroo mother care is not practiced at the hospital despite all parturient being accompanied by birth companions. The neonatal unit will be equipped and transformed into a Mother-Neonatal Intensive Care Unit (M-NICU) for immediate- and conventional- Kangaroo Mother Care (KMC) during the preparatory phase for this study

1.2 Other districts for scale-up

Six other secondary healthcare facilities in Osun State will be involved as follows: State Hospitals Ede and Iwo (Osun West Senatorial district), State Hospital Ikirun (Osun Central Senatorial district) and State Hospitals Ilesha, Okeogbo and Ipetumodu (Osun East Senatorial district). Serial enrollment of the facilities into the study will be done across the senatorial districts, until all facilities are enrolled. All the facilities conduct deliveries but do not handle preterm deliveries as they neither have a Special Care baby Unit (SCBU) nor practice KMC. Mother-Neonatal Intensive Care Unit will be established in all the facilities as part of the implementation research.

2. Established linkages

The research team has longstanding working relationship with the Director of Family Health Department of the Federal Ministry of Health (FMOH), the Osun State Permanent Secretary for Ministry of Health, the Osun State Primary Healthcare Development Board and the head of Osun State Hospital Management Board. The research team therefore did not have any difficulty in securing the written affirmation of the necessary Personnel during the application for this research. Appraisal visits have also been conducted to the learning facility to interact with the staff on ground. The Management of the learning and implementation facilities will also be visited and informed. Courtesy visits would be made to the paramount rulers of the selected communities, who had always been supportive of previous endeavors by the research team.

Agencies with whom the research team enjoy cordial working relationship, including the Private sector (Guild of Medical Directors), Missionary Hospitals Management Boards (Catholic Hospitals, Seventh Day Adventist), Paediatrics Association of Nigeria (PAN), Nigeria Society of Neonatal Medicine (NISONM), Society of Obstetrics and Gynaecology of Nigeria (SOGON), and National Association of Nigeria Nurses and Midwives (NANNM) will be duly informed. The informal sector which includes market leaders, mission birth attendants and antisans will also be duly informed at the preparatory phase as well as during the course of the study.

3. Description of the process that will be followed to identify participants to the study at the site: Identification of participants will be the same as in the Master protocol. The population of interest will be preterm (i.e., <37 weeks of gestation) and low birth weight (<2500gm) newborns in the entire network of health care facilities in the study area, irrespective of their residence. In our setting in Nigeria, we will organize i) advocacy and sensitization meeting with key stakeholders, public and private, engaging MoH in the lead ii) capacity building of clinical providers at iKMC providing facilities; iii) coordinate and engage the local community groups in the study area to create awareness of care-seeking at a health facility, including using antenatal care (ANC), GA dating, and institutional delivery, and identifying and referral of small babies, in case of home births.

Pregnant women at high risk of preterm deliveries from peripheral centres would be transferred with the fetuses in utero to the study facility for the purpose of initiation of IKMC after delivery. If delivery inevitably takes place at the peripheral centres and the newborn is eligible, transfer will be done in KMC position to the study facility. To ensure an effective identification of eligible patients and referral system, a liaison network will be established between the peripheral centres and the study facility, comprising Community Health Extension Workers (CHEWs) and Community Health Influencers, Promoters and Services (CHIPS). Serial reminders will be sent to the healthcare workers in all the peripheral centres about the study, eligibility criteria and referral pathways. There will be ongoing surveillance by the CHEWs engaged by the study to ensure prompt referral of all eligible mother – baby dyad.

4. Process of obtaining consent (and assent)

Information about iKMC within 24 hours of delivery will be offered at arrival to the iKMC implementing facilities will be offered to mothers of eligible babies. This information with be given verbally as well as with the aid of purpose designed information leaflet. Informed written consent will be obtained from mothers of eligible babies who are admitted to iKMC implementing facilities.

Parturient who are less than 18 years will be eligible for enrolment in this study provided they assent to participating in the study and their guardians (husband or parents) consent as well. An independent witness will be required to validate the consent process.

If a woman is illiterate, a witness will be present during the entire informed consent process, using a language that the patient understands. The witness will also sign and date the consent form, along with the individual who obtained the consent.

If the woman refuses to participate in the study or decide to withdraw from the study after initial consent, the mother and baby will continue to receive standard care as per hospital protocols without any penalty. Mothers who chose to withdraw from the study after initial consent will be asked if they consent to using the information obtained from them since enrollment or otherwise.

Eligible mothers will be advised to identify adults of their choice who could act as surrogates for providing Skin-to-Skin (STS) contact when the mothers are not able to do so. If possible, she can bring the surrogate to clinic for her/ their informed consent (s)to be obtained.

After birth, the mother and baby will receive the essential immediate care by the health staff. The baby's birth weight will be taken using standardized Seca weighing scale and babies with weight <2500g will be enrolled into the study.

5. Country context, the risk/benefit assessment for all participating groups

Nigeria records about 7million deliveries annually, with a national facility-based delivery rate of 39% and a neonatal mortality rate of 39 per 1,000 live births. The Infant and under-5 mortality rates are 67 and 132 per 1,000 live births, respectively. From 2013 to 2018 under five mortality in Nigeria decreased at a rate of 2.3 which is inadequate to achieve the Sustainable Development Goals target of reducing U5M to as low as 25 deaths per 1000 live births in all countries by 2030. Preterm and low birth weight babies constitute only 15% of all deliveries globally but are responsible for almost three of every four deaths in the neonatal period. The iKMC has been shown to reduce perinatal mortality by 23% in the first 72hours of life and 25% in the neonatal period compared with conventional management. Scaling up the iKMC will therefore contribute significantly towards achieving the SDG target of 12/1000 livebirths, especially in low- and middle-income countries such as Nigeria, where the neonatal mortality rate is still high.

The community also stands to benefit immensely, as the intervention will reduce the cost of hospital care and encourage breastfeeding with attendant improvement in maternal and children health. In Nigeria, there are no Level 3 Neonatal Intensive Care Units (NICU). Special Care Baby Units (SCBUs) are also not readily available in many Local Governments Areas and States. In addition to these, power supply could be erratic, such that maintaining thermoneutral environments for preterm newborns using incubators could be costly and unsustainable. IKMC is a cost-effective and validated intervention that can be deployed within the community as necessary. The intervention can also be utilized during transfer of preterm and low birth weight newborns from the community, or from a lower tier health care facility to the SCBU.

Despite the afore-listed benefits of IKMC, optimal utilization of the intervention requires training of health care staff to proficiency on the intervention, provision of infrastructures or adaptation of pre-existing structures for Mother- Newborn Intensive Care Units (MNICUs), and adequate facilities for neonatal

monitoring. The Implementation Research on iKMC will aim to address these requirements, thereby scaling up the routine utilization of the intervention. Ultimately, the programme will ensure that the services are initiated and sustained across many facilities within the intervention area in Nigeria.

6. Types of services/interventions to be offered by referral, and the linkages that will be established with such institutions/services, in order to ensure the smooth referral.

The support of Local government chairman, PHC coordinator and traditional rulers will be sought. Community awareness creation will be done continuously to educate members of the community on the benefits of the intervention including ease of accessibility and affordability. Mass media will also be utilized including radio jingles and panel discussion programs to disseminate the information about the program. Communication channels will be established between the study facility, peripheral centres and the community using the hub and spokes model. This will be facilitated via closed user group phones and designation of personnel for interfacility liaison. Training will be conducted for all health workers in the facilities on early identification of eligible women and their available referral pathway. These trainings will be mainly on accurate weighing at birth and provision of reliable weighing scales to all birthing homes. Advocacy and mobilization will be conducted for the opinion leaders and gatekeepers in the community in order to minimize community related delays in presentation at the study facility. Engagement of various men groups, artisan groups and unions on IKMC will be conducted to acquaint the men and help to mitigate the delays that arise when permission from heads of households are delayed. Discussions are ongoing with the state government for resuscitation of ambulance services as well as waiver for out of pocket expenditure as these will enhance compliance with referrals. Community health Insurance which is presently being piloted in the State will be leveraged as a means of financing hospital admissions into the implementing facilities. The National Road Transport Union in the State will be engaged to provide to provide ambulance services when required especially at night. Trained supervisors will be available at the study facility to ensure seamless provision of care to patients at arrival. At the implementing facilities, the staff will be trained on identification of eligible babies and institution of IKMC within 24 hours of birth. Training to competence and proficiency on WHO essential care for small babies, the management of the novel M-NICU model of care and monitoring of newborns and their mothers would also be conducted in the implementing facilities as well as adequate record keeping. Appropriate feedback will be provided to the referring facilities about their patients and two way referral will be strengthened. The government and community leaders will be updated from time to time about the program.

7. Dissemination Strategy

Currently, the conventional KMC is one of the evidence-based interventions captured in the Nigeria Every Newborn Action Plan as well as the National Guideline on KMC with the aim of ensuring the well-being and survival of preterm and LBW infants**.** Therefore, the outcome of the IKMC study will be used to reshape the existing policy document, as well as develop strategy for the scale up of iKMC nationally.

The outcome of the study will be communicated through formal and informal meetings through the existing maternal, newborn and child health platforms of RMNCAEH + N, National Child Health Technical Working Group and Newborn sub-committee comprising of relevant stakeholders using the bottom-up approach:

i) Government

- Community level- Gate keepers, women's groups and beneficiaries
- **Local Government Area (**LGA) dissemination- Policy makers at LGA, Programme officers and health workers.
- State level – Policy makers/ Programme managers-State Ministry Of Health, State Primary Health Care Development Board, Health Management Board, Chief Medical Directors (CMDs) of State Teaching hospitals and health workers
- National level – Policy makers, Programme managers, CMDs of Teaching hospitals, Health workers, Regulatory bodies, Professional associations, Civil Society Organisations (CSOs), NGOs and Development partners).
  - Presentation as Honourable Minister's memo at the National Council on Health comprising of Honourable Commissioners of Health, the highest decision-making body on health in the country.

ii) Professional associations-Annual Scientific conferences of Paediatricians, Obstetricians, Public Health practitioners, Nurses and Group of private practitioners

iii) Research community

Interim reports will be presented to World Health Organization mid-way into the study and the final report at the completion of the study.

In addition to meetings, information, education and communication materials such as policy briefs will be developed in the 3 major Nigerian Languages and distributed to relevant stakeholders.

Findings from the study will be published in reputable peer-reviewed high impact journals.

8. **Data Analysis**: The analysis will be conducted jointly in accordance with the master protocol.

9. **Sample Size**: For stepped-wedge design phase, sample size will be calculated. During model optimisation, coverage and quality will be calculated among newborns either born or referred to the study facility.

10. **Dissemination Strategy (How the study outcomes will be treated and communicated within the research community and the populations involved paying particular attention, if applicable, to the risk of stigmatization.)**

Two key approaches of dissemination will include scientific dissemination through publication in peer reviewed journals and the policy and programmatic dissemination. The findings of the implementation research will be disseminated at ground level with the community, local health authorities, professional organizations within the country and internationally through community meetings conducted locally, national and international seminars, workshops and conferences.

11. **Additional ethical considerations at the study site:**

We do not anticipate any additional ethical concerns other than what is written in the master protocol.

12. **Translated consent forms:** forms have been shared with the IRB.
13. **Local Ethical Approval or proof of submission:** please refer to the table of IRB submission.
14. **The CVs of the investigators:** CVs have been submitted with the Master Protocol.