Implementation research to develop and evaluate a mother-infant centred, pandemic-resilient, scalable model for improving the identification and management of possible serious bacterial infections in young infants in Uttar Pradesh, India

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Abbreviations

ANM	Auxiliary Nurse Midwife
ASHA	Accredited Social Health Activist
AWW	Anganwadi Worker
CHC	Community Health Centre
CHO	Community Health Officer
CSI	Clinical Severe Infection
FBNC	Facility Based Newborn Care
F-IMNCI	Facility-based Integrated Management of Newborn and Childhood Illnesses
HBNC	Home Based Newborn Care
HWC	Health and Wellness Centre
IMCI	Integrated Management of Childhood Illnesses
IMNCI	Integrated Management of Newborn and Childhood Illnesses
INAP	India Newborn Action Plan
IR	Implementation research
JSSK	Janani Shishu Suraksha Karyakram
JSY	Janani Suraksha Yojana
KMC	Kangaroo Mother Care
MAA	Mother’s Absolute Affection (Breastfeeding promotion programme)
NBCC	Newborn Care Corner
NBSU	Newborn Stabilisation Unit
NMR	Neonatal Mortality Rate
PM-JAY	Pradhan Mantri – Jan Arogya Yojana (health insurance scheme)
PSBI	Possible Serious Bacterial Infection
SAANS	Social Awareness and Action plan to Neutralise Pneumonia Successfully
SNCU	Special Newborn Care Unit
UP	Uttar Pradesh
WHO	World Health Organization

Executive Summary

Infections account for nearly half of all deaths in under-5 children globally, and more than a third of all newborn deaths in the state of Uttar Pradesh (UP), India. In developing country settings, infants aged <60 days are particularly vulnerable with their nascent immune systems, compromised breastfeeding and hygienic care practices, and lack of protection from vaccine-induced immunity. Due to the risk of rapid deterioration in condition and paucity of suitable diagnostic resources, infections in the 0-59 day age group of infants (referred to as 'young infants') are identified using clinical sign-based algorithms, and are therefore referred to as 'possible serious bacterial infections' (PSBI). The incidence of PSBI in South Asia and sub-Saharan Africa is approx. 10% of all livebirths.

The World Health Organization (WHO) recommends a comprehensive approach to address PSBI in young infants, including primary prevention, early identification and care-seeking and rational management, based on an extensive body of evidence. Within India, PSBI prevention, identification and management is spread across several policies and programs, with untested assumptions and gaps in policy and implementation. The COVID-19 pandemic has also led to widespread disruptions in maternal and child health services that has impacted PSBI care as well. The proposed implementation research aims to apply a **mother-infant centred approach** to develop and test a scalable model in UP to identify and manage PSBI in young infants, that is robust to pandemic-related disruptions.

Previous PSBI implementation research studies conducted in Haryana, Himachal Pradesh, Maharashtra and UP adopted a service-strengthening approach to operationalise WHO's policy on community-based PSBI management where referral is not possible, and faced several implementation challenges which could not be adequately resolved. These include differences between national and WHO guidelines on PSBI identification and management, lack of trust in the health system and preference for private providers, poor coverage and quality of home visitations by Accredited Social Health Activist (ASHA) workers, low feasibility of utilizing Auxiliary Nurse Midwives (ANMs) – the primary provider for community-based management designated in the Indian guidelines, requirement of intensive handholding support for medical officers and staff nurses in lower level facilities, blind referrals to higher facilities, and systemic problems of dysfunctional equipment and medicine supply shortages.

The proposed implementation research will be conducted in Kanpur Nagar district with a population of 4.8 million with a third of the population living in ten rural blocks surrounding a vibrant city centre. The health system infrastructure in Kanpur Nagar consists of 3 district-level hospitals (including one with a medical college) equipped with special newborn care units and 10 rural community health centres providing secondary level care. There are also several private clinics and hospitals catering to the paediatric age group, some also equipped with neonatal intensive care units. Two of the district level facilities and one private charitable hospital are also sites for an ongoing WHO-sponsored trial on optimising place of treatment and care regimens for young infants with PSBI that is led by the same team of investigators. Kanpur Nagar also has a large number of unqualified healthcare providers who serve an unmet need for medical care across underserved areas in UP and other Indian states. These providers exist in the same ratio of 1:1000 population as ASHA workers and are currently the preferred providers for primary care of young infants in rural blocks.

Prior to operationalisation of the trial, which was impeded due to the impact of the COVID-19 pandemic, we conducted formative research during December 2020 – March 2021 to understand the broader context of PSBI prevention, identification and management in the district and how it was impacted by the pandemic. Based on this formative work, we developed a strategy for improving early identification of danger signs and facilitating care-seeking. These have informed our theory of change for prevention, identification and management of PSBI in young infants, and have laid the foundations for this work.

The **primary outcome** of the research is **PSBI identification coverage**, defined as the proportion of young infants identified with PSBI by trained providers as compared to an assumed PSBI incidence rate of 10% of all young infants. The model will be designed to achieve a PSBI identification coverage of at least 80%, and achieve a near universal coverage of treatment in the infants identified with PSBI. We will also do a cascade analysis to assess effective coverage and barriers and bottlenecks at each step of the cascade.

We will follow the Design-Outcome Cascade implementation research framework in order to design and evaluate the PSBI model, and therefore begin by first designing solutions to meet user-level endpoints (mothers and family members), and then by designing solutions to meet provider-level service delivery endpoints. The model development and refinement process will be based on a generic pathway for illness identification and management and optimization of corresponding process outcomes using an iterative human-centred design approach. This will be strategized, reviewed and guided through quarterly **plan-do-study-act cycles** with co-investigators and key block and district-level health system and community stakeholders.

The model development, refinement and evaluation will be conducted in a rural block (population ~150,000; annual birth cohort ~3,000) in Kanpur Nagar over a period of 12 months across 4 plan-do-study-act cycles of 3 months each. Each cycle will have a specific focus on aspects of model development and refinement, and specific goals with respect to model outcomes for each cycle will be identified based on the results of the previous cycle.

The target population for the evaluation consists of all live births of usually resident mothers in the study area, who will be registered upon notification and concurrently followed up, after due consent, for 60 days at age 15, 30, 45 and 60 days. Infants identified with PSBI will be followed up at treatment initiation and 8 days after treatment initiation or upon discharge from facilities (based on place of treatment) for study-related outcomes. Further, verbal autopsies will be conducted for all deaths reported in enrolled young infants.

The sample size requirement is based on an assumed PSBI incidence rate of 10% among all young infants. In order to conclude with 95% confidence that the PSBI identification coverage attained through the model is 80% or more of the assumed PSBI incidence rate with a precision of 10%, we will need to enrol at least 2,828 young infants. Thus, one block with a population of approx. 150,000 and approx. 3,300 births per annum is sufficient to provide this sample size over a 10 to 12-month follow-up period.

Evaluation data would be collected on Android-based tablet devices, with inbuilt checks for missing values, inconsistencies and skip logic. Measures to conduct aggregate-level data quality checks and ensuring timeliness of data collection for each young infants will be put in place.

The study will be reviewed by the Ethics Review Committee at the WHO and the Institutional Ethics Committee of the Community Empowerment Lab (CEL). It will be led by investigators at CEL who have a proven track record of conducting high quality implementation research in partnership with the government. Collaborators will include investigators at GSVM Medical College and Shyam Children's Charitable Hospital, the district administration and health system leadership in Kanpur Nagar who are already involved of the ongoing PSBI trial. State-level collaborators will include the UP National Health Mission and the UP Technical Support Unit.

Introduction

Despite a steady rate of decline in childhood mortality, the global burden of under-5 deaths is still immense at 5.3 million per annum, with more than 80% of these deaths occurring in sub-Saharan Africa and South Asia.[1,2] The proportion of newborn deaths among under-5 deaths has been steadily rising, currently accounting for 46% of all under-5 deaths. Infection is amongst the most important causes of death, accounting for nearly half of all deaths among children aged 1-59 months,[1] and more than a third of all newborn deaths.[3] In Uttar Pradesh (UP), India – the site for the proposed implementation research (IR), severe neonatal infections account for 39% of all newborn deaths.[3] This amounts to 67,000 deaths annually across UP in the newborn period alone, nearly all of which could be averted through appropriate and timely measures for prevention and management of infections.

The term 'possible serious bacterial infections' (PSBI) was coined for the 0-59 day age group of infants, as these are typically identified and treated based on clinical signs without waiting for confirmatory lab results, given the paucity of diagnostics in low-resource settings and the likelihood of rapid deterioration in condition without antibiotic treatment of bacterial infections in this age group. Further, with regards to PSBI, the epidemiological profile, clinical signs and management of infants in the age group of 28-59 days is the same as newborns (age 0-27 days), and therefore they are grouped together into a single age category of 0-59 days called 'young infant'.[4] A systematic review across 22 studies estimated the pooled global PSBI incidence risk in newborns alone as 7.6% with a case fatality rate of 9.8%,[5] however a wide variation in PSBI incidence has been reported across countries.[6] More recently, IR studies on community management of PSBI cases in young infants in the states of Haryana, Himachal Pradesh, Maharashtra and UP in India succeeded in identifying respectively 7.0%, 8.0%, 5.7% and 5.3% of live births with PSBI signs. [7–10] However the actual incidence rate was unknown in the absence of rigorous surveillance, and is expected to be higher in regions with higher mortality rates. Further, the incidence also depends on the algorithm used for identifying PSBI and cut-off values for temperature, respiratory rate, etc.

A significant body of research has focused on identifying clinical sign-based diagnostic algorithms[11–13] and treatment regimens for PSBI[14–17] that are amenable for implementation in low-resource community settings through minimally trained health workers.[18,19] The WHO recommends a comprehensive approach to address PSBI in young infants along the continuum of care from community to facility (and back), that involves prevention, timely identification of PSBI symptoms and care-seeking, hospitalization for antibiotic treatment and supportive care, and subsequent follow-up of sick young infants post-discharge.[4] Current WHO guidelines regarding identification and classification of PSBI based on clinical sign-based algorithms and corresponding treatment recommendations are provided. Multiple IR studies have focused on operationalizing WHO guidelines for managing PSBI in young infants where referral is not feasible to expand treatment for the maximum possible infants.[7–10,20–27]

Within India, prevention, identification and management of PSBI is spread across several programs such as Janani Suraksha Yojana (JSY), Janani Shishu Suraksha Karyakram (JSSK), Home Based Newborn Care (HBNC), Facility Based Newborn Care (FBNC), Integrated Management of Newborn and Childhood Illnesses (IMNCI), breastfeeding promotion programs such as Mother's Absolute Affection (MAA), and the recently launched Social Awareness and Action plan to Neutralise Pneumonia Successfully (SAANS) program. Yet, the high rate of infection-related deaths implies that there continue to be implementation gaps that need to be addressed at scale.

The 4 recently conducted IR studies in India in Haryana, Himachal Pradesh, Maharashtra and UP assessed the feasibility of operationalizing the WHO guidelines involving simplified treatment regimens for PSBI management in young infants where referral is not possible. While these studies found it feasible to operationalize these guidelines, they identified several challenges that need to be addressed at scale. Challenges identified related to timely identification of PSBI included limited ability of mothers to recognize danger signs, poor ability among community health workers (ASHAs) to recognize danger signs despite prior training, dysfunctional equipment like thermometers and weighing scales with ASHAs, and non-compliance of ASHA workers to the expected schedule and frequency of home-based newborn care visits. Challenges identified related to care-seeking included a general mistrust among families towards the public health system, preference for private providers including unqualified medical practitioners, and poor referral support. Challenges identified related to community case management of PSBI included low feasibility of utilizing Auxiliary Nurse Midwives (ANMs) – the designated primary care provider for case management as per existing guidelines, and further, the requirement of intensive handholding support over a long duration for medical officers and staff nurses in primary and secondary care facilities.

While the studies addressed the above challenges to some extent through intensive interventions within a single district, there is a need to develop solutions that can be rapidly scaled with high fidelity for large state/ country-wide deployment in order to achieve impact at scale. Further insights highlighting key gaps and issues in PSBI implementation based on formative research and activities within an ongoing PSBI trial being conducted by the investigators have also contributed to shaping the proposed IR strategy, which is presented later in this protocol. Overall, a quantum improvement in PSBI outcomes requires a fundamental shift from a service delivery-centred paradigm where multiple health programs are implemented in parallel without sufficient integration, to a mother-infant centred paradigm that integrates care around every young infant regardless of the delivery channel, and is tuned to address their unmet needs and implicit barriers. Additionally, the COVID-19 pandemic has led to a widespread disruption in maternal and child health services across the spectrum, thus magnifying pre-existing challenges and introducing new ones with respect to prevention, identification and management of PSBI. **The proposed IR, therefore, aims to apply a mother-infant centred approach to develop and test a scalable model for improving the identification and management of PSBI in young infants, that is robust to pandemic-related disruptions.** Specific outcomes that will be addressed through this IR are highlighted in a subsequent section.

Implementation Context

State & district implementation context

UP, with its population of 241 million, is comparable in size to the fifth largest country globally, and therefore, requires review, adaptation and integration of policies and programmes to suit its health system and sub-regional contexts. In line with the national policy guidelines, UP's current approach to PSBI management is spread across several programmes. An integrated and child-centred approach to PSBI management would be instrumental in bridging programmatic gaps and achieving planned reductions in infection-related deaths.

This research would be conducted in Kanpur Nagar district of UP. The district is the site of an ongoing individually randomised trial on optimizing the place of treatment and antibiotic regimens for young infants presenting with PSBI signs. It was chosen to leverage the synergy between the two studies without compromising on research integrity.

Figure 1. Location of Kanpur Nagar district

Kanpur Nagar district (Fig 1 & 2) comprises Kanpur city and 10 rural blocks with a total population of 4.8 million. The district center is located about 95kms from the state capital of Lucknow. It is amongst the most densely populated districts (1521 persons/sq km) with a two-thirds population residing in urban areas. The female literacy rate of 81% is the highest in the state, with 40% of rural women and 68% of urban women having more than 10 years of education. Figure 2 shows the administrative map of the district, with secondary-level health facilities and key population and health system indicators summarized in Table 1 .

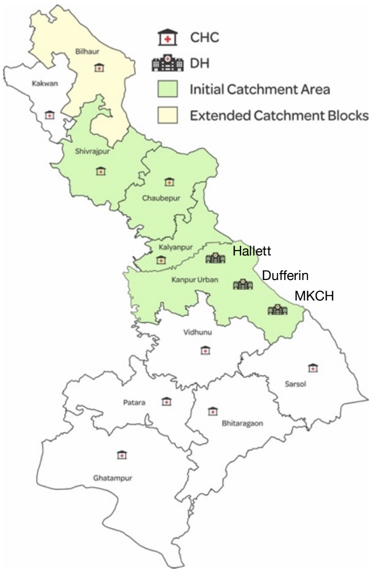


Figure 2. Map of Kanpur Nagar district with key facilities and catchment area for the WHO-sponsored PSBI trial to optimize hospital stay

Table 1. Public health system indicators for Kanpur Nagar district

Birth cohort	100,000 live births per annum
Institutional births	76% (urban: 78%, rural: 74%)
Births in public health facilities	49% (urban: 41%, rural: 63%)
NMR (based on AMANHI study)	42 per 1000 Severe neonatal infections: 39%
Estimated PSBI prevalence	10,000 per annum (based on ANISA & SATT studies)
District-level hospitals with delivery facility & SNCU	• Hallet District Hospital (operated by GSVM Medical College) • Dufferin District Women's Hospital • MKCH District Hospital
Community Health Centres	10 (of which 5 have paediatricians)
Primary health facilities	92 (urban: 50, rural: 42)
Private birthing facilities	207 (urban: 157, rural: 50)
Community health workers	Urban: ANM-263, ASHA-457 Rural: ANM-345, ASHA-1688

UP districts that are predominantly rural typically have a district women's hospital that provides delivery and newborn care (0-27 days only) services and a district common hospital that caters to the rest of the paediatric age group, including 28-59 day old infants. Being an urban centre, Kanpur Nagar district has four district-level government health facilities – three of them are equipped with Sick Newborn Care Units (SNCU). The District Women's Hospital, called Dufferin Hospital, mainly serves urban Kanpur, but does not provide any services for infants older than 28 days except for follow-up care for infants discharged from the SNCU. MKCH hospital is the referral hospital for the rural blocks in the south of Kanpur Nagar district and provides care for all paediatric age groups with an SNCU that caters only to the newborn age group. Hallet is a large hospital providing comprehensive services for all age groups, including delivery and newborn care. It the main referral facility for rural blocks in the north of Kanpur Nagar district. It has an associated medical teaching college and is therefore the highest referral facility in the district. Kanpur city also has a primary health care setup for the urban slum population that consists of 50 urban primary health centres with medical officers in-charge, 263 urban auxiliary nurse midwives and 457 urban ASHA workers. There is also a vast network of private practitioner paediatricians, and multiple private hospitals offering referral care for newborns and young infants.

Each rural block (population 150k-200k) has a community health center (CHC), which is a secondary care facility. At the block level, the medical officer in-charge of the CHC, Block Community Process Manager and Health Education Officer are key stakeholders. At the population level, ASHA workers are meant to be deployed for every 1000 population, though this is highly variable at a ground level. Other grassroot level workers include the Sangini who are ASHAs designated as team leads for a group of 18-25 ASHAs; the Anganwadi workers (AWW) who mainly focus on nutrition and early child development; the ANM – a trained rural midwife who administers vaccines and conducts deliveries; and the CHO – a trained nurse, as a recent addition as part of the government's Health and Wellness Center initiative but not yet fully deployed and integrated in most districts. Rural areas also have unqualified healthcare providers, who are often the first point of care for many families due to proximity, availability and many other factors. From an administrative and governance perspective, the gram sabha (population ~3,500) is the smallest unit of self-governance, with a governance chain consisting of elected representatives at the block and district levels.

All aspects of district level administration and governance are led by the District Magistrate, who also chairs a monthly meeting to review all district-level health system related programs and initiatives. The District Magistrate is assisted by the Chief Development Officer in coordinating day-to-day operations at the district level. All health-related programs and their budgets are coordinated through the office of the Chief Medical Officer of the district, who belongs to the medical services cadre.

Objectives

Research Objectives

The primary research objectives of the study are:

1. To develop a scalable mother-infant centric model to improve the identification of PSBI and coverage of recommended treatment in young infants with PSBI. We aim to develop an integrated model that overcomes the challenges identified in previous PSBI studies and builds on the insights gained through the PSBI trial and formative research in Kanpur Nagar district.
2. To compare the PSBI identification rate achieved through the model against an expected PSBI incidence rate of 10% of all young infants (based on a pooled PSBI incidence of 9.5% in South Asia found by the Aetiology of Neonatal Infection in South Asia – ANISA study, and the assumption that incidence of PSBI in UP would be higher than the pooled PSBI incidence.)[41]. The model will aim to achieve at least 80% coverage of PSBI identification based on an expected incidence rate of 10%. In other words, at least 8% of all young infants should be identified with PSBI through the model.

Secondary research objectives include:

1. To conduct a cascade analysis using the ‘health service coverage cascade’ approach to measure effective coverage of PSBI management and identify barriers and bottlenecks at each step of the cascade[42]
2. To assess process outcomes captured during the course of model refinement (see Table 2, column 2)
3. To document the evolution of the model and strategies over time

Methods

Study Design

This study is designed as a mixed methods implementation research that will involve human-centred design techniques to co-design the PSBI implementation model as an integrated set of scalable components with relevant stakeholders, followed by implementation, concurrent evaluation and data-driven refinement over 12 months in one rural block (population approx. 150,000; annual livebirth cohort approx. 3000) of Kanpur Nagar district.

Population

The Shivrajpur block of Kanpur Nagar district has been chosen for this study, which has a population of approx. 146,000 without about 29,000 households. Shivrajpur has one CHC, which is located approximately in the centre of the block, at a distance of approx. 32km from its nearest referral centre, Hallet hospital in Kanpur city. The CHC is visited by a paediatrician thrice a week, and is designated as a newborn stabilization unit (NBSU), which is not currently functional. Shivrajpur has 4 primary health centres, 140 ASHA workers, 7 ASHA Supervisors (Sangini), and 27 ANMs. All live births of usually resident mothers in this block (notified through sentinel surveillance and key informant networks) will be enrolled after due consent and followed up until age 60 days.

Implementation Science Frameworks

We will utilize the Design-Outcome Cascade Framework developed by CEL, which is useful for designing a cascading set of interventions focused on health impact (see Figure 3). The framework consists of multiple levels. Starting from the bottom-most, these are: (a) beneficiary or user level, where we aim to have the intended health impact – these users may be expected to adopt and adhere to certain behaviours that will contribute to the intended impact; (b) provider/ service level, which are the various intermediaries or services through which interventions will be provided to the ultimate users/ beneficiaries in order to achieve the intended impact; (c) program level, which will involve a set of interconnected components that will need to be integrated and harmonized such that intermediaries are able to achieve the desired performance outcomes needed to translate into outcomes lower down in the cascade; and (d) systems level, which involves higher level elements such as policies, organizational design, resources, infrastructure, manpower, supplies, etc. The outcome cascade flows from top to bottom, and outputs of higher-level elements flow as inputs to the lower-level elements.

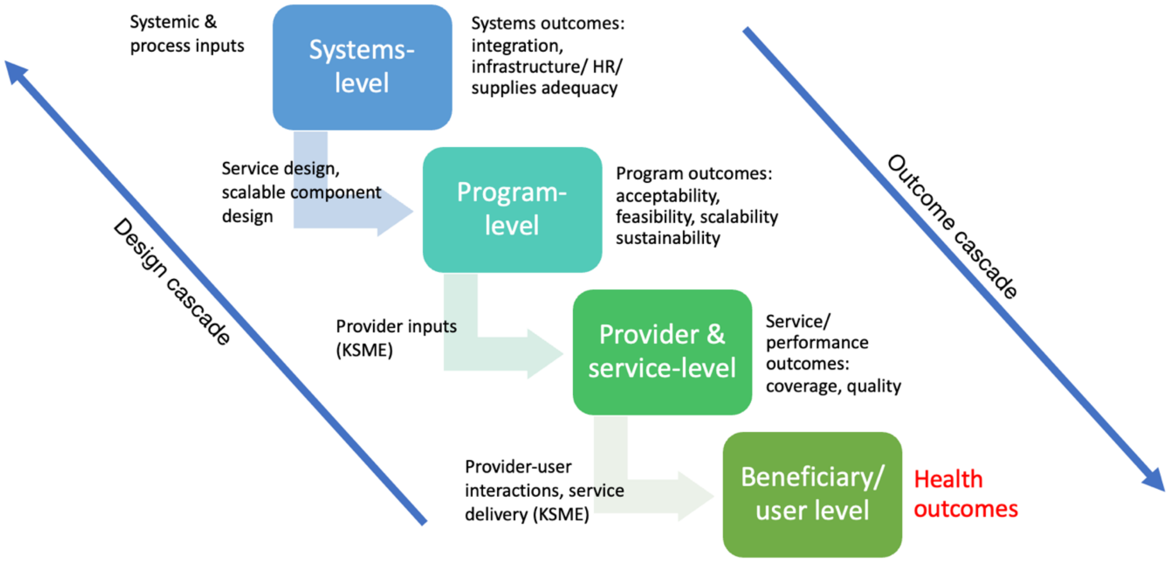


Figure 3. Design-Outcome Cascade

However, in order to design for precision and impact, an optimal strategy is to design from the bottom-up, i.e., from the actors and factors most proximal to the intended health outcome, and then moving up at every level to design the elements that are need to influence outcomes at the next lower level.

We will utilize the Knowledge-Skills-Motivation-Enabling Environment (KSME) framework[40] that explores barriers and enablers along these four domains to understand the needs of users/ providers and design model elements and interactions for successful behaviour change.[43]

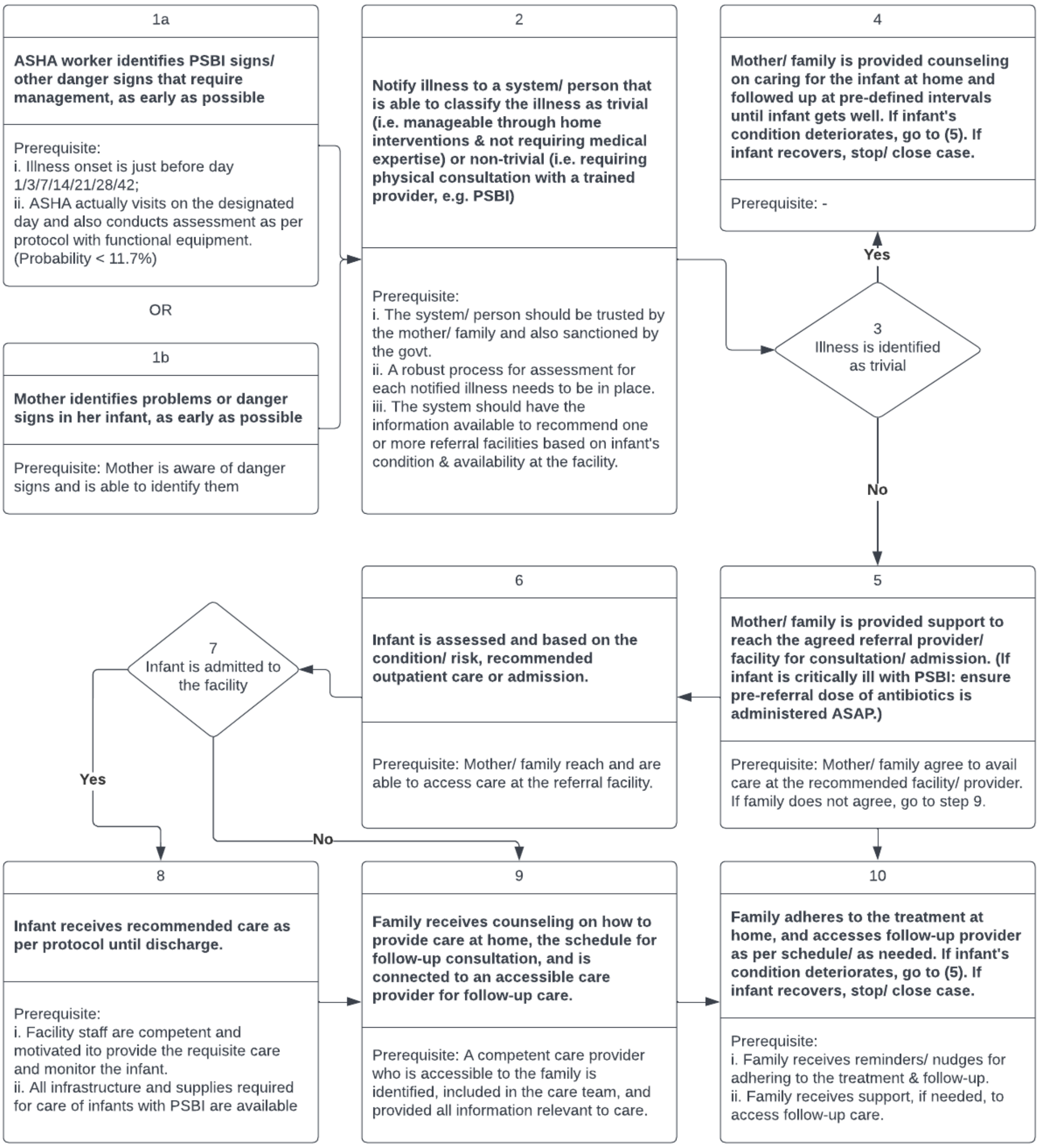
The Design-Outcome Cascade is also helpful in building a robust theory of change and in applying diagnostics to identify gaps and challenges. The theory of change will inform model requirements, which will form the basis for model development.

Model design

Needs assessment of mothers

As per the Design-Outcome Cascade framework, we will design from the bottom-up, and therefore first map the needs of mothers (and family members) in order to identify danger signs and illnesses in their young infants and to be able to access appropriate care and adhere to treatment for young infants identified with PSBI.

From a mother-infant centric perspective, we have identified the following pathway for timely and appropriate care of sick infants (see Figure 4). The pathway caters to any reported illness, and not just PSBI, as from a mother/ family perspective any problem, complaint or illness needs to be managed, and the entity that is able to address a wide range of problems faced will also enjoy greater trust, making it a preferred care provider.



1a **ASHA worker identifies PSBI signs/ other danger signs that require management, as early as possible**

Prerequisite:
i. Illness onset is just before day 1/3/7/14/21/28/42;
ii. ASHA actually visits on the designated day and also conducts assessment as per protocol with functional equipment. (Probability < 11.7%)

1b **Mother identifies problems or danger signs in her infant, as early as possible**

Prerequisite: Mother is aware of danger signs and is able to identify them

2 **Notify illness to a system/ person that is able to classify the illness as trivial (i.e. manageable through home interventions & not requiring medical expertise) or non-trivial (i.e. requiring physical consultation with a trained provider, e.g. PSBI)**

Prerequisite:
i. The system/ person should be trusted by the mother/ family and also sanctioned by the govt.
ii. A robust process for assessment for each notified illness needs to be in place.
iii. The system should have the information available to recommend one or more referral facilities based on infant's condition & availability at the facility.

4 **Mother/ family is provided counseling on caring for the infant at home and followed up at pre-defined intervals until infant gets well. If infant's condition deteriorates, go to (5). If infant recovers, stop/ close case.**

Prerequisite: -

5 **Mother/ family is provided support to reach the agreed referral provider/ facility for consultation/ admission. (If infant is critically ill with PSBI: ensure pre-referral dose of antibiotics is administered ASAP.)**

Prerequisite: Mother/ family agree to avail care at the recommended facility/ provider. If family does not agree, go to step 9.

6 **Infant is assessed and based on the condition/ risk, recommended outpatient care or admission.**

Prerequisite: Mother/ family reach and are able to access care at the referral facility.

8 **Infant receives recommended care as per protocol until discharge.**

Prerequisite:
i. Facility staff are competent and motivated ito provide the requisite care and monitor the infant.
ii. All infrastructure and supplies required for care of infants with PSBI are available

9 **Family receives counseling on how to provide care at home, the schedule for follow-up consultation, and is connected to an accessible care provider for follow-up care.**

Prerequisite: A competent care provider who is accessible to the family is identified, included in the care team, and provided all information relevant to care.

10 **Family adheres to the treatment at home, and accesses follow-up provider as per schedule/ as needed. If infant's condition deteriorates, go to (5). If infant recovers, stop/ close case.**

Prerequisite:
i. Family receives reminders/ nudges for adhering to the treatment & follow-up.
ii. Family receives support, if needed, to access follow-up care.

Figure 4. Generic pathway for illness identification and management

Step 1a/b involves illness identification by either the health worker or the mother. There are only 7 predefined visits by ASHA workers, and for them to identify the illness earlier, the onset of illness should have happened prior to the visit such that the signs are visible during the visit, a probability of 7/60 = 11.7%. Further, as ASHA workers typically make less than half of those visits[7] and may not be able to conduct the assessment as per protocol, the actual probability of

ASHA workers identifying the illness episode first (prior to the mother), is less than 11.7%. The mother has a higher likelihood of identifying that something is wrong with her infant *earlier*, provided she is generally aware of key danger signs. As noted earlier, mothers are more likely to identify and report general morbidities like cold, vomiting, diarrhoea, etc. It is also possible that some of these are also precursors to more serious illness in the future, and therefore early assessment, management and follow-up of these illnesses may reduce the incidence of PSBI overall.

Step 2 involves notifying this illness to a person (for e.g. mothers may notify ASHA workers) or system (for e.g., the call-centre based system that we will be designing) that is able to conduct an assessment and identify whether it is a non-trivial problem and requires care-seeking (e.g. PSBI), or is trivial and can be managed at home with appropriate counselling and simple remedies (e.g. erythema neonatorum). An important pre-requisite for this is that mothers/ families are able to trust this system, such that it becomes the first port of call for any problem or illness that is observed by the family. Further, this system needs the sanction of the health system, such that ASHA workers also report to the same system. A unified reporting system will also be extremely helpful from a policy/ program perspective, in understanding the pattern of illnesses in infants, and improving preventive and curative measures to address them.

Step 3 is a decision borne out of the assessment in Step 2 on whether the illness requires physical consultation from a trained medical officer/ paramedic or potential admission to a health facility. If the illness can be managed at home (Step 4), then the family needs to be provided appropriate counselling or even support with medication if needed. Further, the family can be followed up to ensure that the infant's condition is progressively improving, else the family needs to be redirected for a physical consultation, as appropriate. If the family is in need of physical consultation (Step 5), they need to be provided appropriate options for care-seeking, along with distance & timings, expected cost of treatment, previous client feedback, etc. to help them in choosing a suitable care provider. They need to be provided referral support and facilitation, which will include arranging for transport, alerting the provider/ facility about the patient, checking regarding availability of beds and booking it, etc., and forwarding the necessary details to the referral facility.

Once a sick infant reaches a facility (Step 6), it will be assessed there and advised outpatient care or admission. If the infant requires admission to the facility (Step 8), he/she will need to be provided recommended care and monitoring as per protocol until discharge. An important pre-requisite for this is that the referral facility has all the required competent and motivated manpower, infrastructure, supplies to be able to provide the requisite level of care. At the time of discharge, Step 9 will be followed.

If the patient can be treated with outpatient management (Step 9), the family needs appropriate counselling on how to care for the infant at home, including instructions for administration of medication. They may also need follow-up care, which may include administration of injectable medications, assessment and treatment calibration, etc., for which they need to be made aware of the schedule and connected to a follow-up care provider who will be included in the care team for the baby and will receive the necessary information to be able to provide appropriate care. An important pre-requisite for this is that an accessible follow-up provider needs to be identified who is competent in providing the necessary care to the infant.

Finally, for outpatient/ post-discharge care (Step 10), the family needs to adhere to the treatment at home as per the counselling/ prescription, and also seek follow-up care as per schedule. This might require reminders/ nudges, and even support in accessing follow-up care. The infant's condition also needs to be monitored, and if it deteriorates, Step 5 onwards can be followed.

How the pathway can serve as a template to ***integrate*** *existing services*

It is important to note that the necessary raw elements for the entire pathway are already available. In terms of manpower, there are community health workers (ASHA) for every 1000 population, an auxiliary nurse midwife (ANM) and a community health officer at outreach Health

& Wellness Centres, a medical officer and sometimes a paediatrician and staff nurses at community health centres (some community health centres also have newborn stabilization units with additional nurses), paediatricians and neonatologists along with a team of nurses and paramedics at district hospitals and medical colleges with level 2/3 neonatal intensive care units. Further, there are also a number of private paramedics, doctors and nurses and private facilities with neonatal intensive care units, some of which may be more accessible/ preferred by families. There are services such as the JSSK for transport of sick infants and e-Sanjeevani app for teleconsultation. Further, there is also an ongoing rollout of an app for ASHA workers to register and follow-up every pregnant mother and infant.

The main challenge is that these services are not integrated and optimized around the mother-infant to provide the best possible care, which is what we aim to achieve during the course of this implementation research.

The care coordination system:

The call-centre backbone that we have already established for another project provides the necessary framework for care integration and coordination, and direct accessibility by mothers/families. The process begins at birth, wherein each birth is registered and the mother/ family is provided with counselling on recognizing danger signs, along with a card with a 24x7 helpline number to call in case of any illness. Currently, all births in 22 facilities in Kanpur district are being registered @ about 2,000 births per month. Given that the call centre receives an illness notification for about 35% of all registered infants, it has already been established as a trusted service for mothers/families to seek help with illnesses in the infants. Often, the call centre also receives calls for notifying and seeking help for postpartum problems in mothers as well. Clearly, the helpline serves an important unaddressed need among families.

Further, a physician on call is tele-consulted for each notified illness and if needed, a referral facilitation system is activated for families identified as needing physical consultation or admission. This includes alerting the referral facilities and ensuring that every family is received at the referral facility by a designated worker who ensures that they are attended to by a treating physician/ nurse within 10 minutes of their arrival at the facility.

The system has already been identified as an important innovation within Kanpur district, and we have already received requests by the Chief Medical Officer and district administration system to extend this service to the entire district, also as a centralized information source to guide district health officials.

Model design requirements:

The goal of this IR is to design a system to achieve the ideal pathway in Figure 4 for every sick infant, especially focusing on those with PSBI.

The current call centre backend can easily be improved, extended and integrated with existing services to serve as a central care coordination system for achieving the ideal pathway for illnesses in young infant in the following ways:

1. Building an integrated case management solution around the call centre: This will include detailed information on all registered health workers/ providers/ facilities including public and private in and around the entire catchment area; integrating information for the entire pathway including all interactions with health workers, care providers and services availed including case notes, prescriptions, etc., for each case; nudges and reminders for care teams & families, and feedback from families on the quality of care provided.
2. Co-developing, implementing and refining solutions with concerned stakeholders to meet the pre-requisites for each step of the pathway. For example, for step 2, what

would be the best process to assess each reported case based on the principles of task shifting and efficiency and fidelity at scale. This could be a combination of teleconsultation and physical assessment to maximise efficiency. We would also need to identify who is best positioned to conduct the physical assessment, if needed, ideally at home, to classify illness as trivial or needing physical consultation – is it ASHA workers/ ASHA supervisors/ CHOs, etc. For step 5, we need to understand what are the essential requirements of families in terms of information, counselling and support to agree to avail recommended care. These and other design questions are listed in the following section.

3. Designing a roadmap to integrate existing health system services with the call-centre solution: The call-centre solution will need to integrate with various existing programs and services to optimize care and efficiency, for e.g., (a) ASHA worker app for following up every mother and newborn, (b) JSSK for ambulance services, (c) e-Sanjeevani app for OPD consultations with physicians, etc. During the course of this IR, it will not be possible to achieve complete integration with all the available services. The integration gaps will be identified and a roadmap to achieve integration will need to be laid out.

Design Questions for IR innovations

As noted above, there are multiple aspects of a scalable solution to achieve high coverage of the ideal pathway for all sick young infants with high quality and fidelity of services that need to be co-developed with concerned stakeholders. These are presented in Table 2. IR outcome refers to key steps/ prerequisites that need to be met in order to achieve the ideal pathway, user-level design questions are framed to consider the needs of mothers/ families, and provider-level design questions are framed to consider the needs of intermediaries/ providers in the design of the model. Note: This is not an exhaustive list. There could also be other IR questions that could emerge during the course of this study, and some may be deemed redundant if other solutions have already been identified previously. Further, the values of process indicators mentioned in column 2 of Table 2 are aspirational and are intended to guide the process of design, refinement and optimization of the model over time. In reality, the model may not be able to achieve these aspirational outcomes, but they will help to steer the direction for improving the model and also help in identifying bottlenecks and challenges that need further resolution.

Table 2. Design questions for IR: Target indicator values are aspirational and intended to guide the design, refinement and optimization of the model over time

SNo.	IR Outcome (with process indicators)	User level: Mother-infant centric IR design questions	Provider level: Provider-centric IR design questions
1	All mothers are made aware of the 24x7 helpline number and associated services. (Target indicator, REACH: 80% of all mothers from low SES should be aware of the helpline number.)	a. What channels need to be activated to ensure that all mothers and families are aware of the helpline number, e.g., mass media, ASHA workers, public and private health facilities, etc.?	a. What are the barriers to this strategy?
2	Step 1b: Mothers are aware of danger signs and are able to identify them early.	a. Potential strategies and barriers for coaching mothers to recognize illness early in their young infant and notify it immediately to the	a. What mediums are best positioned to deliver this in a scalable and effective manner (e.g. prior to discharge by staff nurses,

	(Target indicator, Mothers' Knowledge: >70% mothers are able to recall all danger signs of PSBI during the evaluation survey at age 30 days)	system? (For early reporting, we want this identification to be more sensitive than specific – i.e., we don't mind mothers reporting trivial problems or illnesses, as long as serious illnesses are not missed.) For e.g., we could improve counselling prior to discharge from facilities, or have a simple app to connect with mothers and families	at home by ASHA workers)? b. What interventions (e.g. training, job aids, accountability, etc.) are needed to ensure that this cadre delivers the interaction with high fidelity at scale?
3	Step 2 Prerequisite i: The system/ person should be trusted by the mother/ family and also sanctioned by the govt. (Target indicator, Mothers' ADOPTION: >75% of all illnesses reported by mothers in the evaluation survey are notified a priori to the system.)	a. What will it take mothers/ families to trust the system? b. What factors are involved in establishing and degrading trust? c. What are the unmet needs of mothers/ families that the system still does not address by the end of the study?	
4	Step 2 Prerequisite ii: A robust process exists for assessment when an illness is notified to the system. (Target indicator, System FIDELITY: >80% of complaints classified as trivial are actually trivial; >90% of infants who have PSBI are classified as non-trivial by the system)	a. Protocolize the helpline system. b. What would be the criteria used to classify an illness as trivial (can be managed at home without physical consultation with a competent provider, for e.g., erythema neonatorum) or non-trivial (requires physical consultation, e.g., PSBI)? Accordingly, how should the call centre record the complete history of the infant? Potential strategies could be a combination of tele-assessment by a paediatrician/ trained provider and physical assessment by a community-based health worker.	a. Task-shifting: Identify which provider would be the most suitable for doing the physical assessment at home within 2 hours of notification? (e.g, ASHA, Sangini, CHO, private untrained medical practitioners) b. How should these providers be certified for assessment? What measures need to be put in place to ensure accountability? c. Can this process be integrated with e-Sanjeevani service? What are the interface gaps that need to be addressed?

5	Step 2 Prerequisite iii: The system should have the information available to recommend one or more referral facilities based on infant's condition & availability at the facility. (Target indicator, System Optimization: >60% infants with PSBI should be able to receive their entire care at the chosen facility without further up-referral)	a. What should be the criteria for recommending a set of facilities to a family? b. What information needs to be provided to families so that they can choose the option that best suits their care-seeking preferences?	a. How can a database of all facilities/ providers offering various levels of care in each district be populated in the most scalable manner? b. How can newborn stabilization units in districts be activated to ensure complete care for infants with low or moderate mortality risk signs of PSBI?
6	Step 4: Optimal home care for trivial illnesses. (Target indicator, Home care effectiveness: >70% of families do not need to seek care from any other source for trivial illnesses)	a. Identify possible trivial illnesses/ problems and develop a home care protocol and tele-follow-up schedule for each of them that can be advised to families through teleconsultation. This could potentially also be potentially integrated into the app for mothers/ families	a. How can we best use task-shifting for teleconsultation?
7	Step 5: Mother/ family agree to avail care at the recommended facility/ provider. (Target indicators, ACCEPTABILITY: i. >90% families of critically ill infants with PSBI agree; ii. Care-seeking proportion in girl infants with non-trivial illnesses is at least 90% that of boy infants with non-trivial illnesses.)	a. What needs/ fears of mothers/ families need to be factored into negotiating care-seeking with them? b. How can we ensure that >90% of infants critically ill with PSBI are administered antibiotics within 2 hours of being assessed? c. There is a huge disparity between care-seeking for boys and girls. In the PSBI trial, the ratio of boys to girls is 65:35. This level of gender difference is unacceptable, and we need to proactively work out how we can improve care-seeking for girls.	a. How should the system be designed to maximize care-seeking acceptance? (e.g. escalation matrix for tele-callers, etc.) b. Which local care providers (public/ private) can be engaged in administering pre-referral dose of antibiotics? c. How can we enlist sufficient providers such that each baby has access to a provider within 1 hour distance?
8	Step 6: Mother/ family reach and are able to	a. What proportion of cases are able to avail transport	a. What measures need to be taken such that: (i)

	access care at the referral facility. (Target indicator, FEASIBILITY – Facility care: >70% infants with PSBI receive care at the referral facility within 3 hours of referral negotiation)	through the JSSK scheme in a timely manner? b. How can the gap between demand and supply of referral transport be met?	transport is available within 1 hour of successful referral negotiation, (ii) families do not face any problems with respect to admission or accessing care immediately upon arrival at the referral facility, (iii) admission is secured and infant details are already transmitted to the referral facility prior to arrival?
9	Step 8: Prerequisite i: Facility staff are competent and motivated to provide the requisite care and monitor the infant. (Target indicator, QUALITY: >80% infants with PSBI receive rational and appropriate care at the referral facility.)		a. What are the continuing medical education needs of staff nurses and paediatricians in terms of knowledge and skills for newborn illnesses, esp. PSBI? b. What are the motivation and enabling environment needs of staff nurses and paediatricians to ensure high quality care to all sick infants? c. How should the care received by infants be transparently assessed/ audited in order to maintain quality, and identify staff in need of re-skilling?
10	Step 8: Prerequisite ii: All infrastructure and supplies required for care are available. (Target indicator, SYSTEM READINESS: All facilities recommended for PSBI-related referral have availability of infrastructure and supplies based on the level of care.)		a. What processes are in place/ need to be put in place to ensure that supply matches demand?
11	Step 9: A competent care provider who is accessible to the family is identified, included in the care team, and		a. Which local providers are most suitable (optimize accessibility with need for training and handholding support) for providing follow-up care for PSBI

	provided all information relevant to care. (Target indicator, FEASIBILITY – home care: >70% of all infants with PSBI that are discharged/ assigned to outpatient care are able to access follow-up care within 10km distance.)		including administration of prescribed antibiotics & assessment of treatment success? (e.g. CHC doctors, private providers, CHOs, etc.) b. How can these providers be certified and held accountable?
12	Step 10: Prerequisite i. Family receives reminders/ nudges for adhering to the treatment & follow-up. (Target indicator, EFFECTIVE COVERAGE: >80% infants identified with PSBI complete their prescribed treatment.)	a. How can we design the delivery of nudges/ reminders to maximize adherence to treatment. (incl. frequency, content, etc.) We could explore various channels for this, including physical (e.g., nudges by ASHA) and electronic-guided (e.g. app and/or call centre)	
13	Step 10: Prerequisite ii. Family receives support, if needed, to access follow-up care (Target indicator, EFFECTIVE COVERAGE: >80% infants identified with PSBI complete their prescribed treatment.)	a. What are the support needs of families to access follow-up care from the recommended providers? We can also explore the possibility of teleconsultation combined with physical assessment by a community health worker.	
14	Overall functioning of the system.		a. What metrics should be tracked by the system and shared at various levels to monitor and improve the quality of care and respectful care over time?

Throughout this IR, we will follow the process of **human-centred design** to (a) understand the design needs of families and care providers using non-participant observations, in-depth interviews (IDIs), focus group discussions (FGDs), (b) develop prototype solutions based on consultations and co-design sessions with families, care providers and other health system and community stakeholders, and (c) implement and test these solutions with the help of data collected programmatically (e.g. call centre data) as well as data collected through the formal evaluation process described later and (d) identify areas of refinement by repeating this process.

Table 3. The data collection activities for the human-centred design process are tabulated below:

Aim	Participants	Data Collectors	Methods*	Sample and Frequency
1. Map and understand the identification, care-seeking and treatment journey of young infants	Mothers and caregivers who have reported any illness in the first 60 days of life (to the helpline/ ASHAs/identified during quantitative data collection).	Qualitative researchers will obtain informed consent from the mother/caregiver at their home prior to the interview and proceed with the interview if consent is granted.	In-depth interviews (IDIs) conducted physically at home. Purposive sampling to cover participant types across various SES categories, maternal education and severity of disease. Within the category if we get more than adequate number of participants, we will try to get good geographic representation of cases from the study area. The researchers will ask detailed questions on birth and early care, recognition, home-based initial care if any, care-seeking from external providers, referrals, etc., adherence, until final outcome to map the entire journey of the young infant, including who were involved, what was done, where, when and how, and rationale if any.	90 IDIs (with 30 participants at the beginning of the study, and subsequently @ 5 IDIs per month)
2. Understanding the acceptance of model strategies and utilization of key services among caregivers, and suggestions/ feedback on model/ service improvement	Mothers and caregivers of young infants, both sick and healthy	Qualitative researchers will obtain prior informed consent from the mother/caregiver on the telephone to schedule the date, time and place of the FGD and conduct the FGDs at the designated location after administration of the consent. There will also be an additional	Focus Group Discussions (FGDs) with 8-10 participants in the community will be held at a place of convenience. Purposive sampling will be done to cover participant types across various SES categories, maternal education and severity of disease. Within the category if we get more than adequate number of participants, we will try to get good geographic representation of cases from the study area.	24 FGDs (3 separate FGDs with families of healthy and sick young infants, every 3 months.)

		observer/note-taker.	The various themes covered will include various services that participants are able to recall, personal narratives, and their feedback on the services that have been utilized, as well as ways to improve coverage, scope and quality of services.	
3. Documenting how sick young infants are cared for at home to understand various care practices, caregiver involvement, use of medication, challenges, etc.	Non-participant observation of young infants with PSBI being cared for at home/ post discharge	Qualitative researchers will obtain informed consent at the home of the participant and conduct the non-participant observation if consent is given. If CHW is available at home the verbal consent will be taken. This will involve consent from the mother/ primary caregiver to observe the care provided to the YI by the mother and caregivers. In case of refusal, we will not observe the YI.	Non-participant observation at home. Purposive sampling will be done to cover participant types across various SES categories, maternal education and severity of disease. Within the category if we get more than adequate number of participants, we will try to get good geographic representation of cases from the study area. All activities involving the infant will be documented, including what was done, by whom, when, how, etc.	10 observations of 8 hours for each infant at the beginning of the study.
4. Understanding the care of sick young infants in hospitals, including processes of outpatient consultation, emergency care, admission, discharge, treatment, record-keeping, supplies, etc.; common challenges faced by care teams, etc.	Non-participant observation of the paediatric ward and hospital services involving young infants with PSBI admitted to hospitals	Qualitative researchers will obtain informed consent from the facility head and head of paediatrics department at the beginning of the study/ inclusion of the facility into the research. The non-participant observations will be scheduled with facility care providers of consenting facilities each time. The verbal consent will be taken from both care providers and	Non-participant observation of hospital processes for caring for sick young infants. All consenting facilities will be included. The various wards of the facility where young infants receive care – outpatient, emergency, inpatient, patient registration, etc. will be observed to document patient interactions, assessment, care provided, record-keeping, supply chain, etc.	24 observations (24 hours of observation for all consenting facilities once in 3 months i.e. 6 health facilities each 3 months)

		mother/caregivers during observation of the process.		
5. Understanding the existing role, and existing knowledge, skills, motivation and enabling environment for community health workers who may potentially play a role in PSBI identification, care-seeking and follow-up and assessing their suitability for the same.	ASHA workers, supervisors (called Sanginis)	Qualitative researchers will obtain informed consent from the health workers at their home/ work place prior to the data collection activity. If mother/caregiver part of the observation process then verbal consent will be taken prior to the observation	1. Field observations: Community health workers will be shadowed by a qualitative researcher to observe activities conducted in a typical work day, engagement with families, practices, challenges encountered, etc. 2. In-depth interviews (IDIs) will be conducted with the same participants to discuss field observations and explore their beliefs, knowledge, attitude, practices, etc. 3. Focus Group Discussions (FGDs) will be conducted with a different set of workers to triangulate the information and understand their perspectives on their potential role in PSBI identification, care-seeking and follow-up	1. 12 Observations: (4 ASHA workers and 2 Sanginis consisting of high and low performers (as identified by their supervisor) at the beginning of the study) 2. 12 IDIs same as 1. 3. 6 FGDs (Separate FGD with 6-8 ASHA workers from the study block and 6-8 Sanginis from multiple blocks in the study district 1-2 times during the first 2 quarters of the study.)
6. Understanding the existing role, and existing knowledge, skills, motivation and enabling environment for existing service providers (incl. govt. and private) who may potentially play a role in community-based PSBI management and assessing	Staff nurses, ANM, community health officer (CHO), pharmacists, trained and unqualified medical practitioners who reside/ practice in the community	Qualitative researchers will obtain informed consent from the health service providers at their home/ place of work prior to the data collection activity. For government providers, a representative set of both high and low performing providers will be selected based on inputs from their supervisors. For	1. Field observations: Health service providers will be shadowed by a qualitative researcher to observe activities conducted in a typical work day, engagement with families, practices, challenges encountered, etc. 2. In-depth interviews will be conducted with the same participants to discuss field observations and explore their beliefs, knowledge, attitude, practices, etc.	1. 12 Observations (1-2 per provider type (SN, ANM, CHO, Pharmacists etc.) at the beginning of the study.) 2. 12 IDIs: same as above. 3. 2 FGDs (each FGD

their suitability for the same.		private providers, those who already play some role in PSBI management will be selected.	3. Focus Group Discussions will be conducted with a different set of providers to triangulate the information and understand their perspectives on their potential role in PSBI identification, care-seeking and follow-up	with 6-8 participants, providers from various blocks of the study districts.)
7. Understanding the policy and implementation climate, implementation, information and management needs and challenges of health system, political and administrative leaders for improving PSBI management	Program Managers, Facility-In-Charges, and other program implementers at block, district and state levels; Political representatives at village, block and higher levels; Leaders of professional medical and nursing associations.	Qualitative researchers will obtain informed consent from the health service providers at their home/ place of work prior to the data collection activity. We will aim to engage leaders at the district level, and those from various blocks of the district to ensure maximum representation.	1. In-depth interviews from each management/ leadership position will be conducted on various themes related to intersection of PSBI management with their scope of work and accountability. 2. Brainstorming/ co-design workshops: These will be conducted with sets of 4-6 managers/ leaders from time-to-time to share study findings and get feedback and suggestions.	1. 12 IDIs – (beginning of the study with 1-2 from each management/ leadership position) 2. 4 Co-design sessions (at least once every quarter.)

* In cases where we will use purposive sampling, we have mentioned the criteria that it will be based on – to get a good representation of SES, maternal education and severity of disease. Within each category, if we get more than adequate number of participants, we will try to get good geographic representation of cases from the study area.

The sample for each type of qualitative data collection and type of participants is given in above table 3 to get the exhaustive sense of challenges or what happening for each process for model design and further improvement in the process. If we find that we have achieved saturation of new information, we will stop further conducting more IDIs/FGDs/Observations.

A system designed around the helpline as a backbone, with the above considerations, can serve an all-round purpose of facilitating care, integrating various services and programs for mother-infant centric delivery, and providing the necessary metrics to improve care quality over time and refine the system itself. A centralized notification system and subsequent facilitation of care-seeking and care also confers significant resilience to future pandemic scenarios, as the system would have the data to learn and adapt facilitation mechanisms as per emerging needs and challenges.

When the observer observes the processes passively from a distance without participating in the activities, it is known as non-participant observation. Here observer does not try to influence activity or take part in the activities. All non-participant observations will be done after due consent. However, in case of health facilities, permission to observe processes like admission, outpatient consultation, emergency care, etc. will be taken from the relevant authority. The goal in this case is not to do ethnographic research on individuals, but rather a process mapping to identify gaps and opportunities for health service quality improvement. Examples could be: "Patients are made to wait in long queues, but instead could be given a queue number and asked to be seated in a waiting area." Or "Due to high patient load during peak outpatient consultation hours, doctors get about 2 minutes to attend to each patient. We could use task shifting such that paramedics could note down detailed patient histories, allowing doctors to focus on clinical diagnosis and prescribing care.” Or “Mothers are not allowed into the sick newborn care units. This is not in accordance with the national guideline on family participatory care.”

Implementation Plan

An initial version of the core of the model, i.e. the helpline, with some integrations, is already in place. Since the helpline is the core of our intervention strategy for PSBI management, we will continue to operate it by the CEL team in order to refine processes through the course of the study. The assumption is that a helpline-based model by itself is inherently scalable, and has demonstrated prior success within the health system in UP, for example emergency transport, COVID-19 management, etc. How we integrate all other programmatic components, including service delivery by public and private providers into this helpline-based model for achieving high scalability, acceptability, adoption, fidelity and effective coverage is at the heart of this IR. This will be done through iterative cycles of implementation, evaluation and refinement of strategies.

Based on a survey in Uttar Pradesh (UP), 86.63 per cent households have mobile handsets in 2015[*], and is now expected to be nearly universal. We have been registering patients with mobile numbers for multiple studies over the last 5 years, and have not had a single case where they could not share a mobile number from either their household or their nearest neighbor (who also typically happen to be close relatives). We have been following up with mothers registered from multiple delivery points as part of another project, and have not had the problem of not being able to follow-up through mobile phones.

Preparatory work

The preparatory phase (prior to initiation) will involve the following activities:

- Identification of a pilot area consisting of 2 ASHA supervisors (called Sanginis) and approx. 30-40 ASHA workers
- Stakeholder identification, engagement and informal consultations in the entire study area
- Recruitment, training and deployment of the study team
- Finalization of protocols and study instruments and securing IRB approvals
- Establishing the data management system
- Mapping and profiling of all health facilities and providers in the study area
- Establishing existing rate of PSBI identification by the health system through ASHA workers by examining submitted records of home based newborn care visits
- As part of the pilot phase, we will refine the existing helpline-based model by addressing the user-level design questions and some provider-level design questions outlined in Table 2 within the small pilot area of the study using a human-centred design approach
- The overall implementation of the study and initial goals for each quarterly cycle will be planned with key stakeholders.

Model implementation, evaluation and refinement

The generic pathway for illness identification and management (see Figure 4) and the corresponding design questions at the user and provider-level to optimize the process outcomes outlined in Table 2 will form the basis of model design, implementation and refinement. During the pilot phase (preparatory work), some of these design questions and corresponding strategies will be explored to finalize a basic implementation model that can be rolled out across the study area during the first quarter.

Table 2 with its aspirational targets of process outcomes in column 1 will steer the entire IR towards an optimized model. Throughout the IR, we will apply **human-centred design** to (a)

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[*] http://timesofindia.indiatimes.com/articleshow/47926636.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst

understand the design needs of families and care providers using non-participant observations, in-depth interviews, focus group discussions, (b) develop prototype solutions/ improvements based on consultations and co-design sessions with families, care providers and other health system and community stakeholders, and (c) implement and test these solutions/ improvements with the help of data collected programmatically (e.g. call centre data) as well as data collected through the formal evaluation process described later and (d) identify areas of improvement by repeating this process.

The initial focus would be on optimizing the design of the solution to fulfil user-level design requirements as per the Design-Outcome Cascade framework. Initially, any gaps in the system identified on an ongoing basis during care facilitation by the helpline will be supplemented by the study team, including health workers and providers. The gaps in service delivery thus identified will be recorded, and fed into the refinement of the model to optimize the provider-level design and leverage and strengthen existing health services and infrastructure – including public and private and wean dependencies on the study team over quarters 2, 3 and 4.

The quantitative evaluation of the model will be done concurrently, as described in the subsequent section. Evaluation data will be shared with health system stakeholders on a monthly basis to feed into ongoing quality improvement. Physical assessment of health facilities using structured surveys, along with unstructured/ semi-structured in-depth interviews, non-participant observations, consultations and discussions with health workers/ potential providers/ health facilities, will be undertaken to optimize the design of provider-level model components.

Model refinement will involve collaborative goal-setting, strategy review and action through quarterly **plan-do-study-act cycles** with co-investigators and key block and district-level health system and community stakeholders. The optimization goals (for the primary and process outcomes in Table 2) for each quarter will be decided in the beginning of the quarter with these stakeholders, and progress towards attainment of these optimization goals will be tracked on a monthly basis. Key decisions and actions taken during the course of optimization and refinement of the model will be documented along with evidence and rationale. This will serve as a reference for future adaptions of the model at larger scale.

We would also like to emphasize that the goal of this research is not just to generate knowledge, but develop an evidence-based scalable model that can significantly reduce the burden of infection-related mortality in the state by providing simplified recommended treatment. The data generated through the research will be used to optimize and improve the model in order to help it achieve its envisaged goals, as well as generate evidence related to the effectiveness of the model in achieving its objectives.

Policy alignment

To our knowledge, the WHO guidelines for PSBI are in the process of being included in the latest version of the national guidelines in India. However, this document is not currently available to the general public. Any policy recommendations emerging out of this IR will be shared with key decision-makers at the state and national levels.

Outcomes

Primary Outcome

The first primary outcome of this study is the model itself. The other primary outcome of this study relates to the performance of the model, measured by the coverage of PSBI identification achieved by the model. This has been chosen since identification of PSBI is fundamental to subsequent management. We will assume that the actual incidence of PSBI is 10% of all young infants – this is based on data from a previous study in South Asia and the fact that UP would in general have poor indicators when compared to other states in India, or even Bangladesh.[41]

Therefore to aim at a PSBI identification coverage of 80%, the model should correctly identify PSBI in 8% of all young infants. **PSBI identification will be based on confirmation of PSBI by a trained provider.**

Secondary outcomes

Secondary outcomes of the study include:

A. Effective coverage of PSBI estimated through cascade analysis, and analysis of barriers and bottlenecks at each step of the effective coverage cascade. We have mapped the effective coverage cascade for PSBI as follows:[42]
    a. Target population (population in need): all live births in the study area
    b. Service contact coverage (contacts health service):
        i. proportion of infants who receive at least one ASHA visit or call through the helpline
        ii. proportion of infants who received home-based screening (telephonically or physically) for PSBI at least once (infants assessed by ASHA workers will be considered screened-in but not confirmed cases of PSBI)
        iii. proportion of infants who were screened-in for PSBI and recommended consultation by a trained provider
    c. Input-adjusted coverage (contacts health service that is ready, i.e. referral success, PSBI assessment and confirmation):
        i. proportion of infants who were assessed by a trained provider
        ii. proportion of infants who were assessed by a trained provider and confirmed as PSBI
    d. Intervention coverage (receives health service): Proportion of infants who were initiated treatment as per existing guidelines
    e. Quality-adjusted coverage (receives health service according to standards):
        i. Proportion of infants who were initiated treatment within 24 hours of notification to the system (by mother or ASHA worker)
        ii. Proportion of infants who receive complete treatment dose by health providers (as per existing guidelines for hospital and/or community-based care depending on place of treatment)
    f. User adherence-adjusted coverage (user adheres to treatment): proportion of infants who completed follow-up as recommended and completed the treatment dose at home (as per existing guidelines)
    g. Outcome-adjusted coverage (positive health outcome achieved): proportion of infants who were clinically well 8 days after treatment initiation (if discharged prior to treatment completion/ cared at home) OR successfully discharged after recovery from hospital (as applicable)
B. Process outcomes, as outlined in Table 2, column 2.
C. Process of model development & refinement, i.e. the evolution of the model over time.

Sample size

The primary outcome of interest is the PSBI identification coverage. In order to evaluate if the model is able to identify PSBI in at least 80% of the expected number of infants with PSBI (based on an assumed incidence of 10% of total number of young infants), we will require the following sample size:

$$N = \frac{Z^2 P(1-P)}{d^2}$$

where

Z = Z-score for desired level of statistical significance

P = expected coverage in the population

d = desired level of precision

80% of young infants with PSBI translates into 80% of 10% of all young infants in the population = 8% of all young infants in the population. Thus, P = 0.08. A precision of 1% will allow us to estimate P at 8±1%, and therefore PSBI identification coverage of 80±10%.

Thus, for a desired confidence level of 95%, precision of 1%, we get N = $(1.96/0.01)^2$ * (0.08)*(0.92) = 2,828 young infants in the population. In order to conclude with 95% confidence that the PSBI identification coverage attained through the model is 80% or more of the assumed PSBI incidence rate with a precision of 10%, we will need to enrol at least 2,828 young infants. Thus, one block with a population of approx. 150,000 and approx. 3,300 births per annum is sufficient to provide this sample size over a 10 to 12-month follow-up period.

Evaluation

Evaluation will be conducted through a system of concurrent evaluation, that would involve notification and registration of all live births in the study population after due consent and follow-up at days 15, 30, 45 and 60 to track incidence of morbidities, PSBI, etc. and assess process outcomes of the model (like reach of the helpline, etc.) that need to be optimized. Infants identified with PSBI will be further followed up upon notification, treatment initiation and 8 days after initiation of treatment. Verbal autopsy will be conducted for all deaths among enrolled young infants.

The methods for the concurrent evaluation are as follows:

- A system will be set-up to identify all livebirths based on inputs from key delivery facilities (institutional deliveries), ASHA workers and other community informants. Data collectors will visit the facility/ home where the newborn and mother are located as soon as possible after the birth has been reported in order to administer consent for enrolling the babies into the study and conducting follow-up visitations. Newborns of consenting mothers will be enrolled and a birth registration form with basic details of the delivery and birth will be administered.
- All infants will be followed up by field surveyors at age 15 days (delivery details, newborn care practices, morbidities, ASHA visitations, infant vaccination history), 30 days (newborn care practices, morbidities, ASHA visitations, mother's knowledge and skills in assessing danger signs), 45 days (infant care practices, morbidities, ASHA visitations) and 60 days (socio-economic status, infant care practices, morbidities, ASHA visitations, infant vaccination history). If any morbidity is reported at each of these visits, then a detailed questionnaire will also be administered to capture details related to signs & symptoms and care-seeking.
- The Socio-Economic Status (SES) form is very important information collection tool to analyze relationships between social status categories and other variables for example sickness episode or care-seeking etc. The questionnaire used is a standard questionnaire

which is also used in Demographic and Health Surveys (DHS) across the world, with a standard analytic methodology that assigns SES categories based on principal component analysis. In India, we also have a standardized Kuppuswamy socioeconomic scale to classify the patient's socioeconomic status.

- ASHA visitation will be asked on each follow-up day i.e. D15, D30, D45 and D60. ASHA is a community health worker who is supposed to conduct home visits for baby care called home based newborn care (HBNC) for a minimum 7 time from birth to post 42 days of birth i.e day 3, 7, 14, 21, 28, 35 and 42. However, we know that this is rarely the case. We wish to assess the frequency and timing of visits and also gather some information on the content of the visit to get some measure of quality. The goal of this implementation research is to strengthen the health system such that it improves the coverage and quality of health services for sick young infants. ASHA visitations are an important part of the overall service offering of the government, and it is an important study outcome which needs to be suitably measured.
- Any registered young infant identified with PSBI through the health system/ helpline or confirmed by any other competent provider outside of the system will be further followed up upon treatment initiation (referral, treatment, delays), and 8 days post treatment initiation (treatment outcome, adherence, service satisfaction, etc.).
- Verbal autopsy will be conducted for all deaths among enrolled young infants using the latest WHO verbal autopsy instrument. Verbal autopsies will help us track the cause structure of young infant deaths over time to assess if there is any cause-specific reduction in mortality, especially for infections as a cause of death. The WHO verbal autopsy (VA) tool has been validated globally and used for several large studies. We have conducted more than 5000 verbal autopsies of newborns since 2012 using the same instrument, as part of two studies – AMANHI (published in Lancet Global Health) and Emollient therapy (published in PLOS Medicine). The team is well-trained in conducting these sensitive interviews and providing grievance support to the mother and family members. Our team members belong to the same community, and have several years of experience in conducting these interviews. They act with utmost sensitivity and their first intention is to visit the family and express their condolences and togetherness in their grief. Whenever there is a death notification, either independently, or discovered during the time of a pre-scheduled data collection visit, the data collectors will first express their heartfelt condolences. After the initial period of grief, the supervisor will call or physically visit the family to take an appointment for the verbal autopsy. The typical procedure for conducting verbal autopsies is not to ‘administer’ the questionnaire. Rather, interviewers are trained to have a qualitative and empathetic conversation with the family after due consent, to understand the sequence of events that led to the death, which is documented as such. The interviewers then fill out the verbal autopsy questionnaire based on the narrative, and only ask the questions from the structured questionnaire if they have not been covered during the empathetic conversation. Such conversations between family members and visitors (relatives, neighbors, friends) who come to meet them and offer condolences are common in this culture, and are typically cathartic for the family.Social and spiritual support is a strong part of the culture of this community, and is preferred over professional counselling. Relatives, friends and neighbors provide ample support to grieving mothers and families in such conditions.

Data collectors with a minimum of 15 years education and the ability to understand aspects of research ethics and engagement with families, use tablet devices, understand and correctly record information will be recruited for the evaluation. Verbal autopsies will be conducted by the supervisor who will have superior rapport-building and community engagement skills with at least 10 years of experience in data collection, including previous experience with sensitive data such as verbal autopsies. They also work closely with members of the community to ensure adequate social support is provided to a family that may be somewhat isolated

Data management, governance & confidentiality

Qualitative research data will include audio recordings of IDIs and FGDs; their transcriptions and any other profile or background information captured of the participants; and photo/ video documentation of the observations (where consent is granted) along with detailed notes of observed activities and other background information on the family. Audio recordings of IDIs and FGDs will be assigned a unique case identifier and backed up on a secure and password protected database accessible only to authorized research team members for transcription and erased from the recording device. The digital recording of interviews, focus group discussions, etc. will be transcribed verbatim in the language of data collection. All transcripts will be anonymized to ensure privacy and confidentiality of participants. The audio recordings will be subsequently verified by a senior researcher to finalize the analytical datasets, and will be completely destroyed at the end of the study. Photo/ videography of observation sessions will be assigned unique case IDs, tagged based on activities, and preserved in a secure and password protected database accessible only to select members of the research team for future analysis and/ or publication as per the consent granted by the participant. Detailed observation notes will be assigned a unique case id, anonymized and stored in a secure and password protected database for further analysis by authorized research team members.

Data for the concurrent evaluation will be collected on Android-based tablet devices. The data tablet devices will be secured through a device management software which allows for remote management through a central system. The device management system protects the data on the tablet devices and does not allow unauthorized apps to be installed on the device any other application to be installed or delete the data on it. 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. The study forms will have built-in checks for missing values, inconsistencies and skip logic. The collected data will be synchronized in real-time (or upon availability of network) to the cloud server. Data will also be backed-up on a daily basis on an in-house encrypted MySQL database, as well as an encrypted MySQL database on a cloud server located in India. Once the data is downloaded, the system will run basic and aggregate checks for data quality. Any discrepancy found will be daily emailed/communicated to the respective data collectors and their team leaders by the system for necessary rectification. An overdue forms report will also be generated and sent to ensure timeliness of data collection. Discrepancies flagged to concerned team leads and discussed in routine review meetings for feedback and quality improvement.

The entire data management system will be GCP compliant and will protect participant data in every aspect of data management from data collection to data analysis. Protecting the confidentiality of the data will be a high priority. The following safety measures will be employed to ensure data protection and safe handling. At the time of registration of birth, each young infant will be given a unique identification number. Data will be linked to participant identification numbers, and the table linking the identifier to identifying information will be stored in a separate encrypted database which will only be accessible to the data management steward during the course of the study. The consent form, and any other physical forms linking participant personal information to the study ID code number will be kept in securely locked filing cabinets. Proper documentation and storage of the metadata and any files or protocols relevant to data management will be handled with utmost care. Regular backups of the existing data will be done in appropriate intervals. All computers being used in the study will be password protected and will have restricted access to specific study staff to protect confidentiality. None of the participants' names or identifiers will be used in any publications or discussions regarding the study. Data will be accessible only to authorized research team members.

The analytical datasets will be created from the de-identified raw data by merging various tables, as required, into a flat database. The raw data and consent forms will be stored for 7 years and subsequently destroyed. The table linking the participant identifiers with the identifying information will be maintained indefinitely by the data management steward under direct supervision by the principal investigator, to allow for future follow-up studies, if needed.

The call-centre solution will store the programmatic data of beneficiaries as well as providers, tracking each case of reported illness with facilitation of care until recovery. It will have a robust, secure and encrypted database backend to ensure confidentiality. All analysis will be performed on de-identified data.

COVID-19 related measures

The study will be conducted during the ongoing pandemic of COVID-19. We will adopt the following measures to ensure that we have safeguarded our team as well as participants:

- Obtain required clearance from relevant authorities if movement restrictions in place
- Make everyone in the team (team leaders, enumerators, drivers, logisticians etc.) aware of the most recent information from the WHO, government of India and UP, and adhere to their guidelines
- Make everyone in the team aware of referral mechanisms for suspected COVID-19 cases to share with respondents if asked
- Make sure that the relevant IEC materials on COVID-19 (factsheets, brochures, etc.) are available and shared with all staff
- Develop and train staff on appropriate reporting and communication channels to ensure safety and early response (if needed). We will have a notification system to ensure that all COVID-19 cases in the study team are notified within the organization as well as to health authorities, as per government guidelines.
- Inform everyone involved in data collection of the following protocol and clarify that this applies both during and outside of data collection activities:
    - Check temperature every morning. In case of a high temperature (above 37.5 Celsius), or any other mild symptoms such as tiredness, dry cough (common symptoms), shortness of breath, aches and pains, sore throat, or runny nose (other symptoms), inform the team leader. Any person with these symptoms should not engage in data collection and self-quarantine for 14 days. Inform your team leader immediately if feeling unwell with any other symptoms, and follow his/ her guidance.
    - Team leader to ask if enumerators have been in contact with any confirmed or suspected case of COVID-19. If yes, the person should not be participating in the activity and self-quarantine for a minimum of 14 days.
    - Wash hands thoroughly and regularly (ideally every 1 to 2 hours and definitely in between each interview conducted) with soap and water or alcohol-based hand rub.
    - Follow the recommended cough etiquette at all times.
    - Do not touch your (or anyone else's) face – particularly eyes, nose and mouth.
    - Keep at least 1 metre distance from other people at all times. Close-up contact should be limited to less than 15 minutes. Keep distance also in cars, i.e. use enough cars so you are maximum 3 people per car. If not enough cars, see if you can use fewer enumerators and extend data collection time.
    - Sanitize all data collection items prior to each interview (pens, phone, tablets, notebooks, ID cards, etc.)
    - Don't spit in public

- Additionally, for team leaders:
  - Ensure you know the protocol to follow and referral mechanisms to use to inform the right people about any observations of symptoms or sickness among field staff during data collection
  - Procure relevant supplies for staff screening and sanitation (for individuals as well as of common and personal objects): Thermometers, Hand hygiene items (hand sanitisers and soaps, ideally liquid soap instead of soap blocks)
  - Each staff travelling to the field should have their own hand sanitiser with them
  - Enough soap should be available at all times in the office and for all staff
  - Soap should also be brought along with the data collection teams, together with water, so that team members can wash their hands properly once field activities are done for the day
  - Hand-disinfectant rub for enumerators and others involved in data collection (e.g. drivers) and other cleaning material to sanitize common spaces including office, cars, and data collection equipment

Oversight

Oversight for the study will be provided by the WHO, Geneva. The study progress and data will also be shared on a regular basis with the district administration and state health system leadership as part of program review and corresponding action, as needed.

Ethical & regulatory considerations

The study activities will be conducted in accordance with international norms and standards on ethical research practice, including the Declaration of Helsinki and National Ethical Guidelines for Biomedical and Health Research involving Human participants of India.

The study will be reviewed by the Ethics Review Committee at the WHO, Geneva and the Institutional Ethics Committee of the Community Empowerment Lab. Although not a clinical trial and therefore, not a requirement, the study will also be registered in the ISRCTN registry.

Current national guidelines for PSBI are well communicated to the hospitals who treat young infants with PSBI. The studies in past have find the challenges in identification, seeking care of the YIs with PSBI. Therefore, supporting in care seeking, and treatment recommendation from hospitals will not require a consent from participant or care providers. For formative research, model co-design and improvement and outcome measurements that includes direct data collection from mothers, caregivers, health workers, health managers, a written consent will be requested. As described above, all the birth notification of study area will be approached for permission for follow-up visits on specific days. The consent form will be translated into Hindi and back translated to English to ensure equivalence. All research data will be collected after administration of due consent, kept confidential and analyzed after de-identification.

Once a participant has been identified, the consent process involves the researchers introducing themselves and the study, and thoroughly explaining the contents of the consent form applicable to the participant & activity, including right to voluntary withdrawal, no impact on care due to participation in the study, confidentiality, risks/ benefits, etc. Participants will provided the information sheet in the local language, and requested and given ample time and opportunity to ask questions and clarify doubts, and only after they are thoroughly satisfied and the researcher is convinced that they understand what participation entails, they will be provided the consent form for their verification and signatures. If the participant is illiterate, their thumb impression will be taken, and a literate person who they trust and is present during the consenting process, and in a position to verify the same will also sign on the consent form on their behalf. The families keep a copy of the information sheet as well as the consent form, and the researcher takes back a copy of the consent form for internal filing.

Timelines

The study will be conducted over a period of 17 months. The preparatory phase will be conducted over a period of 3 months under the aegis of the existing PSBI trial. Subsequently, the implementation, concurrent evaluation and refinement will be done over a period of 12 months. Final data analysis and report writing will be done over 2 months.

Limitations, Risks & Mitigation

This study aims to co-develop a model to significantly improve the coverage of PSBI identification and management in a rural setting in northern India, based on lessons and insights gained through previous work, and has multiple limitations. It does not address primary prevention of PSBI through appropriate counselling/ coaching of mothers/ family members, which is an important need identified by the study team, but not feasible within the budget and timelines for this study. The study therefore mainly focuses on developing a scalable model to improve identification and management of PSBI, and in the process, accommodates the need to cover other illnesses perceived as important/ needing attention by the family. Further, given the limited timeframe and budget, the study does not promise to eliminate all barriers with respect to identification and management of PSBI, but instead aims to optimize the model to achieve certain process targets, gain a better understanding of the needs of mothers and families, and document gaps in service delivery that are identified during the course of implementation that were both addressed and unable to be addressed during the course of the study. Unaddressed gaps can subsequently be taken up as a subject of future implementation research.

As part of the study, an evaluation team will be enrolling births and following up to document the care practices, morbidities, etc. There will also be a qualitative team who will be observing families and health workers and providers, conducting in-depth interviews and focus group discussions. During home visits to families, it is possible that these workers will observe practices that may potentially cause unintended harm to the baby, including when the baby appears to be very sick but the family is unwilling or unable to act in the child's interests. In such cases, the appropriate steps for the researchers to take are informing the health worker assigned to the family, as well as notifying the helpline for care coordination. The interventions for strengthening and supporting care-seeking are part of the overall package of care that this implementation research seeks to implement.

The purpose of this research is to design scalable systems that can address this issue. The appropriate course of action for refusal to seek care or comply with the prescribed treatment is built into the research design, and involves reviewing the qualitative and quantitative data concurrently to improve the system response. Even for individual cases, the helpline and network of health workers and providers are meant to respond to such situations, and the researchers have to simply notify the corresponding health worker and helpline.

Verbal autopsies are used to identify the biological cause of death and do not investigate risk factors or culpability. There is no risk of the mother being blamed.

Pandemic related disruptions are the main risks to the study, but also present an opportunity to make the model robust to these disruptions. This risk will be mitigated by ensuring engagement of key district and state level government stakeholders throughout the period of the study.

Study team & partnerships

The study will be led by investigators at the Community Empowerment Lab (CEL) that have a proven track record of high-quality implementation research and scale-up through the government health system. The study will be conducted in collaboration with investigators at the GSVM Medical College and Shyam Children's Charitable Hospital in Kanpur Nagar, and the district administration and health system leadership that are already involved in an ongoing PSBI trial. The implementation research will be conducted in close partnership with the UP National Health Mission and the Technical Support Unit for Reproductive, Maternal, Newborn and Child Health and Nutrition to the Government of Uttar Pradesh that closely supports the health system across 75 districts of the state. Other institutional partnerships will also be sought, as needed.

Aarti Kumar is a public health researcher & bioinformatician who currently leads all major research initiatives at CEL as its CEO. She has led several large community-based epidemiological studies, cluster randomized controlled trials and implementation research as Co-PI, and has published in The Lancet, PLOS Medicine and other international peer-reviewed journals. **Dr. Vishwajeet Kumar** is a physician, public health scientist and co-founder of CEL who has laid the foundations of community-entrenched public health research in Uttar Pradesh. Dr. Kumar has previously served as faculty at Johns Hopkins University and has led several seminal research studies on newborn and maternal survival in Uttar Pradesh that have informed global and national policy, and has published in NEJM, The Lancet, and PLOS Medicine, among other peer-reviewed medical journals. The evidence-based model for scaling up Kangaroo Mother Care developed by the CEL team as part of a WHO-coordinated implementation research led by Dr. Vishwajeet and Aarti Kumar, is currently being scaled across UP, making it the leading state in the country for KMC scale-up. **Dr. Rashmi Kumar** is a senior technical advisor at CEL, and recently superannuated as Head of Department of Paediatrics from King George's Medical University, Lucknow. Dr. Kumar is a paediatrician-scientist with a focus on paediatric neurology, and has done seminal work in the field of paediatric infectious diseases, particularly, tuberculosis and Japanese encephalitis. Including vaccine efficacy trials. She has published widely, including The Lancet and NEJM. **Dr. Jai Vir Singh** is a senior technical advisor at CEL, and has previously served as Head of Department of Community Medicine at King George's Medical University, Lucknow, and recently retired as principal of a reputed private medical college. Dr. Singh has led several community-based studies and surveys, and has worked with a broad spectrum of stakeholders on the implementation of various public health programs in Uttar Pradesh.

Dr. Yashwant Kumar Rao is the Head of Department of Paediatrics at GSVM Medical College, Kanpur Nagar. He established the 34-bedded SNCU-NICU unit at the college, which is one of the best performing units in UP and serves as a center for clinical care, research, education and training. He is also the co-PI of the WHO coordinated multi-country trial on PSBI evaluating inpatient vs outpatient care. **Dr. KK Dokania** is a highly regarded paediatrician based in Kanpur Nagar, who has established a sustainable model of care to provide low-cost maternity and paediatric clinical services to disadvantaged communities, and is also a co-PI of the WHO coordinated multi-country trial on PSBI. **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.

Besides the above team of investigators, a consultative committee consisting of the General Manager, Child Health, National Health Mission, Govt. of Uttar Pradesh, The District Magistrate, Chief Development Officer and Chief Medical Officer of Kanpur Nagar will be involved in decision-making roles for action on PSBI management within the Kanpur Nagar district and at the state level in Uttar Pradesh. Besides these government officials in key administrative positions, health system functionaries at the community (frontline ASHA workers, ASHA supervisors called Sanginis), block (medical officers in-charge of community health centres, Block community process managers, etc.), district (chief medical superintendents of the district hospitals, district program manager, etc.) and division (divisional program manager, etc.) levels in Kanpur Nagar district will participate regularly in co-design workshops to discuss findings from the study and co-develop appropriate strategies. Further, community representatives, including political representatives at the village, block, assembly and parliamentary constituency levels, self-help groups, medical and health provider associations, other non-governmental and community-based organizations, and representative groups of mothers, family members, traditional health workers, etc. will also be part of co-design workshops to come together and develop solutions that integrate 360° perspectives.

The above representatives will be engaged as stakeholders through various informal meetings during the initial preparatory stage of the study. This implementation research that is aimed at strengthening the government health system as well as citizen-led initiatives in order to ensure that infants with illnesses, in particular those with possible serious bacterial infections, are identified early and receive timely treatment to reduce preventable deaths in the community. Therefore, this research has direct benefits for the community, and explicitly aims to align the interests of all the above stated community representatives with the interests of the mother and the young infant, to create value for all.

The roles and responsibilities of the study investigators are as follows:

Investigator Name	**Institution**	**Role**	**Key areas of responsibility**
Aarti Kumar	Community Empowerment Lab	PI	Overall responsibility for the study, including finalization of the study protocol, instruments, review, audits, ethical and regulatory compliances.
Dr. Vishwajeet Kumar	Community Empowerment Lab	Co-PI	Key inputs on study design, evaluation, strategy review, and overall guidance to the study team.
Dr. Rashmi Kumar	Community Empowerment Lab	Co-PI	Clinical guidance and inputs into study design and strategy, study instruments and evaluation, etc.
Dr. Jai Vir Singh	Community Empowerment Lab	Co-PI	Public health guidance and inputs into study design and strategy, engagement with key stakeholders, policy feedback, etc.
Dr. Yashwant Kumar Rao	GSVM Medical College, Kanpur Nagar	Co-PI	Local leadership for the study in Kanpur Nagar district, clinical guidance and facility management of sick children, and inputs into other aspects of study design, strategy and evaluation.
Dr. KK Dokania	Shyam Children's Charitable Hospital, Kanpur Nagar	Co-PI	Clinical guidance, strategy for inclusion and engagement of private providers to expand the net for ethical, appropriate and affordable PSBI treatment, and inputs into other aspects of study design, strategy and evaluation.

Dr. Vasanthakumar N.	Uttar Pradesh Technical Support Unit	Co-PI	Strategic inputs for health system interventions, state-level policy and programming, scale-up, and inputs into other aspects of study design, strategy and evaluation.

Dissemination of results

Data from the study will be shared with key stakeholders on an ongoing basis. Final results from the study will be published in international peer-reviewed journals, through formal presentations at appropriate forums with experts and policy-makers at a state, national and global level, and also through other news media for the wider public.

References

1. Perin, J. *et al.* Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet Child & Adolescent Health* (2021) doi:10.1016/S2352-4642(21)00311-4.
2. United Nations Inter-agency Group for Child Mortality Estimation (UN IGME). *Levels & Trends in Child Mortality: Report 2020, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation*. (2020).
3. Alliance for Maternal and Newborn Health Improvement (AMANHI) mortality study group. Population-based rates, timing, and causes of maternal deaths, stillbirths, and neonatal deaths in south Asia and sub-Saharan Africa: a multi-country prospective cohort study. *Lancet Glob Health* **6**, e1297–e1308 (2018).
4. World Health Organization. *Guideline: Managing possible serious bacterial infection in young infants when referral is not feasible*. (2015).
5. Seale, A. C. *et al.* Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. *Lancet Infect. Dis.* **14**, 731–741 (2014).
6. Hibberd, P. L. *et al.* Trends in the incidence of possible severe bacterial infection and case fatality rates in rural communities in Sub-Saharan Africa, South Asia and Latin America, 2010-2013: a multicenter prospective cohort study. *Reprod. Health* **13**, 65 (2016).
7. Mukhopadhyay, R. *et al.* Lessons from implementation research on community management of Possible Serious Bacterial Infection (PSBI) in young infants (0-59 days),

when the referral is not feasible in Palwal district of Haryana, India. *PLoS One* **16**, e0252700 (2021).

8. Goyal, N. *et al.* Management of possible serious bacterial infection in young infants closer to home when referral is not feasible: Lessons from implementation research in Himachal Pradesh, India. *PLoS One* **15**, e0243724 (2020).
9. Awasthi, S. *et al.* Identification and management of young infants with possible serious bacterial infection where referral was not feasible in rural Lucknow district of Uttar Pradesh, India: An implementation research. *PLoS One* **15**, e0234212 (2020).
10. Roy, S. *et al.* Feasibility of implementation of simplified management of young infants with possible serious bacterial infection when referral is not feasible in tribal areas of Pune district, Maharashtra, India. *PLoS One* **15**, e0236355 (2020).
11. Bang, A. T. *et al.* Simple clinical criteria to identify sepsis or pneumonia in neonates in the community needing treatment or referral. *Pediatr. Infect. Dis. J.* **24**, 335–341 (2005).
12. THE WHO YOUNG INFANTS STUDY GROUP. Clinical prediction of serious bacterial infections in young infants in developing countries. *Pediatr. Infect. Dis. J.* **18**, S23 (1999).
13. Young Infants Clinical Signs Study Group. Clinical signs that predict severe illness in children under age 2 months: a multicentre study. *Lancet* **371**, 135–142 (2008).
14. Lokangaka, A. *et al.* Simplified antibiotic regimens for treating neonates and young infants with severe infections in the Democratic Republic of Congo: a comparative efficacy trial. *Matern Health Neonatol Perinatol* **4**, 8 (2018).
15. Tshefu, A. *et al.* Oral amoxicillin compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with fast breathing when referral is not possible: a randomised, open-label, equivalence trial. *Lancet* **385**, 1758–1766 (2015).
16. Mir, F. *et al.* Simplified antibiotic regimens for treatment of clinical severe infection in the outpatient setting when referral is not possible for young infants in Pakistan (Simplified Antibiotic Therapy Trial [SATT]): a randomised, open-label, equivalence trial. *The Lancet Global Health* **5**, e177–e185 (2017).

17. Baqui, A. H. *et al.* Safety and efficacy of alternative antibiotic regimens compared with 7 day injectable procaine benzylpenicillin and gentamicin for outpatient treatment of neonates and young infants with clinical signs of severe infection when referral is not possible: a randomised, open-label, equivalence trial. *Lancet Glob Health* **3**, e279-87 (2015).
18. Darmstadt, G. L. *et al.* Validation of community health workers' assessment of neonatal illness in rural Bangladesh. *Bull. World Health Organ.* **87**, 12–19 (2009).
19. Tripathi, A., Kabra, S. K., Sachdev, H. P. S. & Lodha, R. Home visits by community health workers to improve identification of serious illness and care seeking in newborns and young infants from low- and middle-income countries. *J. Perinatol.* **36**, S74–S82 (2016).
20. Ahmed, S. *et al.* Implementation research to support Bangladesh Ministry of Health and Family Welfare to implement its national guidelines for management of infections in young infants in two rural districts. *J. Health Popul. Nutr.* **38**, 41 (2019).
21. Berhane, M. *et al.* Implementation research on management of sick young infants with possible serious bacterial infection when referral is not possible in Jimma Zone, Ethiopia: Challenges and solutions. *PLoS One* **16**, e0255210 (2021).
22. Ayede, A. I. *et al.* Management of possible serious bacterial infection in young infants where referral is not possible in the context of existing health system structure in Ibadan, South-west Nigeria. *PLoS One* **16**, e0248720 (2021).
23. Leul, A. *et al.* Innovative approach for potential scale-up to jump-start simplified management of sick young infants with possible serious bacterial infection when a referral is not feasible: Findings from implementation research. *PLoS One* **16**, e0244192 (2021).
24. Bhura, M. *et al.* Evaluating implementation of "management of Possible Serious Bacterial Infection (PSBI) when referral is not feasible" in primary health care facilities in Sindh province, Pakistan. *PLoS One* **15**, e0240688 (2020).
25. Wammanda, R. D. *et al.* Implementation of the WHO guideline on treatment of young infants with signs of possible serious bacterial infection when hospital referral is not feasible in rural Zaria, Nigeria: Challenges and solutions. *PLoS One* **15**, e0228718 (2020).

26. Guenther, T. *et al.* Feasibility of implementing the World Health Organization case management guideline for possible serious bacterial infection among young infants in Ntcheu district, Malawi. *PLoS One* **15**, e0229248 (2020).
27. Rahman, A. E. *et al.* Managing possible serious bacterial infection of young infants where referral is not possible: Lessons from the early implementation experience in Kushtia District learning laboratory, Bangladesh. *PLoS One* **15**, e0232675 (2020).
28. 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).
29. Mohan, P. *et al.* Assessment of implementation of integrated management of neonatal and childhood illness in India. *J. Health Popul. Nutr.* **29**, 629–638 (2011).
30. Maheshwari, A., Kumar, P. & Dutta, A. K. Facility based IMNCI. *Indian J. Pediatr.* **79**, 75–84 (2012).
31. Neogi, S. B. *et al.* Inpatient care of small and sick newborns in healthcare facilities. *J. Perinatol.* **36**, S18–S23 (2016).
32. Ministry of Health & Family Welfare, Government of India. *Guidelines for Janani-Shishu Suraksha Karyakram*. http://nhm.gov.in/images/pdf/programmes/jssk/guidelines/guidelines_for_jssk.pdf (2011).
33. Ministry of Health and Family Welfare, Government of India. *Use of Gentamicin by ANMs for management of sepsis in young infants under specific situations: Operational Guidelines*. https://www.healthynewbornnetwork.org/hnn-content/uploads/Operational-Guidelines_India.pdf (2014).
34. Ministry of Health & Family Welfare, Government of India. Addendum to Operational Guidelines on Use of Gentamicin by ANMs for Management of Sepsis in Young Infants under Specific Situations. *Addendum* https://nhm.gov.in/New_Updates_2018/Om_and_orders/rmncha/child_health/Addendum.pdf.

35. Ministry of Health & Family Welfare, Government of India. *Childhood Pneumonia Management Guidelines*. https://nhm.gov.in/index1.php?lang=1&level=4&sublinkid=1336&lid=716 (2019).
36. About Pradhan Mantri Jan Arogya Yojana (PM-JAY). *About Pradhan Mantri Jan Arogya Yojana (PM-JAY)* https://pmjay.gov.in/about/pmjay.
37. Zaidi, A. K. M. *et al.* Scientific rationale for study design of community-based simplified antibiotic therapy trials in newborns and young infants with clinically diagnosed severe infections or fast breathing in South Asia and sub-Saharan Africa. *Pediatr. Infect. Dis. J.* **32 Suppl 1**, S7-11 (2013).
38. Tshefu, A. *et al.* Simplified antibiotic regimens compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomised, open-label, equivalence trial. *Lancet* **385**, 1767–1776 (2015).
39. Puri, D. *et al.* Prevalence of clinical signs of possible serious bacterial infection and mortality associated with them from population-based surveillance of young infants from birth to 2 months of age. *PLoS One* **16**, e0247457 (2021).
40. Kumar, V., Kumar, A. & Darmstadt, G. L. Behavior change for newborn survival in resource-poor community settings: bridging the gap between evidence and impact. *Semin. Perinatol.* **34**, 446–461 (2010).
41. Saha, S. K. *et al.* Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study. *Lancet* **392**, 145–159 (2018).
42. Marsh, A. D. *et al.* Effective coverage measurement in maternal, newborn, child, and adolescent health and nutrition: progress, future prospects, and implications for quality health systems. *Lancet Glob Health* **8**, e730–e736 (2020).
43. Kumar, V. *et al.* Enculturating science: Community-centric design of behavior change interactions for accelerating health impact. *Semin. Perinatol.* **39**, 393–415 (2015).

44. 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).

APPENDIX I. Review of barriers and enablers identified through PSBI implementation research studies conducted in India

Four implementation research studies were conducted in India to understand the feasibility of operationalizing the WHO guidelines with simplified treatment regimens for PSBI management in young infants where referral is not possible. These studies were conducted in Palwal district of Haryana, Sangrah district of Himachal Pradesh, Pune district of Maharashtra and Lucknow district of UP, and reported a treatment coverage of 70%, 80%, 57% and 53% respectively.[7–10] The studies did not measure actual incidence of PSBI cases, but estimated coverage of identification and treatment based on an assumed incidence of 10% of live births in the first two months of life. This assumption was based on previous research that involved rigorous surveillance for PSBI, such as the AFRINEST study in sub-Saharan African countries which reported a PSBI incidence of 11.7% in the young infant period[38] and the ANISA study in South Asian countries that reported a PSBI incidence of 9.5% in the neonatal period.[41] Crucially, both these studies had a fever cut-off of 38.0°C as per WHO guidelines, while the PSBI implementation research studies in India employed a fever cut-off of as 37.5°C as per IMCI. The 0.5°C difference in fever cut-off is likely to yield a much higher number of cases of PSBI in the Indian studies. Therefore, **the assumed incidence of 10% likely underestimates the actual incidence of PSBI in the population based on the fever cut-off and overestimates the treatment coverage.**

The key challenges identified, strategies adopted, and lessons learnt are summarised below.

Policy

A national policy dialog at the inception of these studies led to a consolidation of PSBI signs from previously 11 to 7 signs as per the WHO guidelines, with the exception that the cut-off for fever was retained as 37.5°C as per IMCI vs. the WHO guideline of 38.0°C, and led to an addendum to the previously released guidelines for community-based case management by ANMs.[33,34] Two other policy decisions reported in these studies include alignment on the dosage of amoxycillin as well as non-requirement of referral and treatment with oral amoxycillin alone for infants aged 7-59 days with fast breathing as the only sign of PSBI.[8,10] However, these seem to not have been formally integrated or possibly reversed, as none of the subsequent guidelines reflect these decisions. **Policy alignment and consensus among major stakeholders is an important priority.**

Identification of illness by mothers

Across studies, mothers had limited ability to recognise danger signs. All studies succeeded in improving danger sign recognition by mothers to various extents through a combination of one or more approaches including mass media, group as well as individual strategies. At an individual level, messages around danger signs were communicated variously at antenatal clinics, during discharge and during HBNC visits, typically with the help of visual aids. None of the studies reported any efforts in improving counselling mothers on promotive-preventive care.

Care-seeking preferences

Other than Himachal Pradesh where there was a dearth of private practitioners, all other sites reported communities' general lack of trust in the health system and preference for private providers including unqualified healthcare providers. Despite significant interventions for health system strengthening by the study teams, 31.4% and 42.0% families in Maharashtra and Haryana respectively preferred to seek care from private providers as against only 18.6% in the Lucknow, UP site. Given the local health system context, this likely reflects under-reporting of PSBI cases managed by private providers in UP, rather than a true reduction in care-seeking from private providers. Thus, **private providers present a huge untapped opportunity to improve coverage of PSBI treatment.**

Home visits by ASHA workers

There were several challenges with HBNC home visits of ASHA workers. While ASHA workers had received prior training on HBNC through typical cascade-based training approaches, their ability to recognise danger signs was found to be poor. All studies put focused efforts in retraining ASHAs to build their skills in newborn assessment and classification of danger signs. There were also issues with equipment issued to them being non-functional and needing replacement.

During formative research across all studies, mothers reported a much lower frequency of HBNC visits than the HBNC guideline. However, coverage of ASHA home visitations during the study was measured based on self-reported data by ASHAs, which showed significant improvements across all sites. Importantly, the Haryana site compared the self-reported coverage of ASHA home visits with maternal reports and found a drastic difference. ASHAs reported a coverage of between 80% to 96% for the 6 visits starting from day 3, whereas mothers reported a coverage of 39-54%, with 17% families not receiving a single visit. The Haryana site did not find improvements in actual frequency of visits, record-keeping by ASHAs and supervision of ASHA workers despite intensive efforts including 12 training and re-orientation sessions. Thus, **it is critical to introduce effective measures to ensure accountability of ASHA workers.**

The proportion of PSBI cases reported by ASHA workers in Haryana, Himachal Pradesh, Maharashtra and UP was 11.4%, 28.0%, 35.4% and 81.3% respectively. The unexpectedly high proportion of PSBI cases reported by ASHA in UP likely reflects a high incidence of PSBI cases that went undetected. All other sites found that the majority of PSBI cases were reported by mothers. Thus, **scalable solutions for PSBI identification cannot just rely on ASHA workers and need to keep the mother in the centre.**

PSBI care by community-based providers

All sites reported challenges with utilizing ANMs as the primary provider of PSBI case management in the community. Challenges reported included many ANM sub-centres being non-functional, ANMs not being aware of their role in PSBI case management, and hesitancy of ANMs in handling sick babies as their role primarily involves immunisations, preventive care and conducting non-complicated deliveries. The Haryana, Himachal Pradesh and Maharashtra sites could not successfully overcome these challenges and had to involve medical officers and ayurvedic medical officers in PHCs and CHCs in community-based case management. Even these medical officers were reluctant to treat young infants and typically referred them to higher centres prior to the studies. Intensive handholding by study staff and paediatricians over six months was conducted to improve their confidence in managing sick young infants. Widespread non-compliance with treatment documentation by ANMs and medical officers was reported despite intensive efforts. Thus, the **feasibility of utilizing ANMs for community-based case management appears to be low.** Since these studies, health and wellness centres co-located with ANM sub-centres have been established in many parts of UP where resident trained nurses called Community Health Officers (CHO) have been deployed – feasibility of their role in PSBI case management should be explored. The long periods of intensive handholding required even for medical officers implies that the typical programmatic approach of 2-7 days long cascade-based training and refresher trainings may not be adequate for ensuring PSBI management in non-critically ill young infants in lower-level facilities. **Scalable solutions are needed to provide intensive handholding support to medical officers and staff nurses for PSBI management in lower-level facilities.**

Referral

Lack of referral facilitation to district level facilities was reported as another major problem across the sites that largely remained unresolved. **The problem of blind referral**, i.e., referring patients for care to higher level facilities without adequate documentation, counselling and without confirming with the referral facilities regarding availability of beds and services **is extremely common and needs effective solutions.** Availability of referral transportation was not a problem in other sites except for Himachal Pradesh, where the hilly terrain poses unique challenges. PSBI treatment in higher district and sub-district level facilities was not a focus of these studies but has its own challenges that will need to be addressed in the proposed research.

Systems

Common systemic issues related to infrastructure and supplies included dysfunctional equipment at various levels right down to ASHA workers, and shortage of the key PSBI medications including inj. gentamicin, inj. ampicillin and oral/ dispersible amoxycillin. Some of these issues remained unresolved during the studies, probably since their resolution required engagement of other stakeholders and departments within the health system at the state, rather than district level, which was beyond the mandate of these studies. **Scalable solutions for equipment and supplies-related problems may include automation of resource planning and inventory systems.**