Implementation research to develop & evaluate a health system model to integrate immediate Kangaroo Mother Care into the routine care of preterm or low birth weight infants in Uttar Pradesh

Study Protocol

Lead Research Organization:

Community Empowerment Lab
A-6/14, Vineet Khand 6, Gomti Nagar,
Lucknow 226 010, Uttar Pradesh, India

Principal Investigator: Dr. Vishwajeet Kumar

Date: March 10, 2023, Version: 3.0

Partnering Institutions:

Govt. of UP
UP-NHM
UP-TSU
G.S.V.M Medical College, Kanpur
S.N Medical College, Agra
J.N.M College, AMU, Aligarh
B.H.U, IMS, Varanasi
R.M.L.I.M.S, Lucknow
Hind Institute of Medical Science, Lucknow
Shyam Children & Maternity Center, Kanpur
World Health Organization

Partnerships will continue to expand in due course.

Protocol version

Version	Key changes	Date
Version 1.0	First draft	17 September 2022
Version 2.0	Revisions based on WHO generic study protocol 1st December 2022	31 January 2023
Version 3.0	Revisions based on WHO generic study protocol 9th January 2023 revision after WHO ERC comments	10 March 2023

Implementation research to develop & evaluate a health system model to integrate immediate Kangaroo Mother Care into the routine care of preterm or low birth weight infants in Uttar Pradesh

Executive Summary

Uttar Pradesh (UP) accounts for nearly one-third of India's burden of neonatal mortality and lies on the critical pathway to achieve national and global goals for newborn survival. Low birth weight newborns account for about a third of all livebirths in UP, but two-thirds of all newborn deaths. Kangaroo Mother Care (KMC) is a simple, low-cost, natural intervention that involves close skin-to-skin contact between preterm or low birth weight infants and their mothers, along with exclusive breast milk feeding and other supportive care. With more than 40 years of accumulated scientific evidence, KMC has been found to reduce the risk of mortality in low birth weight infants by 40% when initiated post clinical stabilization, as compared to conventional incubator care. This definitive evidence led to its inclusion as foundational care for low birth weight infants in the global Every Newborn Action Plan (2014), and subsequently into the India Newborn Action Plan. India has committed to achieving the global target of at least 90% coverage of KMC among all low birth weight infants by 2030, which is expected to avert at least 110,000 newborn deaths annually.

Until recently, the global recommendations for KMC specified initiation only upon attainment of clinical stabilization in unstable infants. However, going by these recommendations, half to two-thirds of deaths among preterm/LBW babies would have already occurred by the time these infants became stable enough to be provided KMC. The mounting evidence on the superiority of KMC to conventional incubator care in the case of stable infants begged the question of whether KMC could also contribute towards the attainment of clinical stabilization and therefore if it should be initiated as early as possible after birth. Two small randomized controlled trials found that KMC, when initiated as soon as possible after birth was safe, and improved early attainment of stabilization and overall health outcomes of low birth weight newborns. This led to a large multi-country randomized controlled trial coordinated by the World Health Organization, Geneva, that found that KMC when initiated as early as possible after birth, even in unstable infants, contributed to a further 25% reduction in neonatal mortality rate. The trial enrolled 3,211 infants and was stopped early due to the finding of reduced mortality in infants given immediate KMC, and the data safety and monitoring board recommended that it was no longer ethical to deprive infants in the control group of this life-saving intervention. India was also one of the participating countries in this trial, with Safdargjung Hospital being the study site.

The accumulated evidence from various randomized controlled trials has informed the revised WHO guidelines for preterm or low birth weight infants (2022), where immediate initiation of KMC as soon as possible after birth is recommended for all low birth weight infants, regardless of clinical stability. However, given the current standard of incubator care being nearly universally implemented by healthcare providers, it is non-trivial to scale-up this intervention. Therefore, the need for implementation research to develop and evaluate models to integrate immediate initiation of KMC into the care of preterm or low birth weight infants.

This proposed implementation research study in UP is part of a multi-country study coordinated by the WHO, Geneva in India, Bangladesh, Nigeria and Ethiopia. Apart from UP, this study will also be implemented in Haryana in India. The first phase of the study will involve the development and optimization of a healthcare model to integrate immediate KMC into the existing care of preterm or low birth weight infants in a single district. The second phase of the study is designed as a stepped-wedge evaluation to assess the impact of this model on reduction in neonatal mortality rate and other outcomes in three additional scale-up districts.

UP has been a pioneer in KMC implementation, and has thus far, been leading the country in the scale-up of KMC among stable low birth weight infants, with 240 public health facilities providing KMC services. These include district hospitals, community health centers and lower centers with high delivery loads. The model for scaling-up KMC was developed through implementation research in close partnership with the government of UP and the Community Empowerment Lab (CEL). The ongoing scale-up of KMC to include more birthing facilities and quality improvement in existing KMC facilities is being facilitated by the Community Empowerment Lab as part of the UP Technical Support Unit. An MNCU app designed to support health providers – nurses in particular, in the overall care of preterm or low birth weight infants has been deployed in 217 of the 240 facilities, and is the fulcrum for quality improvement. The data from the app is not only useful for healthcare providers in the immediate care of admitted newborns and mothers, but is also used to generate quality improvement dashboards for the facility and district leadership. Every mother enrolled in the app is followed up directly for her feedback on the quality of services received – which is unprecedented in UP.

Key components of immediate KMC in the proposed study will involve – initiation of skin-to-skin contact within 2 hours of birth or admission to the KMC facility; prolonged skin-to-skin contact or 8 or more hours per day; support for early and exclusive breast milk feeding for the mother; required medical care (including non-invasive ventilation) to be provided while in skin-to-skin contact; and other supportive interventions including hygienic and respectful care and regular monitoring of infants and mothers.

Our approach to scale-up immediate KMC in UP involves a strategic partnership with medical colleges involving faculty in the obstetric, paediatric and community health departments as part of the team of investigators. This will be done under the aegis of the PRAMAAN network coordinated by CEL, which stands for 'Partnership for Research in Advancing Maternal and Newborn health'. At present, medical colleges in UP (with only a couple of exceptions) do not provide KMC services, and are following the conventional model of incubator care. Given that immediate KMC would herald a major shift in healthcare practices, it is critical to integrate this practice within medical colleges such that it becomes standard of care not only for existing doctors and nurses, but for those under training, and enables health system mentors from these medical colleges to support the integration of the practice in other public (and potentially, even private) health facilities. We will accordingly choose districts that have both a medical college with a well-functioning neonatal intensive care unit or special newborn care unit (SNCU), as well as a district hospital with an SNCU. Potentially, other facilities with the basic infrastructure and meeting the minimum care requirements, including private facilities, may also be included as immediate KMC facilities. Integration of immediate KMC would also require the corresponding strengthening of the referral system from lower-level facilities.

Overall, the study would involve a strong partnership between the health system, the research team and community stakeholders. Formative research and context mapping as per the 'Consolidated Framework for Implementation Research' would be conducted during the first phase of model development. This will inform the initial implementation model at the facility and district levels, which will continue to be refined over multiple iterations as part of a co-development process with health system and community stakeholders in order to achieve high coverage and quality of immediate KMC for all infants admitted to SNCUs in the participating immediate KMC facilities. The SNCUs in these facilities will be converted into M-SNCUs to support the co-habitation of the mother and surrogate caregiver with the admitted newborns and facilitate prolonged high-quality KMC. Other requirements will include changes in hospital policies, strong process coordination between the labour room/ operation theatre and the SNCU, unlearning and relearning of providers for changes in practices and providing the requisite support and care to mothers and newborns. Overall, phase I will be conducted over 21 months.

Phase 2 of this research will involve the evaluation of the impact of the model on neonatal mortality and other outcomes in 3 scale-up districts through a stepped-wedge evaluation design. (Similarly, there will be 3 scale-up districts in Haryana, so overall 6 districts in India.) The participants in this study will be all preterm or low birth weight infants that require care in the SNCU of the participating immediate KMC facilities who are either born in the facility or are admitted within 24 hours of birth. All participating facilities within the scale-up districts would initially start as control facilities that are implementing the minimum package of care for preterm or low birth weight newborns that includes initiation of KMC after stabilization of the infants. The districts would then roll over into intervention districts one by one based on a randomized sequence every 6 months. The primary outcome of this study would be neonatal mortality rate, and secondary outcomes include coverage and quality of KMC and other infant outcomes such as breastfeeding, hypothermia, hypoglycaemia and sepsis. An independent evaluation team will collect data on the impact, coverage and process outcomes. All data will be collected after due consent and following both international and national norms and standards of ethical research practice.

The impact analysis will be conducted as a pooled analysis of data from all the countries. A sample size of 500 low birth weight newborns per year per district, i.e. 1000 newborns per district over the 24 months study period, would yield a total of 24,000 newborns across all the study sites (4 countries with 6 districts each). The combined multi-country analysis conducted by the WHO on this sample 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 (i.e. 150 per 1000 livebirths in this population) to 12% mortality (i.e. 120 per 1000 livebirths) in the intervention periods. The data management across all the global sites will be done by the Translational Health Science and Technology Institute (THSTI), an autonomous institute of the Department of Biotechnology, Ministry of Science & Technology, Govt. of India. THSTI will develop a common data platform for both phases of the study, which will be adapted as per the needs of each site. The data for the UP site will be stored on a cloud server managed by CEL, and clean, de-identified data will be shared with the WHO for review and feedback at regular intervals.

There are several mechanisms of oversight for this study. Ethical approval will be sought from the WHO Ethics Review Committee for the overall study, the Institutional Ethics Committee of CEL for the study in UP, and the ethics committees of the various medical colleges that will be participating in this study for enrolment of study participants in their respective facilities. The UP study will be registered with the Clinical Trials Registry of India (CTRI), and clearance will also be sought from the Health Ministry Steering Committee (HMSC). The WHO will provide close oversight to the study across all study sites, which will involve annual field visits as well, besides regular monitoring of data and study progress. The WHO will convene a steering committee for the study that will be comprised of each of the principal investigators from all the study sites, the study coordinators from WHO, a representative of the Ministries of Health of the four countries and 2-3 experts. The Steering committee will be responsible for coordinating activities in the various sites, supervising implementation, reporting of study progress, planning and review of the analysis, and dissemination of study results. The WHO will also appoint a data safety monitoring board (DSMB) before the initiation of the stepped-wedge trial to monitor its overall conduct and quality and safeguard the interests of study participants and stakeholders. Serious adverse events of neonatal deaths will be reported to the DSMB for quarterly monitoring of the trends of neonatal mortality in each of the 24 clusters for safety reasons.

This implementation research will be conducted in close coordination between the research team, the UP government (medical education and health departments) and the community. The research in UP will be led by CEL under the leadership of Dr. Vishwajeet Kumar as Principal Investigator. Dr. Kumar previously served as faculty at the Johns Hopkins University and founded the Community Empowerment Lab. He has conducted several large and complex community and health system-based studies, published widely including in The Lancet, NEJM, BMJ and PLOS Medicine, and serves on various scientific advisory boards, including that of the Indian Council of Medical Research and the national technical advisory group for KMC acceleration. The research will be co-led by representatives from the medical education and health departments of the Government of UP and scientists who are part of the PRAMAAN network.

Table of Contents

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

1. Background

With more than 170,000 newborn deaths each year*, Uttar Pradesh (UP) accounts for nearly one-third of India's burden of neonatal mortality and lies on the critical pathway to achieve national and global goals for newborn survival. Low birth weight (LBW) newborns account for 30% of all livebirths in UP[2], but two-thirds of all newborn deaths†.

A promising, evidence-based, low-cost intervention, Kangaroo Mother Care (KMC), can significantly reduce deaths in preterm and LBW infants. KMC involves prolonged and continuous skin-to-skin contact between a mother and her LBW infant along with frequent and exclusive breastfeeding.[4] Until recently, both the study (with few exceptions) and practice of KMC was restricted to stable LBW infants – conventional care continues to be recommended for unstable infants until attainment of stabilization.

The latest Cochrane Review on KMC from 2016 conducted a meta-analysis of 21 randomized controlled trials that compared KMC initiated post-stabilization with conventional incubator care for low birth weight infants, and found a 40% overall reduction in mortality among infants in the KMC group.[5] In addition, it found a 55% reduction in nosocomial infections, 64% reduction in hypothermia, and several other benefits, including improved breastfeeding, weight gain and mother-infant attachment.[5] A 20-year follow-up study on KMC found that infants who were provided KMC in the first few weeks demonstrated higher academic achievement and more pro-social behaviors than those not provided KMC.[6]

Based on incontrovertible scientific evidence, KMC was incorporated into the global *Every Newborn Action Plan* in 2014 as an essential intervention for low birth weight and preterm infants, with a global target to achieve universal coverage of KMC among all infants with birth weight <2000 grams by 2030.[7] India was an early adopter of this policy and soon after released the *India Newborn Action Plan* (INAP) that aligned with the Every Newborn Action Plan on the recommendations and targets for KMC.

Guidelines for operationalizing KMC within facilities[8] and establishing Maternal & Newborn Care Units (MNCU)[9] to promote developmentally supportive care in special newborn care units (SNCUs) were issued in 2014 and 2018 respectively, but with poor translation into implementation. Further, the care of LBW infants is split across multiple national guidelines that compartmentalize facility and home based newborn care, and are inconsistent regarding the recommendation for KMC as standard of care.[10,11]

Recognizing the need for evidence-informed models to bridge the policy-implementation gap for achieving universal coverage of KMC, the World Health Organization (WHO) coordinated a multi-site implementation research in India and Ethiopia focusing on infants with birthweight <2000 grams. The study aimed to develop contextualized and scalable health system models to programmatically integrate KMC for <2000g newborns across the facility-community continuum. This study took the coverage target one step further from initiation of KMC into targeting 'effective' coverage, defined as skin-to-skin contact of at least 8 hours with exclusive breastmilk feeding.[12] In India, this study was conducted in the states of Haryana, Karnataka and UP, with all sites achieving similar levels of initiation and effective coverage of KMC.[12] In UP, this study was conducted jointly by the Community Empowerment Lab (CEL) and the UP government, and demonstrated a 93% coverage of KMC initiation, and an effective coverage of 53% within facilities and 65% at home following discharge.[2] Since 2016, the innovations developed during this implementation research have been scaled up in 240 health facilities (District Women's Hospitals/ Special Newborn Care Units as well as Community Health Centres/ Newborn Stabilization Units) across UP, described in the subsequent section.

The current national recommendations of initiating KMC only post clinical stabilization of infants, however, limit the potential impact of KMC, given that half to two-thirds of deaths among preterm or low birth weight infants would have already occurred prior to clinical stabilization. For example, in the UP site of the above implementation research, 4.6% of all infants were born with birth weight <2000g, of whom 24% died within the newborn period, with 67% of these deaths occurring within the first 72 hours.[2]

Given the strong evidence with a 40% reduction in mortality and other key benefits from KMC when initiated post stabilization against conventional incubator care, an important hypothesis emerged whether KMC could also contribute to the stabilization of preterm infants and reduce pre-stabilization mortality. Two small trials conducted in 2004 and 2015 comparing initiation of KMC soon after birth with conventional care in infants with birthweight 1200-2200 grams and 1500-2500 grams respectively, found significantly improved transition to extrauterine life and cardio-respiratory stabilization in the KMC group, suggesting that KMC may accelerate and improve stabilization in LBW infants.[13,14] Subsequently, a large multicenter randomized controlled trial was coordinated by the WHO in five hospitals across India, Tanzania, Nigeria,

* Based on NMR of 31.7 per 1000 livebirths from national sample survey data, 2017 [1]
† Based on secondary analysis of data from the Emollient trial.[3]

Ghana and Malawi, that compared the effect of KMC initiated immediately after birth against KMC initiated post stabilization on neonatal mortality rate (NMR) among infants weighing 1000-1800 grams, and found a 25% reduction in deaths in the immediate-KMC group.[15] The large reduction in mortality observed in the intervention group prompted the data and safety monitoring board to recommend that the trial be stopped early as it was no longer ethical to deprive the control group of the intervention.[15]

Based on the findings of the WHO iKMC trial, immediate initiation of KMC in infants with birthweight <1800 grams would contribute to a 25% reduction in mortality over and above the 40% reduction achieved when KMC is initiated post stabilization. These and other new research findings have contributed to a revision of the previous WHO guidelines that recommended initiation of KMC only after stabilization of the infant. The new WHO guidelines for care of preterm or low birth weight infants released in 2022 are based on a systematic review of all available scientific evidence until 2020, and strongly recommend the following:[16]

- KMC should be provided as routine care for all preterm and LBW infants for at least 8 hours daily
- KMC should be initiated as soon as possible after birth with close monitoring of the infant's condition, regardless of clinical stability, unless the infant requires mechanical ventilation or is in shock
- Preterm and LBW infants should be provided mother's own milk, if available (failing which donor human milk and nutrient-enriched preterm formula may be considered in this order of priority) with initiation of entereal feeding as early as possible after birth
- Family involvement in the routine care of preterm and LBW infants admitted in health facilities

Despite advancements in the global scientific evidence and consequently, WHO recommendations, separation of mothers from their sick newborns in Special Newborn Care Units (SNCU) and Newborn Intensive Care Units (NICU) is still the norm in most health facilities in India and in UP. Overall, emerging scientific evidence on the superiority of family-centered, physiologic, and humanized care such as KMC comes into conflict with the traditional medical care paradigm that has been deeply entrenched over decades through medical education and practice. This fundamental shift in newborn care practices amongst care providers and medical institutions requires a design-thinking approach with participation of all key stakeholders, with implementation research informing an evidence-based model for scale.

Given the extraordinary strides made in Uttar Pradesh towards scaling up and institutionalizing KMC within public health institutions, integrating immediate KMC within the roadmap for achieving universal coverage is a logical and critical step forward. The goal of the proposed implementation research is to develop and evaluate a suitable model to achieve the integration of immediate KMC that can be scaled through the public and private health delivery systems with high fidelity and coverage to accelerate NMR reduction.

1.1 Uttar Pradesh Context

A thorough understanding and mapping of the context is fundamental to the conduct of implementation research and critical to designing a suitable strategy for accelerating adoption. We briefly discuss the existing context of newborn care, model for scaling up KMC, and ongoing scale-up of KMC in UP.

1.1.1 Sick and small newborn care in UP

Institutional deliveries now constitute 83% of all births in UP, with two-thirds of all institutional deliveries happening in public health facilities.[17] UP follows the national guideline for Facility-based Newborn Care (FBNC), with 4 levels of newborn care. All delivery facilities are expected to provide essential newborn care services along with basic resuscitation support. Specialized newborn care begins at the level of newborn stabilization units (NBSUs) established within community health centers designated as first referral units, that are expected to provide services for management of stable LBW infants >= 1800 grams, stabilization/referral of sick and LBW infants <1800 grams, phototherapy and newborn sepsis management. The next higher level of specialized newborn care is provided within special newborn care units (SNCUs) established within district-level hospitals that provide Level 2 Neonatal Intensive Care services such as management of LBW infants <1800 grams, management of sick infants not requiring mechanical ventilation and developmental follow-up of discharged infants. UP has also envisioned the establishment of medical colleges in every district in order to make tertiary care available at district-level, and already has 39 state-level govt. medical colleges, in addition to a handful of national-level medical institutes and some private medical colleges as well. Medical colleges are expected to host a neonatal intensive care unit (NICU), which will provide Level 3 neonatal intensive care services such as sustained life support, comprehensive care for the smallest babies, sustained life support with full range of respiratory support including continuous positive airway pressure and mechanical ventilation, and advanced surgical and other specialized tertiary newborn care services.

The above system still has a long way to go in terms of optimal and high-quality functioning. At present, there are 101 designated SNCUs of which 87 are functional, and 180 designated NBSUs with a basic level of functioning. Existing well-established medical institutions have fully functional NICUs. However, some of the newly established medical colleges are likely to experience a slow transition from SNCU (level 2) to NICU (level 3) care.

1.1.2 The UP KMC Model

UP has had a long history of KMC. It witnessed one of the first community-based studies in the world on KMC in 2004-5, where KMC was used as a strategic intervention within an overall package of essential newborn care, to improve the uptake and success of breastfeeding in the first week of life for all newborns, regardless of birth weight, and to bring focus to hypothermia as an important risk factor in home births and home-based newborn care.[18,19] The composite intervention package led to a 54% reduction in NMR.[19] The findings from this study were incorporated into the state's 'Comprehensive Child Survival Programme' launched in 2007, that included community-based KMC into the training curriculum for all newly appointed ASHA workers. However, without sufficient follow-up, supervision, incentive and accountability mechanisms of these workers, noticeable changes in community-based KMC practice were not observed.[20]

Fast forward to 2016, the implementation research for scaling up KMC was initiated at an opportune time when the state government was struggling with poor implementation of the newly released KMC guidelines in SNCU facilities and eager to undertake accelerated innovation development in partnership with CEL. The UP KMC model was thus developed in very close consultation and partnership with the state government, and under the joint leadership of the Secretary Health/ Mission Director, National Health Mission and the Principal Investigator from CEL. It integrated inputs from various stakeholders – mothers and other community stakeholders, all functionaries within the health system from ASHA workers to the bureaucratic leadership, and with strong political backing by the political leadership.

The UP KMC Model was an end-to-end model across the facility-community continuum to achieve universal high-quality coverage of facility-initiated and community-sustained KMC in stable <2000 gram infants, as per the existing WHO guidelines.[2] Where referral was not possible, identified LBW infants were also initiated to KMC at home. The main strategy involved establishing specialized KMC services within existing public health facilities, and establishing them as centers of dissemination and training for mothers and family members, health providers and health workers. Further innovations for improving identification and referral of LBW infants and improving home adherence of KMC completed the KMC facility-community continuum.

A key innovation was the 'KMC Lounge' – a comfortable temperature-controlled safe space for mothers to receive respectful care and provide long duration KMC to their infants within health facilities. Figure 1 contrasts a typical postnatal care ward with a KMC Lounge. The KMC Lounge addressed one of the most fundamental barriers for high-quality, prolonged KMC within health facilities – a lack of privacy and basic comfort and amenities for mothers. Besides creating a respectful and conducive environment for mothers for the practice of KMC, the KMC Lounge also generated visibility and championship for KMC across stakeholders – from the community to the media, and the district leadership to the political leadership at the state level. Thus, it also contributed to a conducive environment for accelerated uptake, scale and institutionalization of accountability mechanisms, and was recognized as a national best practice in 2017.

Figure 1. (a) Typical postnatal care ward in a public health facility (b) The KMC Lounge

The UP model focuses on **integration of KMC across existing programs**, and introduced the concept of the KMC chain (see Figure 2b) with **mother-newborn dyad centric coordination of care** across multiple locations and stakeholders, including district and facility leadership, obstetric and pediatric teams, nurses and frontline health workers. KMC was promoted as a composite package with five components – position, nutrition, hygiene, monitoring and respectful care (see Figure 2a) and corresponding care protocols.

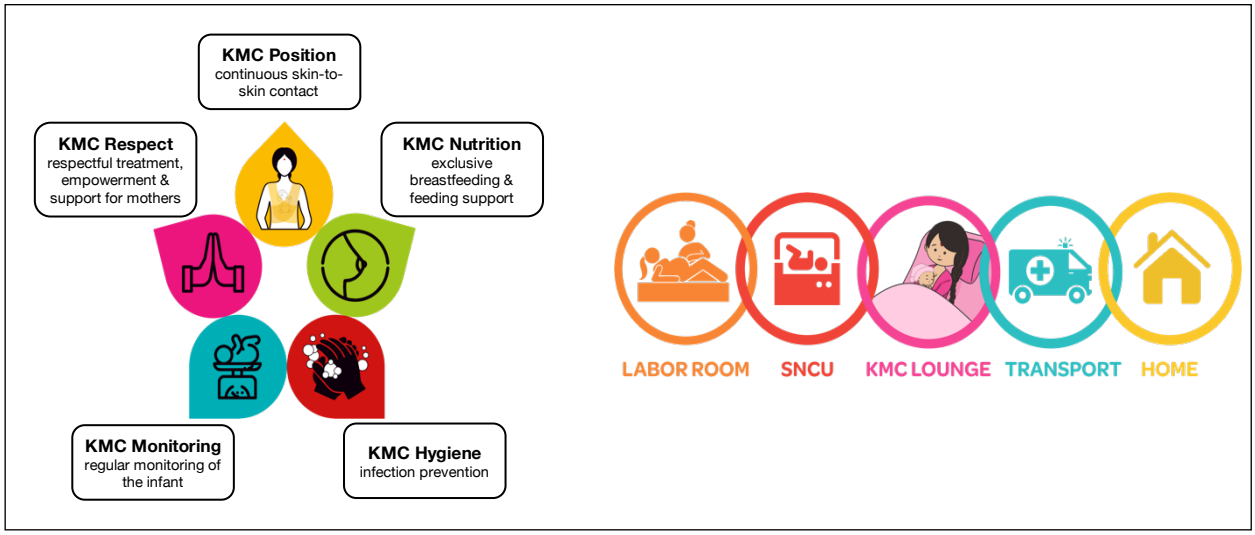


Figure 2. (a) Five-components of KMC (b) KMC Chain

The various components of the entire model are listed in Table 1.

Table 1. Final implementation model for KMC based on 'beyond the building blocks' expanded framework

Domain	Sub-domain	Components
Policy & Financing		• Establishment of KMC Lounges with required infrastructure & supplies for stable infants with birthweight <2000 g • Recruitment of additional SNCU nurses for KMC implementation • Meal provision for mothers & surrogates
Leadership & governance		• Clear political buy-in and championship of KMC by the Health Minister • Health system ownership & leadership in implementation • Leadership of senior district functionaries in KMC implementation & review
Health workforce	Facility-based workers	• Additional nurses to support prolonged stay, counseling and monitoring in KMC Lounges • Training & on-demand coaching sessions for nurses • Close partnership between obstetric and paediatric teams
	Community health workers (ASHA)	• Training & supervision of ASHA workers on weighing, KMC initiation & home support; exposure visits to KMC Lounges
	Other workers	• Orientation of ambulance workers on KMC during transport • Orientation of Auxiliary Nurse Midwives, Anganwadi workers, and other block & district level functionaries on KMC
Service delivery	Facility-based services	• Prolonged stay & 24x7 service provision including counseling & monitoring within KMC facilities • Strengthening of weighing at birth & daily weight monitoring of LBW infants • KMC initiation & referral to KMC facilities based on weight & stability criteria • Aligning key stakeholders to provide respectful mother-baby centric care as a team • Ambulatory KMC, involvement of surrogates as needed, & transition to home plan • Discharge counseling adapted to the needs of the mother & family with roster for home KMC • Inter-facility referral coordination

	Community-based services	• Strengthening high-risk pregnancy identification & encouraging delivery in KMC facilities • Weighing for home births and home-initiation of KMC for families refusing referral to KMC facilities • Strengthening home visitation & priority follow-up of LBW infants by ASHA workers • Baby Care Team consisting of doctors, nurses, ASHA, etc. for following up vulnerable LBW infants in the community
	Tele-services	• Remote nudges for home KMC adherence, counseling & support to overcome challenges, and care coordination with health providers/ workers through a call center
Products, vaccines, technology		• Five-component model of KMC with respective protocols • Integration of KMC services within maternal & newborn programs • KMC Chain workflow within facilities, referral pathway • Tools & videos for counseling; monitoring tools
Information, learning & accountability		• Data-driven review processes for KMC implementation at facility, district & state levels • Online communities of practice for facility heads and nurses • Inter-facility performance-based gamification
Community organizations & societal partnerships		• Partnership with media and civil society organizations to build awareness and championship for KMC • Engagement of political representatives and institutions at the district, block and village levels in building championship & social accountability for KMC • Utilizing social events and opportunities to spread awareness of KMC
Household production of health		• Sensitizing family members to the special needs of LBW infants & support needs of mothers • Including family members in the support and care of the mother-baby dyad

1.1.3 Ongoing scale-up of KMC in UP

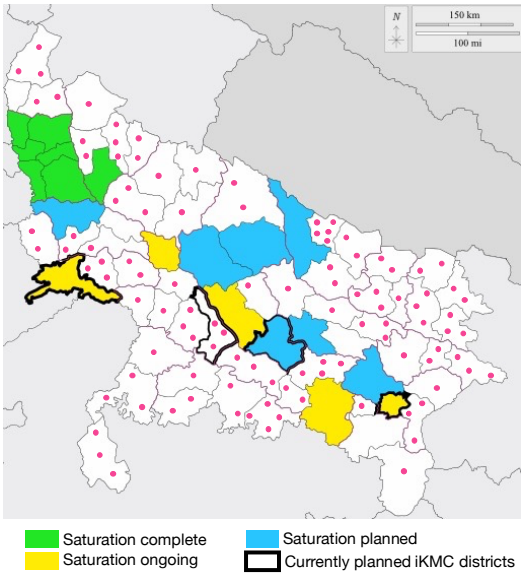


Figure 3. State-wide scale-up of KMC in UP

UP has made tremendous strides in scaling up KMC, with a total of 240 facilities offering KMC services, including 238 district and community health center level facilities, 1 private medical college and 1 private charitable hospital (see Figure 3). Seven of the 75 districts have already saturated the provision of KMC at all district and community health centers. With the Meerut division taking leadership in saturating KMC services in all its 6 districts, an accelerated division-wise saturation of KMC services across the 17 remaining divisions in the state is planned over the next 6 months. The KMC Lounge has evolved into the concept of a 'mother newborn care unit' (MNCU), a respectful and comfortable unit where zero separation is practiced as per the level of care of the facility. Within district level facilities, the MNCU also serves as a step-down ward for the SNCU. Within community health centers, the entire postnatal care ward is being upgraded into an MNCU.

In order to improve the quality of care of LBW infants across all facilities, an 'MNCU app' was developed to support the workflow of nurses in providing high quality care and regular monitoring to LBW infants and their mothers. The data generated by the MNCU app feeds into the performance review of each KMC facility, and monthly meetings are held with each facility to provide specific feedback on improving their processes and provision of care. At present, the MNCU app has been deployed in 217 out of the 240 KMC implementing facilities.

Once high-quality care is established in a KMC facility, it can begin to serve as training and dissemination center for nearby facilities as well as for providers and community health workers within its catchment area.

1.2 High-level strategy for integration of immediate KMC in UP

In order to develop a model for iKMC in UP, we need to identify districts that can lead the way and support the state in scaling up iKMC across the rest of the districts. Successful practice of iKMC per se, requires a certain minimum standard of care within participating facilities, as well as a certain level of confidence and trust among providers in this new and unfamiliar practice, especially when caring for unstable newborns. It must be borne in mind that although it is included in the latest WHO recommendations based on very strong multi-country evidence (including India), iKMC is still not part of the national guidelines. In the UP context, we have learnt that healthcare providers (e.g. paediatricians/ obstetricians) in public health facilities may be averse to following any new practice that is neither part of the national guidelines nor is standard of care in typical care contexts. We therefore need districts, facilities and providers that can play a leadership role as 'early adopters' of this practice and system of care. Specifically, we need model districts that are ready to adopt new evidence-based practices that are life-saving, and ideally, well-functioning medical colleges that are willing to integrate iKMC as standard of care within their care provision and pedagogy.

At present, KMC services are not being provided in medical college hospitals as part of routine care of LBW infants, barring few exceptions. This is also a key barrier for institutionalization of KMC as the medical workforce continues to be trained in a scientifically outdated and inferior system of care, and will therefore end up propagating the same system. This will continue to generate new streams of providers who are unfamiliar with KMC and family-centered care, and who will therefore, require a lot of unlearning of practices that were entrenched over several years of medical education and residency. The integration of immediate KMC provides a great opportunity to mobilize clinical and research teams across the pediatric, obstetric and community health departments in medical colleges to make the necessary foundational changes to integrate KMC as standard of care within their ecosystem, thereby generating a positive momentum for institutionalization and dissemination of KMC as the standard of care, right at the source.

We have established the Partnership for Research in Advancing Maternal and Newborn Health (PRAMAAN) – a consortium of public and private medical colleges and institutions that are keen to apply evidence-based and data-driven approaches to institutionalize KMC for all LBW and preterm infants within their facilities, and support the state in its scale-up. Ten medical colleges in UP are already part of this consortium. This consortium will serve as a strong research platform for future studies/ implementation research related to maternal and newborn health.

We will typically 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. This is in line with UP's plan to have a medical college in each district. Further, the medical college can support the district hospital and other facilities along the referral chain in institutionalizing iKMC. After the study, the participating districts and facilities will serve as dissemination and training centers for immediate KMC integration for other districts in their region.

At a district level, we will establish close working partnerships between the medical college and the district hospital, to leverage local expertise of medical colleges in establishing systems and strengthening quality of care in district hospitals. Similarly, close working partnerships will be encouraged between district facilities and community health centers. This would facilitate greater integration, accountability and referral between these entities and improved quality of care for newborns overall, in the chosen districts.

2. Implementation Research Objectives

2.1 Primary objectives

1. To develop an optimized implementation model that will integrate immediate KMC (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/ SNCUs to Level 2 Mother-Newborn Intensive Care Units (M-NICUs) or Mother-Newborn Special Care Units (M-SNCUs) within the chosen study district.

2. To scale up the model to 3 districts using a stepped-wedge design and evaluate impact of the scale up on health outcomes including neonatal mortality.

3. To support the central government, state governments and districts of interested states to further scale up iKMC.

2.2 Secondary objectives

1. To ascertain the costs and cost effectiveness of immediate KMC implemented at scale

2. To lay the foundation for research implementation platforms that can assess other maternal and newborn health (MNH) interventions and care for preterm or LBW babies.

3. Methods

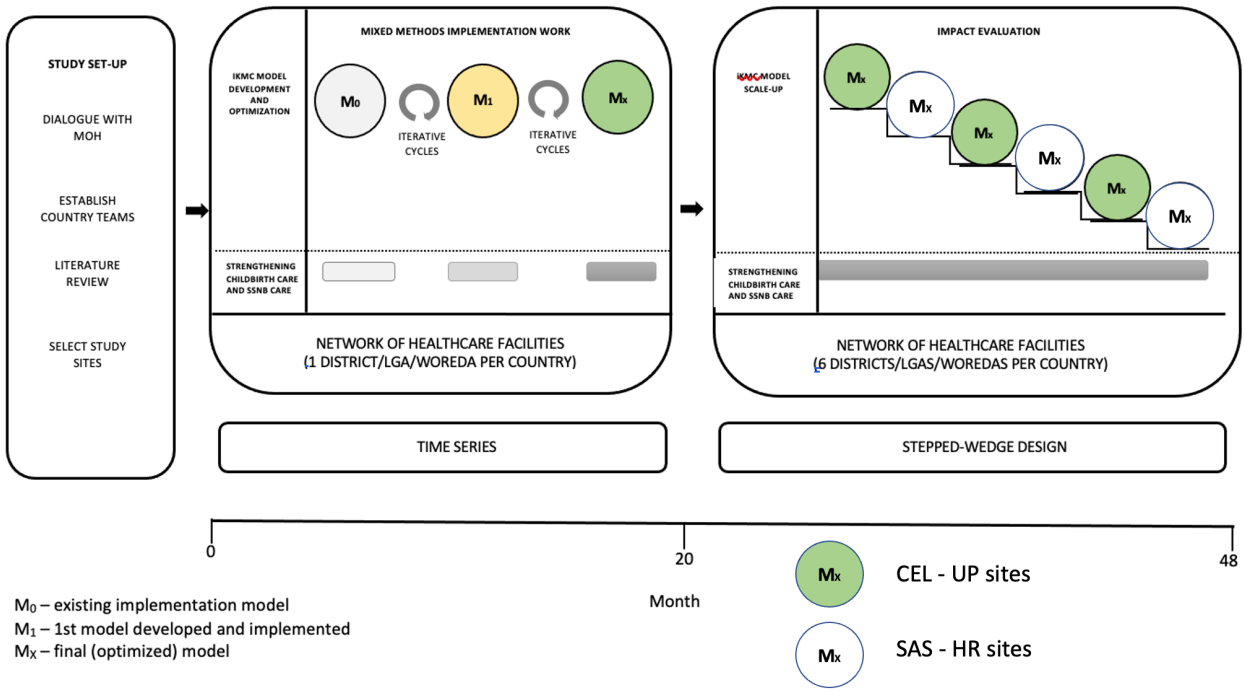
3.1 Study design

This study will be part of a multi-country implementation research and effectiveness study to improve care for preterm or LBW babies. 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.

Phase I is the 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 across 3 additional districts in UP using a stepped-wedge design as part of Phase II, to evaluate the impact of this scale up on neonatal mortality and other important outcomes.

We will choose the Phase I district from central UP in alignment with the high-level strategy. The Phase II districts will be chosen to ensure regional representation across UP, and therefore we will choose at least one district from western and eastern UP regions (see Figure 5). 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%.

Figure 4 – Overview of the study



We will align with the Every Newborn Action Plan (ENAP)[27] 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

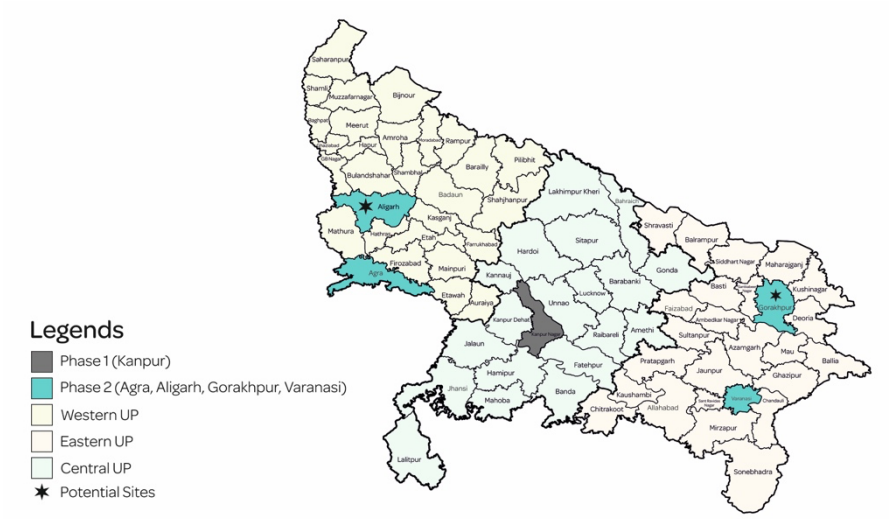


Figure 5. District selection for the study

Uttar Pradesh is one of the two states in India where the study will be conducted, besides Haryana. The states have been chosen based on the presence of a strong implementation research team with the capacity to conduct this study, coupled with a strong commitment of the government to improving hospital-based care for preterm or LBW infants.

The districts and facilities for conducting this implementation research within UP will be in alignment with the high-level strategy as outlined in section 1.2. The provisionally planned districts are shown in the map in Figure 5.

3.2.1 Phase-1: Model development in Uttar Pradesh site

The model development phase is proposed be conducted in Kanpur Nagar district in central UP (Fig 4), although the final district will be chosen in close consultation with stakeholders in the heath 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.

3.2.2 Phase II: Scaling up of the optimized implementation model & its evaluation

During this phase, the optimized iKMC implementation model will be implemented in a randomized stepped wedge manner in 3 districts within UP (chosen on the basis of parameters provided earlier, in consultation with the government and participating institutions) to evaluate its effectiveness on neonatal outcomes.

Each district will have at least one medical college and district hospital as immediate KMC facilities, with potential inclusion of private medical colleges and facilities. The chosen facilities will be supported to become immediate KMC implementing facilities by strengthening the quality of preterm 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-SNCU, including identification of space and organization of infrastructure, procurement of KMC supplies, and training of existing health workers will be done prior to the initiation of iKMC implementation in the district.

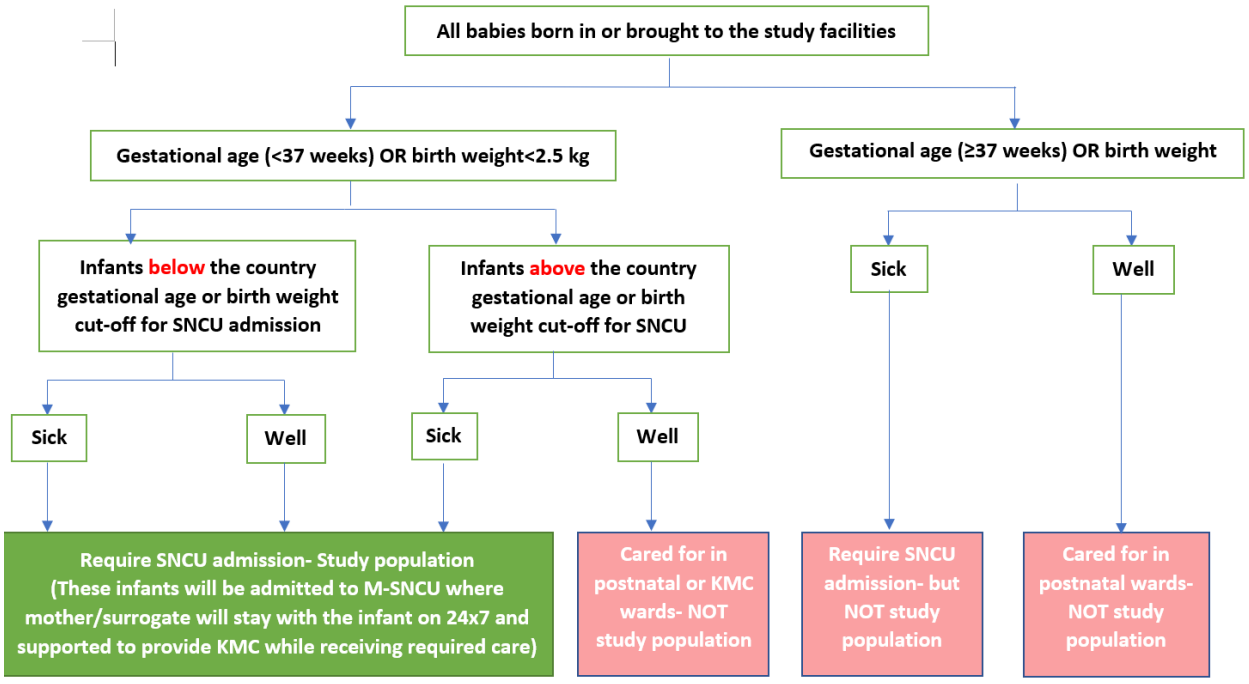
3.3 Study population

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., weighing <1800 grams at birth, or those preterm or LBW newborns who weigh >=1800 grams but are sick and need SNCU admission. See Figure 6 below.

The revised WHO guidelines include a recommendation for KMC for **all** preterm or LBW infants starting immediately after birth unless the newborn is critically sick.[26] 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 NICU/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 of preterm or LBW infants who require NICU/SNCU admission after birth as depicted in Figure 6. During the intervention period, these infants will be admitted to M-NICU/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 NICU/SNCU and KMC will be promoted and encouraged through existing mechanisms.

Figure 6 - 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

This implementation research effort will be conducted in close partnership between the central and state governments and the respective research teams, and will involve the community and other relevant stakeholders. Interventions to support iKMC will be delivered by the health system, potentially with support from community stakeholders; 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. Table 2 below summarizes the composition of the implementation research team.

The research team will consist of three small independent teams: (i) **programme learning & design team**, trained in qualitative methods and review of quantitative analysis, 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, and coordinate activities for co-development of the model along with government/ health system stakeholders and community stakeholders; 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 the IR team

	Government partners	Community stakeholders	Research team		
Overall role	Participate in the co-development of the model, its buy-in, and implementation	Participate in the co-development of the model, its buy-in, & support the implementation.	Implementation, qualitative and quantitative research data collection and evaluation of the implemented programme		
Team members	Health/ administrative leadership, policy makers, implementers, supervisors and health staff/health care providers	Mothers, community leaders & influencers, development partners, etc.	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	Participate in co-design workshops, and offer experiences, insights, suggestions and brainstorm on potential solutions. Lead any other community-driven efforts to improve adoption & quality of KMC. Facilitate institutionalization for accountability, sustainability, and scalability Mothers & surrogates – to provide iKMC to their newborns.	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 trial 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

An important infrastructural modification that is ideally needed for iKMC 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[21], 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 7).

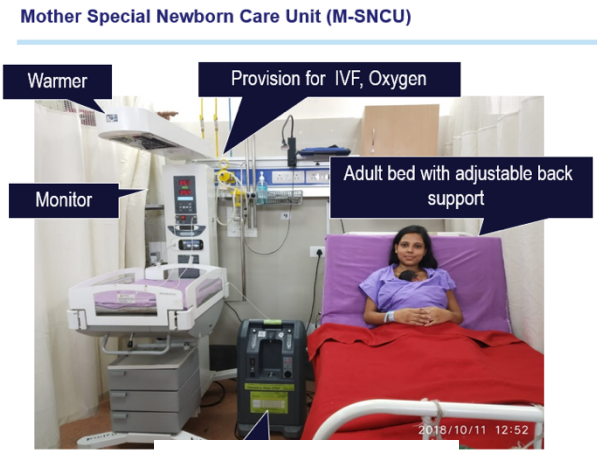


Figure 7 - M-SNCU

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 8). 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.

Figure 8 - Enabling environment

- ***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* [29] 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.[29]

Specifically, we will use the *Consolidated Framework for Implementation Research* in the Generic Implementation Framework [29] to guide the development and process learning activities and include key concepts from the Dynamic Adaptation Process in implementation.[23] 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 Annex 1).

The iKMC trial identified two key common gaps in care: the provision of appropriate respiratory support and periodic clinical monitoring of babies.[23] 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 8 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).[20] Similar methodology will be used during subsequent re-design workshops (see below).

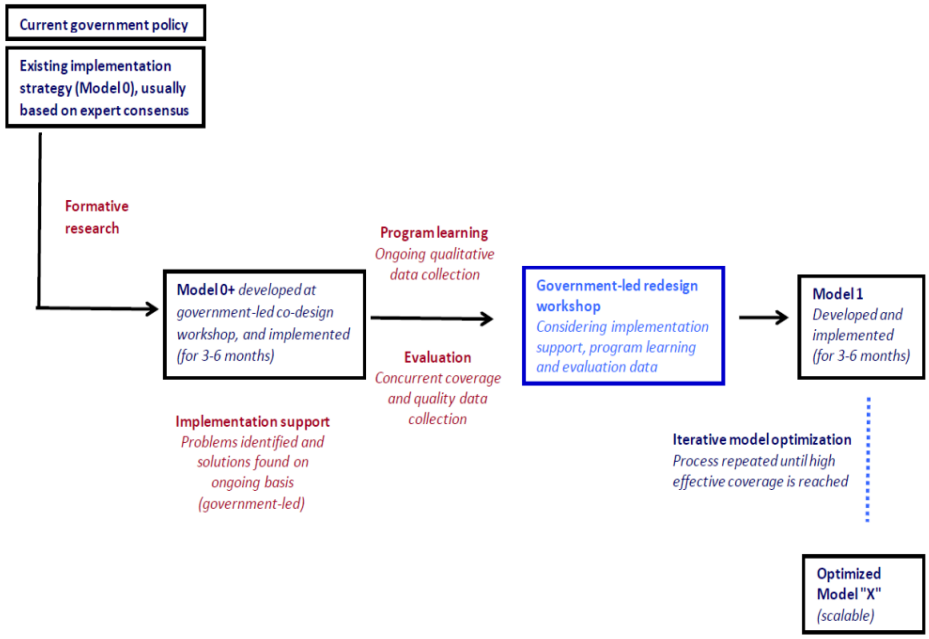
Implementation Model 0+ will be initiated with concurrent programme learning as well as quantitative data collection on coverage and quality outcomes. The quantitative coverage and quality data will be the parameter for optimization of the implementation model, while the qualitative programme learning 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 8 summarizes this process of implementation model development and optimization.

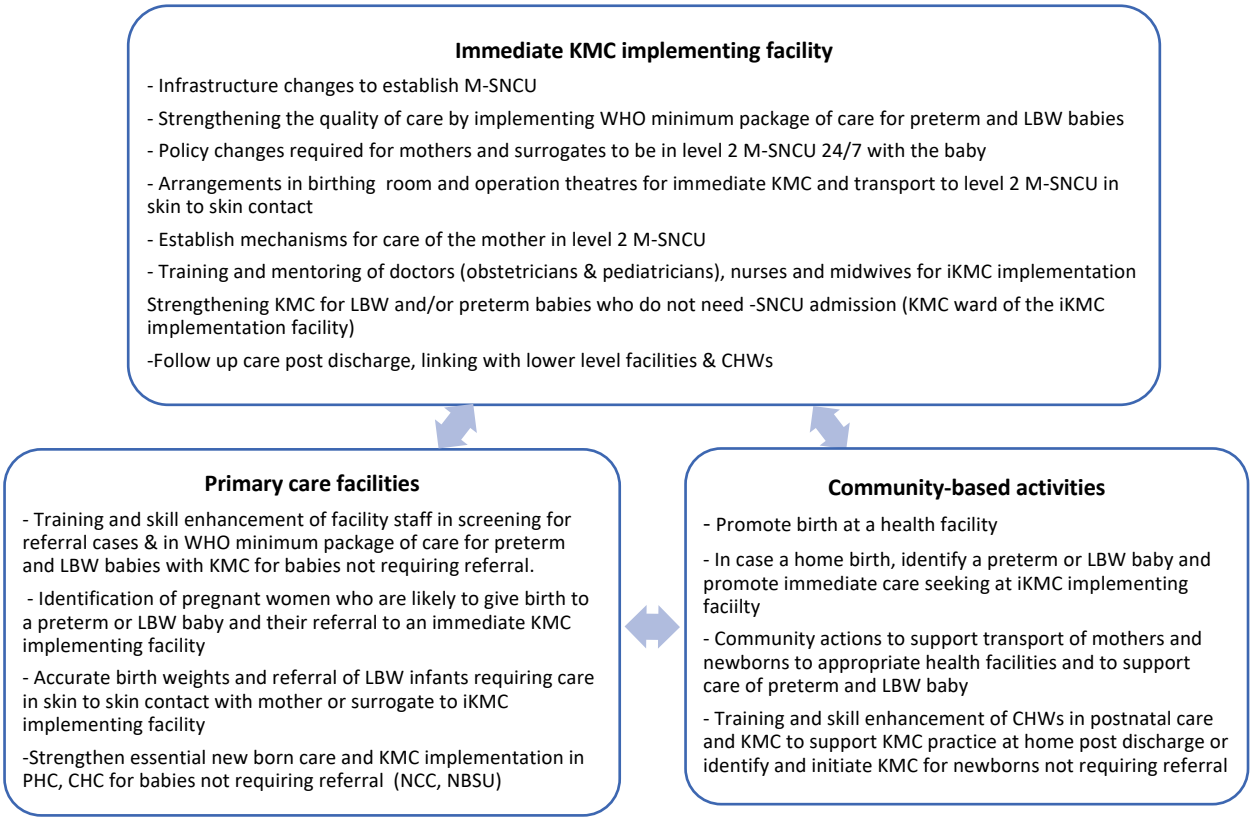
Figure 8 - Process of implementation model development and optimization



Source: reference 25

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 9 below.

Figure 9. 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.[28]

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 3 clusters across the three districts to evaluate its effectiveness on neonatal outcomes.

Each cluster would be one health administrative unit of district/sub-district 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. The health facilities having a functional level 2 SNCU in all the three districts in Uttar Pradesh 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 three identified districts 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 one district 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-randomised trial design in 3 districts over a 24-month duration (Figure 8). The unit of randomization will be a district with 1-2 facilities having functional level 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.

Figure 10. Roll-out of the stepped wedge cluster RCT design in UP

#	Y0	Y1-Q1	Y1-Q2	Y1-Q3	Y1-Q4	Y2-Q1	Y2-Q2	Y2-Q3	Y2-Q4
Cluster 1	Minimum Care Package for small babies implemented	C	T	I	I	I	I	I	I
Cluster 2		C	C	C	T	I	I	I	I
Cluster 3		C	C	C	C	C	T	I	I

C= *Refers to control period in which small or sick newborn care is strengthened.*
T*= Refers to transition period* ***(no measurement)***
I*= Refers to intervention period in which the iKMC implementation model scaled up*

The stepped-wedge design is a unidirectional crossover design where all clusters start in the control phase (i.e., minimum package of care for small and sick newborns) and cross over to the intervention (i.e., the optimized iKMC implementation model) at different timepoints, till all clusters have transitioned to the intervention condition. All 3 clusters in the state will start with the control condition (see Figure 10). At each equally spaced cross-over time, one cluster will transition to the immediate KMC implementation model based on a pre-allocated random sequence. A three-month transition period is included in each cluster to allow for the implementation model to be operationalized. 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 immediate KMC implementing facilities, and strengthening of newborn care to ensure early identification and referral of eligible infants to the immediate KMC implementing facility in skin-to-skin contact with the mother or surrogate, and strengthening of referral pathways. Once each cluster has crossed to the intervention, it will continue to be exposed to it for the remaining duration of the study. The coverage outcomes will be analyzed at the state and country level (along with another similarly designed study to be conducted in Haryana). However, impact outcomes, i.e., pre-discharge and neonatal mortality will be pooled and analyzed at the country level (along with another similarly designed study to be conducted in Haryana) and ascertained at a global level in combination with data from multiple countries by the WHO.

The rationale for a stepped-wedge design in evaluating the effectiveness of the 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 step 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 taken into account.

3.7.3. Randomization

The study will run concurrently in the 6 clusters in 2 sites of India i.e. 3 clusters in UP (by CEL) site and 3 in Haryana (by SAS). 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 6.

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 6, 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 coverage outcomes from the trial will be assessed at the state and country level (to be pooled with data from a similar study in Haryana). The impact outcomes – pre-discharge mortality and NMR, will be pooled at a country level along with Haryana, and ascertained at a global level in combination with data from other countries by the WHO for adequate statistical power.

Due to the paucity of reliable preterm birth data, sample size calculations are based on LBW estimates. The sample size for clusters has been estimated at WHO based on the average characteristics across sites, and is not UP or India-specific. 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%, resulting in estimated 20,000 livebirths. Of which, we assumed that yearly 5% of LBW newborns would require care at SNCU (1000 LBW infants 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 600 LBW newborns). To allow for varying cluster sizes within country/districts, we have assumed a 0.75 variation coefficient.

Parameter	Estimates
No. of LBW newborns requiring care in level-2 units born in facilities or transferred to facility within 24 hours after birth in one district	500/year (125/quarter)
Neonatal mortality before discharge in control periods (based on the WHO immediate KMC trial)‡	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

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.[22] For mortality outcome we have assumed an ICCs of 0.01 (considered sensitivity at 0.005 to 0.02). Considering the

‡ WHO Immediate KMC Study Group, Arya S, Naburi H, Kawaza K, et al. Immediate "Kangaroo Mother Care" and Survival of Infants with Low Birth Weight. N Engl J Med. 2021 May 27;384(21):2028-2038.

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-period 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.

The combined multi-country analysis conducted by the WHO 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 periods. All calculations were done based on a method proposed by Karla Hemming (University of Birmingham, UK) with the Shiny CRT calculator.[31]

With 3 clusters in UP, the total sample size for UP would be around 3,000 LBW births during the 24 months study period. Similarly, with 24 clusters across countries, the total sample size of study would be 24,000 LBW births during the 24 months study period.

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.[32]

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 14.1.
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.

Accordingly, a scale-up strategy will be develop in close consultation with the state and national government with the research team providing the necessary technical support. This is in alignment with the ongoing scale-up of KMC in UP. Findings from the study will be consolidated by the WHO with findings from other countries to propose a global model for scaling up immediate KMC. 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[29] . 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 3.

The 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 3. 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	Outcome measurement team	By checking M-SNCU register / clinical records filled by routine staff in M-SNCU and interviews with mothers at M-SNCU

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
		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)		
Other outcomes				
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

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
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
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 4, 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 4. 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		First outcome will be measured by the outcome evaluation team	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)	in the M-SNCU/SNCU in the trial facilities who are born alive in or brought alive to the trial facilities. 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		Second and third outcomes will be measured using routine M-SNCU/SNCU staff records and maternal interviews. Outcome 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		

	Numerator and denominator	Specific notes to the indicator	Data collected by	
			Who	How and where
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 admitted in the M-SNCU/SNCU in the trial facilities (Expressed as percentage)	Temperature measurement schedule may be site-specific (M-SNCU/SNCU based protocol)		
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 WHO and other research sites, 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.

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 managed by data manager who will be 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 two-layer data quality check for completeness and accuracy will be implemented. Random spot checks and data validation will be coupled with independent audits. Any discrepancies will be immediately addressed. All effort will be made to minimize missing data. Data is owned by study site. We 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 by WHO with study sites 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, Community Empowerment Lab Institutional Ethics Committee (CEL IEC) Boards (IRBs) and in participating institutions institutional ethics board. 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.

Initiation of study intervention Evidence showed 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 Hindi 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 5.

Table 5. 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

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 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 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.

There might be a risk that mothers/caregivers feel that the poor outcome of their children is due to failure to seek care, non-compliance with treatment, or lack of money. However, the healthcare providers will be well trained in asking these questions to mitigate the risk.

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 by the study team within 7 days to the WHO, Geneva team, who will collate data from all the sites and report 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.

11. Implementation research team and partnerships

This implementation research will be conducted in close coordination between the research team, the UP government (medical education department and health system) and the community. The research in UP will be led by **Dr. Vishwajeet Kumar** as Principal Investigator (PI). Dr. Kumar previously served as faculty at the Johns Hopkins University and founded the Community Empowerment Lab to bring science to empower communities and health systems in improving maternal and newborn survival and early child development. Over the last 20 years, Dr. Kumar has led multiple large community and hospital based trials and implementation research in close partnership with the health system and community stakeholders. Dr. Kumar also served as the PI for the implementation research on developing a health system model to scale up KMC for stable low birth weight infants in Uttar Pradesh, that has laid the foundations for the ongoing scale-up of KMC across UP. Dr. Kumar has several high impact scientific publications, including in The Lancet, NEJM and PLOS Medicine. He serves as a member of the National Technical Advisory Group on KMC, and on the Scientific Advisory Board to the Indian Council of Medical Research.

Ms. Aarti Kumar serves as the CEO of CEL, and will also serve as a Co-PI of this study. Ms. Kumar has been leading the current expansion and quality improvement program for KMC in UP. Under her leadership, CEL has also established the Partnership for Research in Advancing Maternal and Newborn Health (PRAMAAN) network that is dedicated to the advancement of research of public health relevance, generation of local evidence and contribution to state and national-level policy making. The network currently consists of 10 medical colleges across UP, and will continue to expand to include nursing colleges and other multidisciplinary institutions of eminence that can contribute to this goal. The entire research team at CEL is well positioned to conduct this implementation research study in close partnership with the government, the **PRAMAAN network** and community stakeholders. The team has been working relentlessly post the completion of the KMC implementation research in March 2019 to make good on its commitment to support the government in scaling up KMC across the state with high coverage and quality. A dedicated team has been constituted for this that has established deep partnerships with every level of the government and health system across the state and is providing all relevant support to attain the goal of universal coverage of KMC for all low birth weight infants. The quality improvement efforts are powered by the MNCU App which was co-developed with clinical experts as well as users.

Mr. Pramod Kumar Singh, who has over 20 years of experience in immersive community and health system-entrenched research and co-development of innovations with key stakeholders, has been at the forefront of KMC scale-up efforts, and will also serve as a Co-PI of this study.

Dr. Rashmi Kumar is a senior paediatrician and scientist and Senior Technical Advisor at CEL, and will also serve as Co-PI of the study, focusing on the clinical care and neurodevelopment follow-up of infants at the immediate KMC facilities. She has previously served as the head of the department of paediatrics at the King George's Medical University, Lucknow, has led multiple research programs at her institution and published widely, including in NEJM, The Lancet and BMJ.

Several partners in the PRAMAAN network will serve as Co-PIs in the proposed study. They are currently leading the obstetrics, paediatrics/ neonatology departments in their respective institutions. We will further also include nodal officers from the community health departments in the various medical colleges. More investigators will be added as the network expands.

Dr. Vasanthkumar Namasivayam, IAS is a member of the Indian Administrative Services and Executive Director of the UP-TSU, which is providing technical support to the Govt. of UP for reproductive, maternal, newborn & child health & nutrition activities across 75 districts. He provides strategic guidance to the GOUP to implement evidence-based policies, scale successful innovative models and health system strengthening including human resources.

Dr. Yashwant Kumar Rao is a neonatologist and Professor and Head of Department, Paediatrics at GSVM Medical College, Kanpur. He did his MD (Paediatrics) from King George's Medical College, Lucknow. Dr. Rao has held several leadership positions in his college and medical associations, and advisory positions with the government. His areas of interest are neonatology, critical care, malnutrition and non-communicable diseases in childhood and adolescence. He is leading multiple ICMR studies and is a Co-PI on the ongoing PSBI trial in Kanpur Nagar.

Dr. Neena Gupta, Professor and Head of Department of Obstetrics & Gynaecology, GSVM, Kanpur, completed her MBBS from KGMU, Lucknow and MS (Obs. & Gynae.) from SNMC, Agra. She received President's Guide Award and certificates of appreciation from IMA on 'international women's day' and 'national safe motherhood day'. She has more than 60 papers published in peer-reviewed journals. Dr. Gupta has presented more than 40 papers in various conferences of state and national level and has supervised over 60 thesis as guide and co-guide. She is Master trainer PPTCT Programme, Laparoscopic tubectomy, community care of new born & SIFPSA, comprehensive abortion care, MIYCN, New contraceptives, Emergency contraceptives, MDR, BEMOC, CEmONC and Competency based PPIUCD technique, Trained in ART and reproductive medicine, basic endoscopy, Good clinical practices, CA cervix screening.

Dr. Smriti Agrawal is Professor and Head of Department, Obstetrics & Gynaecology at RMLIMS, Lucknow. She pursued her MBBS from Madras Medical college Chennai and MD & DNB from PGI Chandigarh. Dr. Agarwal is the nodal officer for RRTC program at RMLIMS Lucknow. She has done significant work on Genital TB, GDM, mycotoxins, extramural and intramural. She has guided 8 thesis and co-guided 1 PhD project along with 32 thesis. She has several publications in reputed peer review journals.

Dr. Dipti Agarwal is Professor & Head of Department, Paediatrics at RMLIMS, Lucknow. Some significant courses that she has been trained in include- Medical Ethics course, Advanced course in vaccinology, Antibiotic stewardship program, PMDT module etc. Dr. Agarwal is a Master trainer in Newborn stabilization unit, Basic Newborn Resuscitation Program, IMNCI, SAANS, Cough Module, National Pediatrics TB guidelines, Standard TB care-WHO. She has organised 15 CMEs and workshops, conducted RRTC training for three districts, NBSU trainings, State training program of SAANS in collaboration with NHM and UNICEF for the District Medical Officers, BNCRP trainings for doctors and nurses. She is the Principal investigator in 5 intramural projects and has 47 Publications (National and International Journals peer reviewed indexed) and 15 Chapters. Apart from this, Dr. Agarwal is also the reviewer of various reputed journals- Frontiers in Pharmacology, Lancet infectious diseases, Pediatrics Infectious Disease, BMC Infectious disease, Indian Paediatrics , Indian Journal of Paediatric.

Dr. Ashok Kumar Gupta, MBBS, MD, PDCC is Assistant professor department of paediatrics (Neonatology) at RMLIMS, Lucknow. He has various publications in his area of interest i.e. neonatal intact survival. He received gold medal in Scientific Article Publication in Journal of the Anatomical Society KGMU, Lucknow. Dr. Kumar has presented poster in Zonal NEOCON and received first prize , along with active participation in various other conferences.

Dr. Uma Pandey is MD (BHU), FRCOG (London). She is Professor and Head of the Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi. She is

Examiner for MRCOG Examinations Fellow Representative, AICC RCOG North Zone 2021-2023. CHAMPION Trial: She was Principal investigator at BHU for various studies and published them in various peer journals. One of the trial findings which published in NEJM were incorporated in WHO PPH recommendations.

Dr. Ashok Kumar is Professor in Pediatrics, In-charge-Neonatal section and Dean-Research, Institute of Medical Sciences, BHU, Varanasi. Dr. Kumar is an enthusiastic researcher with around 180 publications in national and international peer-reviewed journals. His research journey started with observational and descriptive studies, and over the last 6-8 years, has ventured into randomized controlled trials as well - with 8 trials already published so far. Of late, he has taken a special interest in qualitative research and found it of profound value in understanding how mothers and families feel, think, act and make decisions.

Dr. Richa Singh is Professor in Department. of Obs. & Gynae. S. N. Medical College Agra. She pursued her MBBS from Lady Hardinge Medical College , New Delhi and did her MS from S. N. Medical College , Agra. She is the Vice President of Agra Obs. & Gyn. Society and Agra Menopause Society. She has been the Organising Secretary Midterm UPCOG Agra 2018.She has been Awarded Kamini Rao Yuva Oration AICOG Guwahati in the year 2010 and the prestigious Padma Shree Usha Sharma Oration UPCOG 2018 Prayagraj. Dr. Singh has also received the FOGSI CORION Research Award AICOG 2012 Varanasi, the Karan Gupta Award, Jagdishwari Mishra Award, and B.D. Jamuna Prasad Award for best Research Papers. She has published many Paper publications in Indexed Journals.

Dr Poonam Yadav is Associate Professor**,** Department of OBS-GYN at S.N.Medical College, Agra. She pursued her MBBS from KGMC Lucknow and MS from BRDMC Gorakhpur. She has received the FOGSI CORION Award (Junior category) at AICOG 2016, FOGSI – “Dr DC Dutta prize” by FOGSI for best handbook published in 2020. FOGSI- “Jagdishwari Mishra prize” for best poster presentation in AICOG 2020, “Shri Prabhu Dayal Baweja Medal” for best paper published in the journal of U.P Chapter of Obstetrics & Gynaecology, Best paper presentation award in YUVA ISAR 2019 Best paper presentation in 9th conference of South Asian Federation of Obstetrics & Gynaecology & Yuva ISAR 1019 at Agra. Dr. Yadav is the Co-ordinator of various national live workshops on laparoscopy and vaginal hysterectomy (AICOG 2016 and SELSICON). Guest speaker, moderator & panellist at various international and national conferences, Dr. Yadav has received the Achievers Award by AOGS in 2012, 2014,2016,2017. She has been the Joint editor for AICOG 2016 and Editor AOGS 2019-2020. She has more than 30 publications in various international and national journals and books and Published a hand book on “Common medical disorders in pregnancy” as editor AOGS.

Dr. Neeraj Yadav pursued his MBBS from KGMC Lucknow and MD Pediatrics GSVM Medical College Kanpur. His field of interest is Neonatology and Pediatrics Critical Care. He has won Various prizes for paper & poster presentation at state and national level. He did Fellowship in Clinical Neonatology. He has been Fellow at Indian Academy of Pediatrics 2018. National and state course instructor of NRP, EPIC, IMNCI, FIMNCI, PFCCS, FBNC and the Divisional co-ordinator of post graduate quiz of Indian Academy Pediatrics, Dr. Neeraj has been a Guest speaker, moderator & panellist at various international and national conferences. He was honoured as an expert by UP Service Commission, Allahabad on several occasion for Medical officers and Faculty in Pediatrics. Dr. Yadav has more than 30 publications in various international and national journals and books and has also been a reviewer for many reputed journals.

References

1. India State-Level Disease Burden Initiative Child Mortality Collaborators. Subnational mapping of under-5 and neonatal mortality trends in India: the Global Burden of Disease Study 2000-17. *Lancet* **395**, 1640–1658 (2020).
2. Kumar, A. *et al.* A scalable health system model to achieve high coverage and quality of Kangaroo mother care in Uttar Pradesh, India. *Acta Paediatr.* (2022) doi:10.1111/apa.16534.
3. Kumar, A. *et al.* Effect of sunflower seed oil emollient therapy on newborn infant survival in Uttar Pradesh, India: A community-based, cluster randomized, open-label controlled trial. doi:10.1371/journal.pmed.1003680.
4. Whitelaw, A. & Sleath, K. Myth of the marsupial mother: home care of very low birth weight babies in Bogota, Colombia. *Lancet* **1**, 1206–1208 (1985).
5. Conde-Agudelo, A. & Díaz-Rossello, J. L. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. *Cochrane Database Syst. Rev.* (2016) doi:10.1002/14651858.CD002771.pub4.
6. Charpak, N. *et al.* Twenty-year Follow-up of Kangaroo Mother Care Versus Traditional Care. *Pediatrics* **139**, (2017).
7. World Health Organization & Unicef. *Every newborn: an action plan to end preventable deaths*. https://apps.who.int/iris/bitstream/handle/10665/127938/9789241507448_eng.pdf (2014).
8. Child Health Division, Ministry of Health & Family Welfare, Government of India. *Kangaroo Mother Care & Optimal Feeding of Low Birth Weight Infants: Operational Guidelines for Programme Managers & Service Providers*. http://www.nhm.gov.in/images/pdf/programmes/child-health/guidelines/Operational_Guidelines-KMC_&_Optimal_feeding_of_Low_Birth_Weight_Infants.pdf (2014).
9. Jhalani, M. Maternal and Newborn Care Unit Operational Guideline 2018. https://nhm.gov.in/New_Updates_2018/Om_and_orders/rmncha/child_health/As_md_letter_on_MNCU.pdf (2018).
10. Ministry of Health & Family Welfare, Government of India. *Facility Based Newborn Care - Operational Guidelines*. (2011).
11. Ministry of Health & Family Welfare, Government of India. *Home Based Newborn Care: Operational Guidelines*. https://www.healthynewbornnetwork.org/hnn-content/uploads/Revised_Home_Based_New_Born_Care_Operational_Guidelines_2014.pdf (2014).
12. Mony, P. K. *et al.* Scaling up Kangaroo Mother Care in Ethiopia and India: a multi-site implementation research study. *BMJ Glob Health* **6**, (2021).
13. Chi Luong, K., Long Nguyen, T., Huynh Thi, D. H., Carrara, H. P. O. & Bergman, N. J. Newly born low birthweight infants stabilise better in skin-to-skin contact than when separated from their mothers: a randomised controlled trial. *Acta Paediatr.* **105**, 381–390 (2016).
14. Bergman, N. J., Linley, L. L. & Fawcus, S. R. Randomized controlled trial of skin-to-skin contact from birth versus conventional incubator for physiological stabilization in 1200- to 2199-gram newborns. *Acta Paediatr.* **93**, 779–785 (2004).

15. Immediate KMC Study Group, W. H. O. Immediate “Kangaroo Mother Care” and Survival of Infants with Low Birth Weight. *N. Engl. J. Med.* **384**, 2028–2038 (2021).
16. World Health Organization. *WHO recommendations for care of the preterm or low-birth-weight infant*. (2022).
17. International Institute for Population Sciences (IIPS) & ICF. *National Family Health Survey (NFHS-5), 2019-21: Uttar Pradesh District-wise factsheets*. http://rchiips.org/nfhs/NFHS-5_FCTS/COMPENDIUM/Uttar_Pradesh.pdf (2021).
18. Darmstadt, G. L. *et al.* Introduction of community-based skin-to-skin care in rural Uttar Pradesh, India. *J. Perinatol.* **26**, 597–604 (2006).
19. Kumar, V. *et al.* Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial. *Lancet* **372**, 1151–1162 (2008).
20. Vimarsh & State Innovations in Family Planning Services Project Agency (SIFPSA). *Evaluation of Comprehensive Child Survival Program under NRHM in Uttar Pradesh*. http://upnrhm.gov.in/assets/site-files/monitoring_and_evaluation/PDF_CCSP_Final_Report_14.10.13.pdf (2013).
21. Immediate “Kangaroo Mother Care” and Survival of Infants with Low Birth Weight. *New England Journal of Medicine* **384**, 2028–2038 (2021).
22. Taljaard, M. *et al.* Intracluster correlation coefficients from the 2005 WHO Global Survey on Maternal and Perinatal Health: implications for implementation research. *Paediatric and Perinatal Epidemiology* **22**, 117–125 (2008).
24. Immediate “Kangaroo Mother Care” and Survival of Infants with Low Birth Weight. N Engl J Med. 2021;384(21):2028-2038. doi:10.1056/nejmoa2026486
25. Mony PK, Tadele H, Gobezayehu AG, et al. Scaling up Kangaroo Mother Care in Ethiopia and India: a multi-site implementation research study. BMJ Glob Health. 2021;6(9):e005905. doi:10.1136/bmjgh-2021-005905
26. WHO recommendations for care of the preterm or low birth weight infant. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO
27. WHO & UNICEF. Survive and thrive: transforming care for every small and sick newborn. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/publications/i/item/9789241515887
28. World Health Organization. Standards for maternal and newborn health. 2007 (http://www .who.int/maternal_child_adolescent/ documents/a91272/en/).
29. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice : a consolidated framework for advancing implementation science. 2009;15:1-15. doi:10.1186/1748-5908-4-50
30. Taljaard M, Donner A, Villar J, et al. Intracluster correlation coefficients from the 2005 WHO Global Survey on Maternal and Perinatal Health: implications for implementation research. Paediatr Perinat Epidemiol. 2008;22(2):117-125. doi:https://doi.org/10.1111/j.1365-3016.2007.00901.
31. Hemming K, Kasza J, Hooper R, Forbes A, Taljaard M. A tutorial on sample size calculation for multiple-period cluster randomized parallel, cross-over and stepped-wedge trials using the Shiny CRT

Calculator. Int J Epidemiol. 2020 Jun 1;49(3):979-995. doi: 10.1093/ije/dyz237. PMID: 32087011; PMCID: PMC7394950.

32. Hemming K, Taljaard M, McKenzie JE, Hooper R, Copas A, Thompson JA et al. Reporting of stepped wedge cluster randomised trials: extension of the CONSORT 2010 statement with explanation and elaboration. BMJ 2018 Nov 9; 363:k1614

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	

*** 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.*