BetterBirth: A Trial of the WHO Safe Childbirth Checklist Program

NCT02148952

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Instructions: The purpose of this research protocol is to provide IRB members and reviewers with sufficient information to conduct a substantive review. If a separate sponsor's protocol exists, submit it in addition to this document.

Complete all of the sections below. For more detailed instructions, consult the Investigator's Manual or IRB website (links provided below).

GENERAL INFORMATION	
Protocol # (if assigned):	
Version Date: 11 October 2017	**Version Number:**
Principal Investigator: Vishwajeet Kumar, MBBS MPH; Bhala Kodkany, MBBS MPH; Atul A. Gawande, MD MPH; Katherine Semrau, PhD MPH	
Faculty Advisor (if PI is a student**): N/A**	
Protocol Title: BetterBirth Trial of the WHO Safe Childbirth Checklist Program Study Protocol	

1. Specific Aims

Despite well-recognized gaps in maternal and newborn care practices at birthing sites worldwide, no unifying practice tools exist that clearly define minimum care standards and are proven to support their effective delivery. Translation of evidence into reliable and sustainable practice has been a particular challenge to improving outcomes in the regions where mortality rates are highest. The disparity between knowledge and practice in maternal and perinatal care is especially unfortunate because a rich evidence base exists and many proven interventions are relatively inexpensive and easy to perform.

This safety and quality improvement project builds on our prior experiences with health-related checklists. In 2007, the Harvard T.H. Chan School of Public Health led a World Health Organization (WHO) project to reduce deaths in surgery globally. Following experience in aviation and other industries in managing safety, we designed and tested a two-minute, 19-item surgical checklist that was found to reduce surgical mortality more than 40% when adopted by facilities. The WHO Surgical Safety Checklist has now been introduced in over 4,000 hospitals worldwide. Our proposal is to test a similar systems-based approach to reducing harm in low-income childbirth facilities.

The WHO Safe Childbirth Checklist (SCC) is a 29-item tool comprised of accepted standard care practices known to be associated with improved maternal, fetal, and neonatal outcomes (see Attachment). The instrument and associated implementation program (the SCC program) were developed over the past three years by a partnership of WHO and the Harvard Chan School, working with a large international network of experts and stakeholders in maternal, fetal, and newborn health. The aim is to reduce severe childbirth-related harm, including death, in institutional deliveries. Pilot testing of the SCC program at a public-sector birth center in south India demonstrated dramatic improvements in health worker adherence to essential childbirth-related clinical care standards.

The current study is a matched-pair cluster randomized trial of the SCC program in birthing sites in north India to assess its impact on serious maternal, fetal, and newborn harm. The SCC program will be rolled out in approximately 60 birth centers and outcomes of mothers and babies in these intervention facilities will be compared with those from approximately 60 comparison facilities (in which the SCC program is not introduced) on a total sample of over 170,000 births. The data collection for the study will be completed in a 55-month period. Lessons learned are anticipated to guide scale-up and policy-making in India and other high priority countries.

The main objectives of this study are to:

- Measure the impact of the SCC program on maternal, fetal, and newborn survival; and severe maternal harm.
- Measure the impact of the SCC program on secondary outcomes—specifically, (1) selected individual health outcomes for mothers and babies, and (2) rates of successful delivery of selected essential health practices by health workers.

The senior co-PI and Director are based at Ariadne Labs and are responsible for the conduct of the BetterBirthTrial. HSPH staff and faculty are also responsible for trial implementation, trial management, and ethics reporting.

Project management structure will broadly have two arms: implementation (rollout of the WHO SCC program) and evaluation (data collection and management). Investigators will be responsible for overall management of the activities and for providing guidance to program partners for effective implementation and high quality data collection. The Harvard Chan School has contracted local implementation partners who will function through their own program structure to implement the intervention and comparison program in 120 target facilities.

Community Empowerment Lab (Vishwajeet Kumar, PI) is our primary research partner. They will be responsible for providing technical support and advice on the building of local consensus, support in ethical approval, finalize trial procedures, host the primary data server, monitor the trial and review interim and final data analysis, and collaborate on manuscript preparation and results dissemination of the trial results.

PSI–India is our primary implementation partner. They will also be responsible for recruitment and administrative management of the evaluation arm of the project. Technical and programmatic management of research will be conducted under the direction of the investigators.

Dimagi Inc. is our primary data management and technology partner. They will be responsible for developing the mobile applications for data collection for health outcomes and processes data, call center software (interface for entering the CATI data) and will be hosting the database on a HIPAA compliant encrypted server secured under multiple layers of cyber security.

2. Background

2.1 Provide the scientific background and rationale for the study

Checklists have been defined as "formal lists used to identify, schedule, compare or verify a group of elements or actions; used as visual or oral aids to enable users to overcome the limitations of short-term human memory."[1] Checklists range from simple (e.g., a simple handwritten grocery checklist) to complex (e.g. electronic checklists used by large commercial airlines) and are integral to safety operations in many high-reliance industries, including aviation, nuclear power, and product manufacturing.[2] Medicine has in common with these fields the necessary completion of tasks that can be complex and stressful, with human lives dependent on their safe and reliable completion. Inability to reliably comply with high quality clinical practices is associated with adverse patient outcomes, and even hospitals in high-income developed countries have relatively low compliance rates with known best practices.[3], [4] Furthermore, as stress increases, thought processes and breadth of attention becomes narrow, making reliance on

memory alone problematic when attempting to adhere to all known best practices in a complex situation.[5] Checklists are tools employed to improve this adherence. A health-related checklist may be defined as a tool that assists an individual or team in assuring that essential clinical care practices are performed. Health-related checklists can serve as powerful vehicles for change in enhancing patient safety by promoting compliance with best practices, reducing error, and improving patient outcomes.

Summary of relevant research studies

A five-item checklist for central-line placement was found to reduce catheter-related bloodstream infection by two-thirds in a statewide study in the US.[3] The initiative is now rolling out in multiple countries to develop a strategy to reduce deaths globally.[6] A two-minute checklist was devised for surgical teams to assure adherence to 19 practices identified as critical for safe surgery. The tool was implemented in eight pilot hospitals, including St. Stephen's Hospital, Delhi, and a District Hospital in rural Tanzania, in an 8,000 patient trial. As reported in the *New England Journal of Medicine* in January 2009, death rates fell significantly, from 1.5% to 0.8%.[5] The effectiveness of this strategy has been confirmed in independent large-scale trials.[6], [7] WHO established the Surgical Safety Checklist as a recommended global standard of care and more than 20 countries have implemented it as a national policy. Considering world-wide surgical volume is estimated at greater than 200 million cases, this approach offers potential reduction of death and complications at large scale.

Rationale for development of a Safe Childbirth Checklist

Of more than 130 million births that take place each year, up to 350,000 result in the mother's death, 1.2 million in an intrapartum-related (fresh) stillbirth, and another 3.1 million in a newborn death during the neonatal period.[8–12] The major causes of childbirth-related mortality are well described: hemorrhage, infection, hypertension-related disorders, and prolonged/obstructed labor in mothers; and infection, birth asphyxia, and complications of prematurity in babies.[8], [13] The highest incidence of maternal and perinatal mortality occurs around the time of birth with the majority of deaths occurring within the first 24 hours after delivery.[14] Intrapartum-related (fresh) stillbirths often result from complications during labor. Most of these deaths are avoidable if existing knowledge had been applied. The disparity between knowledge and practice is particularly unfortunate in maternal and perinatal care because a rich evidence base exists and proven interventions are relatively inexpensive and easy to perform.

Provision of skilled attendance at every birth has emerged as a global priority. Women in high-risk regions are increasingly being encouraged to deliver in health facilities where potential complications can be optimally managed. However, in practice, poor quality of care at health facilities is frequently observed.[15] Frontline workers deliver essential health care to mothers and newborns, and helping to improve their capabilities and performance is crucial to increasing survival. But no widely applied practice tools clearly define minimum care standards and support their effective delivery. Integrated service packages that build upon existing clinical system frameworks to improve care across the continuum of steps involved in safe childbirth are urgently required.

2.2 Describe the significance of the research, and how it will add to existing knowledge

The WHO Safe Childbirth Checklist program

The WHO SCC program was established by WHO and the Harvard Chan School as a safety initiative to improve health workers' capacity to deliver high quality maternal and perinatal care in instituional births in low income settings with the goal of saving lives.

The SCC was developed from October 2008, to June 2010, through a systematic, stepwise process that included: comprehensive review of existing guidelines and evidence; formal consultation of key stakeholders including international content experts, frontline health workers, policy-makers, and other maternal-newborn health advocates; iterative refinement of checklist content; and usability field testing in 17 birth sites in ten high-priority countries including India, Pakistan, Nigeria, Kenya, Ghana, Tanzania, Mali, and China. The result is a 29-item bedside checklist to efficiently aid health workers in insuring adherence to standards of care associated with improved maternal, fetal, and neonatal outcomes. Each item is a critical action that is commonly missed but proven or considered by expert consensus to reduce deaths and/or major complications. The checklist is intended for use at four critical junctures in clinical care around the time of birth: (1) on admission of the mother to the birth facility; (2) when the mother begins to push or before cesarean; (3) soon after birth (within 1 hour); and (4) before discharge from the birth facility. Checklist items target the major killers of mothers (hemorrhage, infection, prolonged/obstructed labor, and hypertensive-related disorders) and babies (infection, asphyxia, and complications related to prematurity) in low and middle-income countries. Intrapartum-related (fresh) stillbirths are addressed through content focused on improving management of women in labor. The SCC does not represent a protocol, algorithm, or guideline and does not replace existing policies. Rather, it is a bedside tool designed to aid clinicians in adhering to them. Local tailoring of the checklist is encouraged.

Pilot study of the WHO Safe Childbirth Checklist program

A pilot study of the SCC program was conducted from July 2010, to December 2010 in Karnataka, south India. The primary aim of the study was to assess, through a pre-post intervention design, the program's impact on health workers' adherence to a core set of safety standards linked with improved maternal, fetal, and neonatal health outcomes. The study site was representative of large Community Health Centers (CHCs) in India. Data were obtained primarily through direct observation of health workers' practices by independent, third-party data collectors. Observational data were collected on 300+ consecutively enrolled birth events within a period of approximately 3 months during each phase (pre-intervention and post-inervention) of the study. The sample size was calculated to detect a 20% increase in the proportion of births in which selected process measures are met, with a statistical power of 80% and an alpha value of 0.05.

The SCC program led to dramatic improvements in health worker adherence to essential childbirth-related clinical care standards. Health workers provided on average 10 out of 29 (34%) essential clinical care standards at baseline and 25 out of 29 (86%) after introduction of the checklist ($p<0.001$). For example, adequate hand hygiene rate at the time of delivery increased from 11% to 100%; rate of oxytocin administration within one minute after birth increased from 8% to 66%; and rate of breastfeeding within 1 hour after birth increased from 50% to 95%.

Study goals

The goal of the study is to measure the impact of the SCC program on maternal, fetal, and newborn health outcomes. The primary hypothesis is that use of the Safe Childbirth Checklist improves safety and outcomes of child delivery in a low-income setting.

Study Objectives

A. Measure the impact of the SCC program on maternal, fetal, and newborn survival; and severe maternal harm.

B. Measure the impact of the SCC program on secondary outcomes—specifically, (1) selected individual health outcomes for mothers and babies, and (2) rates of successful delivery of selected essential health practices by health workers.

Study outcomes

Primary outcome

The primary outcome in this trial is the rate of a composite measure of "maternal" and "baby" conditions. A composite rate of maternal, fetal, and newborn outcomes was selected because:

- The SCC program is intended to reduce harm for both mothers and newborns, as well as influence intra-partum management thereby potentially addressing fetal health; and
- The baseline event rate must be sufficiently large for feasibility of study design (small baseline event rates necessitate larger sample sizes) and the baseline measurable mortality rate for any of these populations individually would not necessarily be sufficiently large to design a feasible study.

The composite measure will reflect severe maternal, fetal, and neonatal complications that occur around the time of childbirth relative to the total number of birth events. For this study, a birth event is defined as the period from the time of maternal admission for childbirth until the completion of 7 days after birth. A birth event, in essence, considers the mother and baby to be a single dyad given that their health outcomes are many times interdependent. For this reason, multiple gestations will also be considered to be a single birth event. A birth event may result in a stillbirth and/or live birth.

The rationale for including the period from birth to 7 days for mothers and newborns is (1) the SCC program is anticipated to have beneficial effects immediately after delivery as well as after the mother and baby leave the facility; (2) many mothers and babies are discharged or leave the facility soon after birth (many in less than 6 or 12 hours); (3) a substantial number of events comprised in the primary outcome may occur after mothers and newborns leave the hospital and/or after the first 1-2 days after delivery.

Specific outcomes comprising the composite measure are:

Maternal outcomes:

A. **Maternal death within 7 days**: defined as death of a woman at any time from admission to the facility for childbirth, through delivery, until the period of 7 days following delivery.
B. **Severe maternal complications within 7 days**: Defined by the following clinical criteria:
    - Fits (in absence of history of epilepsy),
    - Loss of consciousness retained at >1 hour,
    - High fever and foul smelling vaginal discharge
    - Post-partum Hemorrhage, or
    - Stroke

Fetal/ Neonatal outcomes:

A. **Stillbirth**: defined as a late stage fetal death occurring at ≥28 weeks of gestation OR with a birth weight of ≥1000 gm. at birth. [19] In the study settings, health workers often do not have the capacity or training to differentiate between fresh and macerated stillbirths. It is observed that fresh stillbirths are often misclassified as macerated stillbirths (or intra-uterine deaths). Similar experience has been reported in other studies conducted in similar settings. To avoid missing out on the misclassified fresh stillbirths, both forms of stillbirths will be included in the primary outcome.
B. **Early neonatal mortality**: defined as a newborn death that occurs in the first week of life.

A "positive" outcome for a given birth will be recorded if any one of the 4 above-listed events occurs. A "negative" outcome means that none of the above-listed events occurred. The evaluation component of BetterBirth will attempt to measure whether rollout of the WHO SCC program significantly decreases the incidence of "positive" events so-defined.

Secondary outcomes

Secondary outcomes are:

A. **Combined maternal, fetal and newborn outcome**: composite rate of maternal death within 7 days, fresh or macerated stillbirth, and neonatal death at 7 days.
B. **Maternal outcomes**: Rate of maternal death (measured through 7 days), rate of severe maternal complication described above (measured through 7 days), rate of inter-facility transfer, and the rates of the following maternal procedures: blood transfusion, hysterectomy, need to revisit facility due to a problem, C-section.
C. **Newborn outcomes**: Fresh or macerated stillbirth, rate of early neonatal death (within 7 days), rate of inter-facility transfer, need to revisit facility due to a problem.
D. **Rates of adherence by health workers to essential childbirth practices ("process measures")**: Specifically, the rates of completion of the following practices will be assessed in a sample of approximately 7800 deliveries for each of pause-points 1, 2, and 3: including maternal temperature obtained on admission, maternal blood pressure obtained on admission, partograph use, inappropriate initiation of oxytocin before delivery of the baby, appropriate hand hygiene (use of soap and water, and wearing clean gloves) by health workers at the time of delivery, skin-to-skin care, oxytocin administration within 1 minute after birth, newborn weight and temperature obtained within 1 hour after birth, and initiation of breastfeeding within 1 hour after birth.

Additional outcomes

Additional outcomes to be evaluated are:

A. Rate of SCC use.
B. Impact of the SCC program on the availability of the essential resources including: partograph, oxytocin, antibiotics, Magnesium Sulphate, gloves, water, and soap.
C. Operational changes in workflow introduced independently by the facility staff, induced by the SCC program.
D. Impact of the SCC program on the rates of medication administration; specifically oxytocin, antibiotics for mother, Magnesium Sulphate, antibiotics for baby, antiretroviral for mother, and antiretroviral for baby.

E. Qualitative user impressions of checklist use and facility culture as assessed by survey of health workers.
F. Patient satisfaction as assessed by survey of patients.

3. Study Setting

3.1. Identify the sites or locations where the research will be conducted.

This trial will be conducted in a single state (Uttar Pradesh; UP) in a single country (India). The maternal mortality ratio in UP is 359/100,000 live births.[19] Maternal near-miss data for UP are not available, but estimates from similar low-income settings in Indonesia, Syria, and Latin America range from 14-34/1,000 live births. [20–22] The intrapartum-related (fresh) stillbirth rate in UP is 27.7/1,000 births and the rate of neonatal death on the first day of life is 11/1,000 live births.

India is at a crucial juncture for increased focus on standards of quality of care for institutional childbirth given that the country has the world's highest burden of maternal and neonatal mortality and a recent dramatic increase in institutional deliveries due to its National Rural Health Program's *Janani Suraksha Yojna (JSY)* scheme[8], [24–26]. The proposed study intervention has high potential for integration with existing services in the state. It directly supports the government of India's strategic framework for quality assurance and provides a clear blueprint for strengthening adherence to nationally-mandated protocols and guidelines relating to childbirth.

To maximize representation across UP, and to facilitate administrative ease associated with decentralized management; five geographic regions ("hubs") will contribute sites to the trial. Each region will be comprised of parts of 3-5 districts (for reference, there are a total of 72 administrative districts in UP). The current proposed regions and districts are listed in the table below. The proposed district plan was formulated based on (1) early discussion with and preferences of government of UP; (2) need; (3) relative high rates of institutional births; (4) existing Population Services International (PSI), the primary implementing partner, footprint; and (5) avoiding overlap with similar existing programs. Regions will be named after the major district included, which will act as the regional headquarters. This regional plan of districts will be flexible to allow for potential inclusion of new districts if necessary. On average, twenty facilities will be recruited in each region—approximately 10 in both intervention and comparison arms.

Hub	**Lucknow**	**Agra**	**Meerut**	**Varanasi**	**Gorakpur**
Districts	Lucknow	Agra	Meerut	Varanasi	Gorakpur
	Kanpur Nagar	Aligarh	Bulandshahar	Jaunpur	Basti
	Unnao	Hathras	JP Nagar (Amroha)	Azamgarh	Ambedkar Nagar
	Rae Bareli	Mathura	Muzaffarnagar		
	Gonda		Moradabad		
	Sultanpur				
	Faizabad				
	Hardoi				
	Lakhimpur				
	Sitapur				

It is our understanding that private sector facilities are conducting fewer and fewer deliveries in UP due to the JSY scheme. All health facilities will be enrolled from the public sector, where the majority of births occur and where outcomes are generally thought to be worse.

3.2. Describe the Principal Investigator's experience conducting research at study site(s) and familiarity with local culture

The principal investigator (Dr. Atul Gawande) recently led an evaluation of a WHO Surgical Safety Checklist Quality Improvement program in 8 hospitals around the world. Four hospitals were in developed settings (US, UK, Canada, New Zealand) while four hospitals were in developing settings (Jordan, India, Philippines, Tanzania). The results of this study were published in the New England Journal of Medicine in January 2009 (Haynes, et al). Our group has also worked closely with the World Alliance for Patient Safety at the World Health Organization for the past several years. Dr. Gawande is an international expert in safety and is the current lead for the Safe Surgery Saves Lives program at the WHO.

The co-principal investigator (Dr. Katherine Semrau) has 15 years experience in in maternal and child health research, focused in low and middle income settings. Further, Dr. Semrau has traveled and worked in India, previously. She is an epidemiologist by training and will focus on the proper implementation of the study and data analysis.

3.3. Is the research conducted outside the United States?
☐No ☒Yes: If yes; describe site-specific regulations or customs affecting the research, local scientific and ethical review structure

There will be no significant differences between the regulation of this study in the US and international site.

3.4 Are there any permissions that have been or will be obtained from cooperating institutions, community leaders, or individuals, including approval of an IRB or research ethics committee?
☐No ☒Yes: If yes; provide a list of the permissions (also include copies with the application, if available)

Ethics approval for the study with annual reviews has been obtained from the Institutional Review Boards at:

- Lucknow Ethics Committee, Lucknow, India (Ref no 13/LEC/12 dated 30th Apr 2012)
- J.N. Medical College, K.L.E. University, Belgaum, India (MDC/IECHSR/2012-2013 dated 5th May 2012)
- Harvard School of Public Health, Boston (Protocol number: 21975-101)
- Ethics Review Committee at WHO, Geneva (MDC/IECHSR/2012-2013 dated 5th May 2012)
- Population Services International, Washington, DC (protocol 47.2012 dated Nov 28, 2012).

4. Study Design

4.1. Describe the study design type

Cluster randomized comparison design

This study will employ a matched-pair cluster randomized comparison design. The randomized trial design with a matched comparison arm was selected for this trial since it represents the strongest design with the greatest likelihood of providing clear and accurate assessment of the program's effectiveness. Pairs of facilities will be matched according to known and measured covariates prior to randomization in order to increase power and efficiency. A staggered rollout will be incorporated for practical reasons given logistical challenges of implementing in large number of centers simultaneously.

The checklist program is an intervention that, by its nature, is most efficiently delivered at the facility level. From a research standpoint it would be impossible to prevent contamination of the intervention between individual health workers if rolled out at the provider level within a given facility, particularly in the typical facilities where only a small number of staff attend births. The intervention will therefore be introduced at the facility level; facilities represent clusters in this study and the study will be implemented in a total of 120 facilities. Sixty facilities where the checklist program is implemented will constitute the intervention group (intervention health facilities; IHFs) and the comparison group will be sixty matched facilities (comparison health facilities; CHFs). Outcomes will be measured at the patient level.

The senior co-PI and Director are based at Ariadne Labs and are responsible for the conduct of the BetterBirthTrial. HSPH staff and faculty are also responsible for trial implementation, trial management, and ethics reporting.

Project management structure will broadly have two arms: implementation (rollout of the WHO SCC program) and evaluation (data collection and management). Investigators will be responsible for overall management of the activities and for providing guidance to program partners for effective implementation and high quality data collection. The Harvard Chan School has contracted local implementation partners who will function through their own program structure to implement the intervention and comparison program in 120 target facilities.

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- Indian Council for Medical Research, (ICMR), New Delhi, India (Ref no 5/7/858/12-RHN)

The Universal Trial Number (UTN) the protocol is U1111-1131-5647. The trial has been registered with clinical trial registry at ICMR (www.ctri.nic.in), number: 5/7/858/12-RHN. The trial has also be registered with www.clinicaltrials.gov and is identified by number: NCT2148952.

4.2. Indicate the study's duration - and the estimated date of study completion

The study is anticipated to last up to 60 months, including 24 months of preparation and pilot testing ("preparation phase") and up to 36 months of RCT intervention and data collection ("trial phase") followed by data analysis. Site selection will be completed during the preparation phase and site enrollment will be targeted to be completed by 15 months after the trial phase begins. Site enrollment will take place in batches, or "waves," of facilities for administrative practicality and to be able to take advantage of learning that is anticipated to take place during implementation in the first few waves.

Successfully rolling out the checklist program, and being in a position to accurately measure outcomes in such a large number of facilities and through home visits has risks of delay. Our plan is to ensure that all study tools (relating to both program implementation and data collection) are validated in the preparation phase prior to use in the trial phase in the pilot sites. As described above, we will enroll five and ten sites for training, refining our coaching and data capture tools, testing and improving our software applications, and completing our pilot data collection for reporting on lessons learned for dissemination and validation of our data tools. These sites will start during the preparation phase continue throughout the length of study and the learning from data gathered in these facilities will be reported separately from the RCT.

The trial phase will then roll out in a staggered fashion, based on staffing and observed feasibility. Data collection from each facility will begin after the facility has been enrolled and any training completed and will continue for up to 18 months. Enrollment and data collection will be stopped when the required sample size for the primary outcome from the study sites (171,964 birth events) is achieved. The trial will be monitored for possible early end when the outcome data from the first wave of 15 pairs of sites (Phase II) are captured using appropriate statistical techniques. Anticipated key milestones in the study timeline are as follows:

Activity	**Targeted date**
Preparation phase begins	Month 0 (began Nov 2012)
Trial phase II begins	Month 24 (Oct 2014)
Data on Essential Birth Practices complete (Phase II)	By month 35 (Dec 2015)
All facilities enrolled (Phase III)	By month 40 (April 2016)
Interim analysis	Month 40(April 2016)
Outcome data collection complete	By month 60 (Oct 2017)

Follow-up and early withdrawals

Due to the nature of the intervention, long-term follow-up of patients will not be performed. Data from individual mothers and babies will be collected at two time periods: at facilities at the time of discharge from routinely collected data registries and at a pre-defined period starting 7 days after delivery to ascertain outcomes.

The local co-investigator and the local study staff will be available by phone or in-person meeting throughout the study to answer any questions that study participants may have. This local team will be in regular contact with the Harvard T.H. Chan School of Public Health study staff. In

addition, the School-based staff will spend approximately 4-6 months each year in the field directly supporting study execution and will be available for support and follow-up.

In case a facility's leaders decide to discontinue the intervention before the completion of the study, permission will be sought from them to continue data collection until the overall sample size is reached. In case a center withdraws from the study altogether, data collection will still be continued from the other facility in the matched-pair. At the same time, another pair of facilities may be enrolled in the study to reach the overall sample size.

4.3. Indicate the total number of participants (if applicable, distinguish between the number of participants who are expected to be screened and enrolled, and the number of enrolled participants needed)

Five primary areas of risk were considered in the determination of the sample size for this trial: (1) intracluster correlation; (2) cluster size and number; (3) inter-cluster correlation between facilities in a matched pair (i.e., matching effect); (4) baseline event rate (i.e., primary outcome); and (5) estimated event rate reduction that can be achieved (and measured) by the intervention program. These risks were balanced in the context of operational management considerations, resulting in a total sample size target of 171,964 births (~86,000 in each arm) across 60 pairs of birth facilities (120 sites total).

4.4. List inclusion criteria

For measuring outcomes, we will include all mothers admitted to a study site for childbirth, excluding those who have been referred into the facility by an inter-facility transfer, those being managed for abortion and those who refuse. In case a mother or baby from an enrolled site is referred out to another facility (before or after delivery) the mother-baby dyad will be included in the study and the outcome will be allocated to the referring facility.

For a smaller subset of pause-points during birth events (as detailed above), health worker practices will be directly observed to measure the impact of the SCC program on delivery of essential practices, as a secondary outcome. A convenience sample of women and babies cared for by the health workers around the time of childbirth at the facility during data collectors' duty hours will be included in this component of the study.

Site recruitment

Due to the nature of the program the unit of intervention will be at the facility level. Hence, the recruitment plan will include selecting health facilities conducting deliveries and enrolling them into either the intervention or comparison arms.

Each of the six regions will contribute approximately 20 facilities (approximately 10 each in intervention and comparison arms) leading to a total of 120 facilities. Sites will be spread across districts in each region and will be matched-paired across districts.

Site identification

Study sites will be identified, vetted, and enrolled using a predefined structured selection process. Eligibility criteria include: geographic location of the facility within study districts; facility being a PHC, BPHC,CHC, CHC/FRU or DWH; willingness of the facility leaders and staff to participate in the study; facility being a 24X7 functional National Rural Health Mission (NRHM) accredited birth center; having at least three birth attendant trained at the Auxiliary Nurse Midwife (ANM) level or above; a birth volume of at least 1,000 births annually; willingness to

provide its newborn and maternal outcome data; and having no potentially confounding ongoing research or quality improvement programs at the time of selection.

Site enrollment

Site enrollment refers to the date on which both facilities in a matched pair are entered into the trial. Matched-pairs of facilities will be enrolled together to maintain consistency in the duration of follow-up and data collection. It is anticipated that all facilities will be enrolled by approximately 20 months from the start of the trial phase (see description of preparation and trial phases below in the section entitled, "schedule, project timelines, and sampling time frame"). In each facility, data collection will continue for up to 18 months after the last site enrollment.

Matched-pairing

Matched-pairing of facilities based on available background characteristics prior to randomization helps to ensure that IHFs and CHFs are as similar as possible at baseline, and increases statistical power and efficiency.[27] Within each matched-pair of facilities, one facility will be randomized to receive implementation of the intervention program and the other facility will undergo data collection for maternal neonatal outcomes and be given the implementation package at the end of the observation period.

Matching will be conducted by exact matching on specified variables when possible and within bounded ranges of those variables when exact matching is not feasible. Facilities will be matched based on selected variables from the following list: zone, facility type, level of staffing (number of skilled nurses or ANMs performing deliveries); birth volume, distance to district hospital.

If, after enrollment, either facility in a pair becomes unable to participate, both sites will be excluded from the main analysis from that time point onwards. As an "intention to treat" study if a CHF withdraws from the study, the intervention and associated data collection will be continued in the paired IHF. If an IHF withdraws from the study, data collection will continue at the matched CHF will be offered the intervention according to the original timeline. In the event that a either a CHF or IHF drops out an additional matched pair of facilities may be added.

Preparation Phase and ongoing learning

Five and ten non-study sites will be engaged prior to the RCT for training, refining our coaching and data capture tools, testing and improving our software applications, and pilot data collection for reporting on lessons learned for dissemination and validation of our data tools. These sites will continue throughout the length of study and the learning from data gathered in these facilities will be reported separately from the RCT. All informed consent procedures will be followed for data collection.

4.5. List exclusion criteria

None.

4.6. Describe study procedures

Roll-out

Roll-out of the RCT will be done in 2 phases. In the first phase, 15 pairs of sites will be enrolled. Following confidence that the intervention and data collection are being rolled-out according to the protocols, the remaining 45 pairs of sites will be initiated.

Randomization

Facilities within each matched-pair will be randomized to either IHF or CHF groups. Randomization will be conducted by the epidemiologist using a computer program. All facilities will be matched-paired before any rollout begins. Randomization of specific pairs will be performed prior to enrollment of that pair of facilities into the trial.

Blinding and bias

Due to the nature of the intervention, which will be evident and easily discovered, it will not be possible to blind the facility staff, investigators, trial staff, and data collectors to the allocation.

Contamination of CHFs with the checklist program is possible. We suspect, however, that significant contamination with sustained checklist use in CHFs is unlikely since the program component of the WHO SCC program (not simply the checklist itself) is anticipated to be an important factor in checklist adoption by local staff. Likelihood of bias in observation data collection will be minimized by allocating only IHF or CHF groups of facilities to any individual data collector.

Translations and local adaptation of the study tools

All data collection materials used in the study (e.g., consent forms, study tools) which need translation will be translated into Hindi according to established practices. Steps will be taken to ensure content, semantic, and technical equivalence between the source (English) version and target (Hindi) versions of the material. The process will include review of the content of any clinically-related tools by a group of local experts to align it with the local guidelines and cultural practices; translation, back-translation, and comparison of original vs. back-translated versions; and field testing for appropriateness for use by monolingual (source language) users as indicated.

Intervention

The trial has two study arms: intervention and comparison. The intervention is the implementation of the Safe Childbirth Checklist program.

Modifications to the previously piloted WHO Safe Childbirth Checklist were made in partnership with Government of India and UNICEF-India to ensure alignment with Indian guidelines. The checklist for the trial has been included as an attachment to this document.

The implementation program was developed to maximize the likelihood of successful checklist adoption based on growing appreciation that adaptive solutions, not merely technical ones, better support lasting behavior change.[16] This “Engage-Launch-Support” model is based on the understanding that successful change requires participation and involvement from several levels of leadership as well as front line staff. The engagement includes meeting with district leaders followed by clinical and administrative leaders from each facility. The program is launched with an orientation to the checklist program, which is attended by as many personnel involved in childbirth activities as possible (including physicians, nurses, auxiliary nurse midwives, ancillary staff, and administrators). Support includes ongoing coaching support of facility staff and leadership, and the identification of a local checklist coordinator who supports his/her colleagues in adopting the checklist, ensures that it is integrated it into facilities activities, and continues to champion the quality improvement efforts.

In each hub, an intervention team will be assigned, consisting of a team leader (usually a doctor) and coaches (usually nurses) who provide support for IHF facilities. Coaches will be responsible for on average 2-4 facilities in their hub, aiming for a consistent team leader and coach for each

facility. During the initial engagement or support period, a Childbirth Quality Coordinator will be identified from the facility staff with onsite responsibility for supporting checklist adoption.

Engagement: Once a facility is enrolled in the trial and randomized to the intervention arm, the team leader and coach will engage senior administrative and clinical leaders from the district and the facility to discuss their quality and safety issues and use of the Safe Childbirth Checklist to potentially reduce them. During this period, facility-based criteria and processes for referral will be identified, reviewed, and posted. Availability of essential supplies will also be reviewed.

Launch: Following engagement, the team leader and the coach will provide orientation to the Safe Childbirth Checklist and quality of care at childbirth. They will employ a pictorial flipbook designed for this purpose and a conceptual video to visually illustrate how the checklist could be integrated into care and used correctly. Both childbirth providers and facility administrative leaders will be asked to participate. The orientation is organized as best as possible to ensure that caregivers are relieved from care duties during the sessions. Whenever possible the orientation will be done with staff from two or more facilities at an offsite location. The team leader or coach will individually orient new staff members involved in childbirth that join a facility after the launch.

Support: Following the launch, regular visits by the intervention team will continue. The team leader will visit each facility regularly at increasing intervals (weekly, fortnightly and then monthly) to provide support to the coaches, Checklist Coordinator, and Administrative Leaders. The Coach will visit each facility more than once weekly for approximately three to four months. Following that period the visits will occur, based on observed uptake of the checklist, at decreasing frequency but no less than monthly. Coaching visits will continue through the first eight months after launch with an option to continue in select facilities through the end of their data collection period.

During each visit, the coaches will review progress and provide support for the birth attendants in effective checklist use. Review and support consists of a review of the birth attendant's experience in checklist use, identification of barriers, and brainstorming about potential solutions to encountered problems. By the end of the initial month of support a local champion, or Childbirth Quality Coordinator (CQC) will be identified within each facility. This person will ultimately take responsibility for ongoing evaluation of Checklist utilization and work with the team leader and coach to address any identified problems or barriers and lead efforts for the maintenance and enhancement of any systems needed to support clinical practice during and after the intervention period.

Comparison package

There will be no intervention initially in the comparison arm facilities. At the conclusion of the evaluation component, all centers will receive the intervention (checklist program) package, guided by the evidence generated through the trial.

Quality control and monitoring

A strong quality control and monitoring (QCM) component will be built in the study to ensure quality and consistency in the implementation of the intervention package. The QCM system will have two main components: progress reporting by the implementation teams and in-person monitoring visits by designated supervisors. The intervention teams will input data regarding engage, launch, and support activities at each facility which will be available for use for monitoring the implementation process and identify areas for improvements. Senior management personnel and a designated QCM officer will visit sites regularly to directly observe the quality of

implementation, validate data on implementation progress, and to feedback achievements against predefined benchmarks such as (1) Rate of checklist use (compliance), (2) Proportion of cases for which checklist was completed in all aspect (completeness), (3) Rate adequate frequency of coaching visits maintained, and (4) Training participation percentages.

4.7. Does the study involve the collection of data/specimens (including the use of existing data/specimens)?
☐No ☒Yes: If yes; indicate how, when, where and from whom specimens or data will be obtained

Data collection for Impact and Outcomes

Personnel independent of the implementation teams will collect impact and outcome data. Each team is led by a Data Team Leader and includes a group of Field based Data Assistants (FIDA) who obtain registration and follow-up data, Facility based Data Assistants (FADA) who observe births in the facilities, and Computer Assisted Telephone Interview personnel (CATI) who follow the mothers up by a phone call. Data collected by these teams will not be available to the implementation or Ariadne study team with the exception of the FADA data for implementation sites as described below.

BetterBirth register

Birth event registration (including demographic information relating to the mother and baby; and contact information for the family and the family's community health worker/accredited social health activist (ASHA), and data for in-facility survival outcomes for each mother-baby dyad will be collected from each study site. Local staff (birth attendants) will enter information in their own birth registers and referral registers as they routinely do currently (no change in existing practice), from which FIDA will subsequently extract data required for the study and enter it into a "BetterBirth register" (which is essentially a pre-printed, standardized data collection form). A BetterBirth register will be placed at all facilities recruited in the trial. The BetterBirth register will be stored at the facility and will not be taken off-site, including after conclusion of the study. Additionally, photographs may be taken of facility registers and shared with the local principal investigator to assess data quality of facility data. These photographs will be destroyed after study completion.

Birth event registration

Each facility will be serviced by FIDAs. The FIDA will be responsible for filling the BetterBirth register at the facilities and then uploading the demographic and contact data from the BetterBirth Register onto the mobile CommCare-ODK application (the CommCare-ODK application is described in further detail below). This FIDA will visit each facility at least 2-3 times a week to update the BetterBirth register and upload data. They will also be responsible for conducting home visits for follow-up (see below).

Follow-up through computer assisted telephonic interview (CATI)

Following registration, call center-based data collectors (CATI) will attempt to follow-up all mother-baby dyads between days 8 to 21 post-childbirth in order to ascertain their survival and morbidity outcomes at 7 days. Through a web interface on their computer terminal, CATIs will have access to the mother's contact details and demographic information (for verification of identity) which will have been collected by the facility health workers and entered into the database by FIDAs. CATIs will call the mother (or, in the event the mother is unavailable, the woman's husband or other immediate family member) and conduct interviews to obtain information regarding her 7-day health outcomes and those of the baby. In the event the mother

cannot be reached on her primary contact number, CATI will attempt to reach the mother on additional contact numbers that will have been collected by the facility staff (e.g., husband's and family member's numbers). If the mother cannot be reached on any of the personal contact numbers, the CATI will then attempt to call the relevant ASHA worker and request her to establish contact with the mother. ASHA is an Accredited Social Health Activist appointed by the NRHM in the village and acts as the conduit between the patient and the health system. If contact with the mother (or family member in the case of maternal death or severe distress) cannot be achieved telephonically by any means on the first attempt, the CATI will continue attempting to reach the mother by phone through the process outlined above until day 21 unless she has moved. If at this time, no contact can be made with the mother telephonically then the case will be transferred to field management for follow-up through home visit by FIDAs. If she has moved, the case can be moved earlier the FIDA to attempt to determine outcomes from remaining family members.

In the event a mother or baby was referred from a study facility to another hospital (before or after delivery) the mother-baby dyad will still be followed-up by CATI or home/facility visit.

For follow-up of mothers without telephonic contact details, initial contact will be established with the ASHA with an attempt to obtain telephone number of the mother. Besides the ASHA, the CATI will have also have access to a directory of telephone numbers of other stakeholders in the village (Anganwadi worker, Anganwadi helper and village pradhan). This directory will be developed by the FIDA, CATI, and data team leaders, and will be updated continuously through the duration of the study. These numbers will then become additional contact numbers to reach the mother between 8-21 days. Note that interviews for patient outcomes will not take place with the ASHAs or other stakeholders; these individuals will only be involved to help establish contact with the mother.

CATI will use a computer and headset, and conduct the follow-up interview using a conversation guide and standardized outcomes questions. Data will be entered simultaneously into the database using a web-based form integrated with the CommCare-ODK application. The scripts for the patient interview will be developed in consultation with a local communication specialist to best suit the local language, terminology, and cultural norms.

Mother-baby dyads that could not be tracked through the call center and in cases where the CATI was unsuccessful in completing the follow-up interview will be escalated by her to the CATI – Team Leader, who will review the case and transfer to FIDA who will facilitate a CATI remote home visit.

Follow-up by CATI Remote Home Visit

Cases referred to the FIDA for CATI remote home visit will be followed up in person by FIDAs visiting the family's house. FIDAs will have access to the mother's address which was entered into the database by them at the time of registration data collection. FIDAs will visit the mother-baby dyads at their homes. If the mother is not available, the husband or other close adult relatives (maternal mother or mother-in-law) can answer questions on maternal and infant vital status and maternal morbidity. If none are available, adult household members will be asked only about vital status of the mother and infant if not known. The FIDA confirms a mother's identity and facilitates direct communication between the mother and the CATI, who is available via telephone. The priority is for CATI to ask all outcomes and satisfaction-related questions. If the CATI remote call is successful, the CATI protocol will be followed as described above.

However, if no cellular/ telephone coverage is available, the FIDA uses a standardized script similar to one used by CATI to gather the necessary information and close the case. If the FIDA collects the data, it will be entered simultaneously into the database using the CommCare-ODK application on their Android-based phones. The scripts for the patient interview will be developed in consultation with a local communication specialist to best suit the local language, terminology, and cultural norms.

Directory of stakeholders

Prior to or during conducting home visits, the FIDA will support the development of a directory of telephone numbers of stakeholders in the visited village (Anganwadi worker, Anganwadi helper and village Pradhan). This directory will be developed by the FIDA, CATI and the team leader and will be continuously updated. The objective of developing this directory is to facilitate follow-up of subsequent mothers in that village through CATI.

Data collection for process measures

Adherence by health workers to essential practices outlined on the checklist will be assessed in selected pilot sites and in all of the 15 pairs of sites in Phase 2 of the study. Facility-based data collectors (FADA) will directly observe health workers that attend to mothers and their babies around the time of birth at the first three of the four checklist pause points (including two observations points to cover pause point 3). An estimate of 7800 deliveries will be observed at each of 4 observation points (1 at each of the first 2 checklist pause points and 2 observation points at checklist pause point 3) until approximately 60 observations at each of the 4 observation points has been done at each site per data collection period. Checklist pause point 4 will not be observed due to the uncertain nature of time and place of discharge in these facilities. FADAs will observe and record activities in the admission, labor and delivery, and postpartum wards. Data will be recorded on standardized data collection forms (paper-based) and will immediately then be entered onto a mobile application.

Data observation will also include baseline at the first five pairs of RCT study sites, then after 7-10 weeks of coaching at each of the 15 pairs of the first phase of the study, follow-up at five pairs of sites after 5-7 months of coaching, follow-up at 15 pairs of sites after approximately 11-15 months after coaching, and follow-up at 15 control sites after the implementation package is delivered to those facilities (at the conclusion of the evaluation period). The below table outlines the minimum number of observations at each data observation time frame, as well as the total minimum number of observations by the FADA overall (22,800).

Data Observation Type	**Number of Pairs**	**Number of Observations**
Baseline	5 Pairs (10 sites)	2,400 (240 observations each at 10 sites)
7-10 Weeks Post-Coaching	15 Pairs (30 Sites)	7,200 (240 observations each at 30 sites)
5-7 Months Post-Coaching	5 Pairs (10 Sites)	2,400 (240 observations each at 10 sites)
12 Months Post-Data Collection Start	15 Pairs (30 Sites)	7,200 (240 observations each at 10 sites)
7-10 Weeks Post-Coaching in control facilities	15 Sites	3,600 (240 observations each at 15 sites)
TOTAL		**22,800 Total Observations**

The rates of completion of the following practices which will be assessed in the sample of birth events which will include: maternal temperature obtained on admission, maternal blood pressure obtained on admission, partograph use, inappropriate initiation of oxytocin before delivery of the baby, appropriate hand hygiene (use of soap and water, and wearing clean gloves) by health workers at the time of delivery, skin-to-skin warming, oxytocin administration within 1 minute after birth, newborn weight and temperature obtained within 1 hour after birth, initiation of breastfeeding within 1 hour after birth, and rates of checklist utilization (See Data Collection for Process Measures: Contents of Observation Tool).

Data collection for resource availability

There is evidence to suggest that the checklist program may result in changes in the availability of material resources (i.e., supplies) within facilities. We will attempt to measure this by assessing resource availability in both intervention and comparison arms. Data collection for resource availability will be conducted by the data collection team leaders (DCTL) every three months during a regularly scheduled visit to the facility. The DCTL will check for the availability of materials including partograph, oxytocin, antibiotics, Magnesium Sulphate, gloves, soap, and water at the facility at the time of their visit. They will record the information on a standardized checklist for entry into a database.

Data collection for medication administration & presence of birth companion

We will measure the influence of the SCC program on medication usage by recording the rates of medication administration in the facilities where the births are being observed in intervention and comparison arms. Rates of administration of the following medications will be studied: oxytocin, antibiotics for mother, Magnesium Sulphate, antibiotics for baby, antiretroviral for mother and antiretroviral for baby. FADAs will be responsible for recording medication use during their observations. They will also record whether or not a birth companion was present at the facility during childbirth.

Data collection for user impressions

Health care workers (HCWs)

Data collection for health workers' satisfaction and qualitative evaluation of the checklist program will be conducted through a self-administered survey for all HCWs able to read Hindi involved in birth delivery. Additionally, a semi-structured interview will also be done to collect user impressions from a sample of IHF facility directors and also capture system changes related to implementation of the BetterBirth program.

To measure differences in safety culture, a brief survey will also be self-administered by ANMs, staff nurses and doctors conducting deliveries at baseline, after 6 months of implementation at both CHFs and IHFs, and after about 12 months of implementation at both CHFs and IHFs (near the end of outcomes data collection in the site).

Patients

Three questions aimed at understanding patient satisfaction will be asked in for all mothers-baby dyads during follow-up interviews through CATI calls or FIDA home visits (see attachment).

Data collection for birth attendant characteristics

A series of birth attendant characteristics (e.g., age, caste, education level, Safe Birth Attendant (SBA) training experience) will be collected using a standardized questionnaire (see attachment). The goal of this activity is to assess potential correlations between these characteristics and our primary and secondary outcomes at different study sites.

Birth attendants will be contacted via the telephone numbers held in the study's files. The questionnaire will be administered over the phone. If birth attendants cannot be reached via phone, data collectors will attempt to collect the information in person by visiting the birth attendants at the study facility at which they work. Documentation of informed consent for this activity is not required by the local IRB. Data collectors will verbally provide birth attendants with a general summary of the questionnaire; based on this description, birth attendants may choose to accept or decline participation. Data collected will be coded using a unique identifier and linked with study data (e.g., facility-level outcomes).

Data collection for cost effectiveness

A key piece of understanding the cost of checklist use is the time the healthcare worker spends on the checklist and checklist behaviors. There are two methods we will use to capture this information: Time motion and work-sampling observations. Time motion will tell us how much time is spent on checklist-related activities and work-sampling will provide a synopsis of how healthcare workers at the facilities distribute their time across different categories of activity. Ultimately these methods will provide an understanding of how much health worker time is saved or used up by the checklist. We will also use these observations of time along with estimates of healthcare worker wages to estimate the cost of using the checklist. We will also collect administrative cost information and survey birth attendants on their perceptions related to time and the checklist. Further explanation of the two observation methods, survey, and costs data collection is below.

Costs

Cost data collection will take place in Lucknow by the PSI team. They will work with partners, (such as GOI) as needed, to gather the information. A cost data template that will serve as an input sheet has been created for collation of cost data across the relevant entities in the Betterbirth Trial i.e. The Government of India, PSI and the Ariadne Labs team.

Timing of provision of care

Time motion observations of the healthcare worker will be completed to provide an exact measure of only checklist related activities. FADA-TLs will observe healthcare workers; FADA TLs will randomly select 2-3 healthcare workers in the delivery unit to be observed one at a time throughout their shift/day. We anticipate that observation will take place over approximately 8 days.. This data collection will take place in at least 4 intervention and at least 4 control facilities. Using a stop clock, FADA-TLS will measure the time taken on each activity and record the time on the pre-classified in a paper tool.

Similarly, the work-sampling component of the cost-effectiveness work seeks to measure how healthcare workers spend their time at the facilities. The result will be a snapshot of how health worker time during a work shift is divided between activities in which they are directly interacting with the patient (any interaction with patient, including activities such as handwashing or recordkeeping in the presence of the patient), direct patient care activities where they are not interacting with patients (e.g. meeting about a specific patient, talking with patient's family,

patient recordkeeping, etc.), work activities that do not pertain to specific patients (e.g. taking inventory, attending a general staff meeting), breaks (restroom, lunch, socializing, etc), and down-time (e.g. waiting for patients, no work tasks to do). This data collection will only take place in at least 4 intervention and at least 4 control facilities. FADA-TLs will observe 2-3 healthcare workers at one time and record their individual activities at pre-determined intervals (e.g. every 2 minutes) on a paper form.

Survey for Worker Time Use Questionnaire:
This survey will provide qualitative information on the perception of usability, and time spent or saved using the checklist by HCWs. This survey differs from the checklist utilisation survey, which is currently being administered in the BB study. This survey specifically captures HCW perception of time related to the checklist activities in relation to other clinic duties. However this is a self-administered, similar to the Checklist Utilization Survey or Safety Attitudes Survey process, and will be administered to respondents in intervention facilities only.

Quality Improvement Initiative to understand BetterBirth Trial via Informal Focus Groups and Surveys

A BetterBirth study team member from HSPH held informal focus groups at various trial hubs for BetterBirth study staff (specifically, focus groups were broken down by Coach, CATI, FIDA (field-based data collector), and FADA (facility based data collector)). Each focus group was informal in structure. The discussion was recorded and later transcribed. Verbal permission was obtained from each participant to record and ask questions, and names were never used or recorded. The discussion focused on study staff perceptions of successes, challenges, and other significant experiences regarding the BetterBirth program/trial (both to understand quality improvement from a program perspective, as well as to understand the context of the program within the study facilities).

Additionally, CATI and FIDA data collectors were given informal feedback forms to complete voluntarily. Feedback forms asked about opinions on training received during the BetterBirth program, connectivity/network issues, experience accessing patients for follow-up, and additional information on challenges faced and suggestions for improvement.

Participation in both activities was voluntary and anonymization of the respondents was maintained. It is possible that a respondent may have made a reference to a specific person at a specific facility (ex. MOIC of a certain facility), but names were never used.

This data have been collected. The data was originally collected under quality improvement/program evaluation, in order to better understand perceptions of the BetterBirth program/trial via informal focus group discussions and feedback forms with various cadres of BetterBirth study staff, and to use this information to potentially inform future adaptations of the program or alternate interventions. Presently, this information serves as institutional knowledge, but may be included in future publications.

4.8. Is there a data and safety monitoring plan (required for greater than minimal risk studies)?

☐No ☒Yes: If yes; describe the plan

Data Quality Assurance

The complexity of the data collection process, scale of data collection, and the component of following-up mother-baby dyads after 7 days add considerable challenges in maintaining data quality. We acknowledge the risks that these situations impose and have incorporated a number of quality assurance (QA) measures to reduce the likelihood of errors in data collection and management.

Mapping the data collection process, from the point that the data is recorded into the BetterBirth register to the completion of the follow-up after 7 days post-delivery, QA measures will be installed at every stage. To minimize data entry errors, built-in validation checks will be incorporated in the mobile application (for example, a data collector will not able to enter "90" as mother's age). This will also function as a consistency check for data recorded in the BetterBirth register. Additional built-in features will make it necessary for FIDAs to review each form before its final submission to the database, will time stamp critical points such as start and end time of a new record, time stamp the length of time taken to complete each record, and automatically stamp GPS coordinates of the place of submission. A process of site logging will also be introduced into the data collection process. Before a FIDA starts recording data, he/she will mark his/her attendance at the site by using the site logging module of the mobile application which will capture the GPS co-ordinates of the facility and date and time of site visit.

Similarly, the web interface for CATIs for entering follow-up data will have built-in redirection logic and algorithms to minimize user errors and will have guide text embedded into the data entry forms to guide CATIs continuously throughout the CATI process. A standardized script has been developed for the call center staff (CATIs) with the help of a local communication specialist, so as to ensure effective and meaningful communication between the CATIs and mothers/ family members/ ASHA workers.

We are focused on ensuring a minimum of 95% accuracy in data collection. Using an ROC curve, we have calculated the number of data collection units which need a DQA to be certain that our accuracy is at that level or higher. Each new employee will undergo this minimum DQA and if quality is confirmed, will then undergo ongoing monitoring.

For example, a subset of calls (approximately 20 calls with and 20 calls without a birth outcome of interest) will be evaluated by the call center manager as a quality control and monitoring procedure. A similar number of CATI calls adequate to ensure validity will be sent to the FIDA app to be checked by CATI remote home visits within 42 days of delivery for each of the cases. These will be done as soon as possible after the CATI closes the case and within 7 days. The FIDA will visit the home and pass their mobile phone with a CATI on the line to conduct the outcomes interview. When cell service is unavailable, the FIDA will conduct the outcomes interview.

Regular assessment of FADA skills (confirming they achieve 100% concordance on a sample of three observations) will be conducted. FADAs Team Leaders will also re-enter a sample of paper forms into the mobile device for comparison.

An integrated quality control and monitoring (QCM) framework will support data quality management. The overall framework will be to monitor data collection activities and control the quality of data with respect to its completeness and accuracy.

The three most critical activities involved in the data collection process, which will be monitored closely, are FIDA facility visits, follow-up after 7 days by the call center, and call center validation visits by FIDA. We will monitor the completeness and accuracy of data describing birth registration, health outcomes at discharge, and health outcomes post delivery within 7 days as described above. Double data entry will be performed on a subset of the data for benchmarking and quality control as described above.

Data safety monitoring board
A data safety monitoring board (DSMB) will be established to oversee the safety and scientific accuracy of the study. The DSMB will contain a minimum of three members external to the study team, of which:

- At least two of the members will be maternal-child health experts, preferably an obstetrician-gynecologist and a pediatrician.
- One of the members will be a senior statistician
- One of the DSMB members will be designated as the DSMB Chairperson.
- None of the members will be directly involved in the conduct of the study.

The DSMB will review the study design and protocol, including the data collection protocols and processes. It will also review outcomes data at intervals of 6 months, at the interim point at the end of phase II, and final analyses. The DSMB will advise and decide on the continuation, early stoppage, and/or final termination of the trial based on this periodic data review.

4.9. Are there any anticipated circumstances under which participants will be withdrawn from the research without their consent?
☒No ☐Yes: If yes; describe the circumstances as well any associated procedures to ensure orderly termination

5. Data/Statistical Analyses Plan

5.1. Briefly describe the plan for data analysis (including the statistical method if applicable)

Interim analysis and early stopping
The trial will be monitored by the DSMB for possible early stopping, if a large intervention effect occurs at the time of interim analysis, using a Haybittle–Peto approach.[33] Specifically, an interim Rao-Scott chi-square test will be performed after approximately 25% (45,000) of the total births are enrolled, which should occur approximately 15 months after the trial phase begins (Phase 2 data collection complete). In order to stop the study at this point in favor of the SCC program, the P-value for this Rao-Scott chi-square test must be ≤0.001. The stopping rule for this study will be used as a guideline rather than as a hard-and-fast rule. Any final decision will also consider additional endpoints such as differences in complications, process measures, birth attendant compliance to the checklist, as well as an estimate of the intervention effect adjusted for birth attendant's compliance to the checklist. If the findings of the interim analysis are in favor of stopping the trial due to beneficial effect of the SCC program on the combined measure of maternal and newborn outcomes, the research study will be stopped. For ethical reasons, the

promised implementation support for enrolled sites would continue for the originally planned duration of the trial.

Final analysis

If the study is not stopped, the final analysis will be performed when approximately 86,000 birth events have been accrued in each arm. Using the Haybittle–Peto approach, the P-value for this Rao-Scott chi-square test must be ≤0.05 for the intervention and comparison groups to be declared significantly different. The final analysis is expected to occur up to 35 months after the start of the trial phase.

Secondary analyses

Secondary analyses will use the Rao-Scott chi-square test, adjusted for matching and clustering, to compare groups with respect to selected individual health outcomes and process measures. Since these are secondary analyses, no formal stopping rules will be applied and all tests will be performed at a 5% type I error rate. The following power calculations again assume an intracluster correlation of 0.075 (being conservative here, we use the maximum ICC for newborn outcomes in the 2005 WHO Global Survey on Maternal and Perinatal Health).

The secondary maternal, fetal, and newborn health outcomes will be measured on the entire sample. For a given outcome the Rao-Scott chi-square test statistic will have greater than 80% power (with a 5% Type I error) to detect a minimum absolute difference in rates between the comparison and SCC groups of 7 per 100 if there is no effect of matching (DeffM=1) and 5 per 100 at the most conservative design effect for matching (DeffM=0.55). We note that 5 per 100 is the estimated absolute difference that can be detected without a priori knowledge of the rate in the comparison group, and is estimated assuming that the rate in the comparison group is 50 per 100 (50%); as the comparison group rate gets further from 50%, we can detect a smaller difference between the comparison and SCC groups.

Structured observation of health worker performance will be performed on a subsample of births: an estimate of 7800 births at each of three pause points (1 observation point for the first 2 pause points, 2 observation points for pause point 3) will be observed from 15 matched-pairs of facilities (30 facilities). Thus, we will sample 25% of the total facilities in the study (30 facilities) to observe processes. For a given process measure outcome at 8 weeks of coaching with an ICC=0.01 and DeffM=1 (both most conservative), which will be measured on a sample of 1,800 births (average of 60 births per facility), the Rao-Scott chi-square test statistic will have greater than 80% power (with a 5% Type I error) to detect a minimum difference in rates between the comparison and SCC groups of 8.5 per 100. We note again that 8.5 per 100 is the estimated difference that can be detected without any a priori knowledge of the rate in the comparison group, and is thus estimated assuming that the rate in the comparison group is 50 per 100 (50%); as the comparison group rate gets further from 50%, we can detect a smaller difference between the comparison and SCC groups. Further, based on the results from the SCC program pilot study in Karnataka, we expect to see much larger differences than 8.5 per 100 between the comparison and SCC groups.

We will also do an initial analysis on pre intervention observation (60 at each observation point per facility) and early post intervention (starting 8 weeks after intervention) to qualitatively explore that change is starting, before additional facilities are initiated but no statistical analysis are planned. If no change is seen, then the intervention component will be intensified as the additional 13 pairs are enrolled for the phase II.

5.2. Is there a sample size/power calculation?

☐**No** ☒**Yes: If yes; describe the calculation and the scientific rationale, and, if applicable, by site and key characteristics such as participant demographics**

Intracluster correlation

The nature of the SCC program as a health system innovation precludes its randomization at the level of individual patients and instead incorporates a cluster design (i.e., randomization at the facility, or cluster, level). Estimating intracluster correlation coefficients (ICCs) is necessarily based on extrapolations from prior studies. ICC estimates have been derived for maternal and newborn health from the 2005 WHO Global Survey on Maternal and Perinatal Health (analyzing data from more than 90,000 pregnancies and births taking place in 120 hospitals in 8 Latin American countries). [22] For maternal and newborn outcome variables in this setting, the overall median ICCs were 0.011 (interquartile range 0.007–0.037) and 0.054 (interquartile range 0.013–0.075), respectively. Measures specific to this trial's causal effect for which an ICC was estimated include neonatal death at 7 days (ICC=0.005) and maternal death (ICC=0.0003). The population studied and that in north India are not identical; clinical care delivered in Latin America may be of higher quality than that in UP; the implication is that ICCs may be lower in Latin America. For additional reference, numerous studies evaluating neonatal death in village settings in India and elsewhere in Asia use much lower ICCs, ranging from 0.0005 to 0.006. Considering these available data, and following discussion with biostatistics experts, including a reviewer at The Bill and Melinda Gates Foundation (BMGF), we therefore assume for this study the relatively conservative ICC estimate of ICC=0.01.

Cluster size and number

Clusters (i.e., facilities) of various sizes (i.e., annual birth volumes) will be enrolled in this trial. Public sector facilities to be included in the study are Primary health centers (PHCs), block PHCs, community health centers (CHCs), CHC/FRUs (First Referral Units), and District Women's Hospitals (DWHs). UP has roughly 3,660 PHCs that vary widely in volume, from fewer than 150 deliveries annually to larger, so-called "block PHCs" (BPHC), that manage an average of 1,440 deliveries annually. These constitute a first "port of call" for a population of approximately 20,000-30,000 for most routine institutional deliveries with basic obstetric care. Each CHC acts as a referral center for 4-5 adjoining PHCs (on average) and provides specialist care including obstetrics and pediatrics to a population of 80,000 to 120,000. There are roughly 386 CHCs in UP and each has on average approximately 1,800 deliveries annually including a mix of referred and new cases. We therefore assume, for the sake of sample size calculations, that the expected average cluster size is 1,440 births (which is equal to the average annual birth rate of a BPHC), though we know that a minority subset of facilities will conduct less than 1,440 deliveries/year (e.g., small PHCs) and another minority subset of facilities will conduct more than 1,440 deliveries/year (e.g., CHCs). For operational reasons, we are only including facilities with more than 1,000 births/year by their report.

Matching effect

Matching will be conducted by exact matching on specified variables when possible and within bounded ranges of those variables when exact matching is not feasible. The matching process including matching variables is further discussed in the "methodology section" below.

Baseline event rate

The primary outcome in this trial is the rate of the composite measure of maternal death within 7 days, severe maternal complications within 7 days, fresh or macerated stillbirth, and neonatal death within 7 days.[18], [23] Taken together, data available from UP (described above in "Study Population") suggest that the baseline rate of the primary outcome may be as high as 50-60/1,000 live births. Preliminary data from this study suggest that the baseline rate may actually be greater

than 100/1,000. The baseline rate used in this study will be 60/1,000; this is purposively set lower than the baseline data to (1) maintain conservatism since the preliminary data is based on a small sample and we do not want to risk under powering the study; and (2) to facilitate the possibility of demonstrating significant changes in sub-analyses (i.e., perinatal death rate).

Estimated event rate reduction

Based on knowledge of the relatively poor existing quality of healthcare services in UP, and the results of the SCC program pilot study which demonstrated marked improvement in health worker performance, we feel that achieving up to a 15% reduction in prior outcomes with the SCC program is feasible in this population and, at the same time, will enable the calculation of a practical sample size.

Statistical power

The Rao-Scott chi-square test statistic, which adjusts for the matched-pair cluster randomization scheme, will be used to compare the rates of the primary outcomes in the comparison and intervention groups. For our matched cluster randomized design, the necessary sample size per treatment group, *N*, using the Rao-Scott chi-square test statistic, can be written as a product of three terms:

$N = n \times Deff_C \times Deff_M$, where

n = sample size per treatment group for a simple random sample of independent patients5

$Deff_C$ = Design effect 'for an unmatched cluster randomized design versus a simple random sample, = 1 + (*m*-1) × *ICC, with*

m = average number of patients in a cluster (birth facility) ≈ 1440 patients

ICC = intra-cluster (birth facility) correlation coefficient ≈ .01

$Deff_M$ = Design effect 'for a matched versus unmatched cluster randomized design

In this study, with ICC=0.01, we approximate *DeffC* = 15.4, so that within-facility clustering has a significant impact. The best available estimate for *DeffM* when using our matching algorithm can be obtained from our team member's matched cluster randomized design in Mexico.[41, 47] In the Mexico study (in which 14 outcomes were measured), *DeffM* was at most 0.55 (resulting in at least a 45% reduction in the total sample size); 10 outcomes had a *DeffM* of 0.2 or smaller (giving at least an 80% reduction in the total sample size); and 7 outcomes had a *DeffM* of 0.1 or smaller.

Because our major constraint is the number of facilities that can be enrolled in the trial, and not the number of patients per facility (since we will be able to measure all patients in a facility on the main outcomes), the total number of patients per treatment group in the sample size calculation above *(N*) is mainly relevant in that it determines the required number of facilities. The total number of facilities equals 2 times the total number of patients per group divided by the expected cluster size:

Total number of clusters = 2×*N/m*

We assume that matching will have some effect but do not want to risk overestimating that effect, and will therefore incorporate the smallest matching effect in the sample size calculations The result (using an ICC=0.01 and a matching design effect of 0.55) is a trial enrolling 120 facilities (60 pairs of facilities) for a total of 171,964 births (86,000 births in each arm) that will detect a 15% reduction in the primary outcome from 60/1,000 to 51/1,000 live births with 80% power and an alpha value of 0.05. However, we will have 80% power to detect a smaller reduction in the primary outcome, if the matching effect is ultimately stronger than this conservative estimate.

6. Recruitment Methods

6.1. Does the study involve the recruitment of participants?

☐**No: If no, skip to 7.1**
☒**Yes: If yes; indicate how, when, where, and by whom participants will be recruited**

Please see Section 4.7 as well as Section 9.1 for detailed information on our recruitment.

6.2. Are there any materials that will be used to recruit participants, e.g., emails, posters, and scripts?
☒**No** ☐**Yes: If yes; provide a list of the materials (also include copies with the application)**

7. Available Resources

7.1. Describe the feasibility of recruiting the required number of participants within the recruitment period

BetterBirth sites have been selected in accordance with a minimum average delivery load of 1,000 deliveries per year and data collection period scheduled accordingly. Based on what BetterBirth has observed to date, consent refusal and lost to follow up cases have been minimal. Therefore, BetterBirth does not anticipate any challenges in recruiting the required number of participants within the recruitment period.

7.2. Describe how the Principal Investigator will ensure that a sufficient amount of time will be devoted to conducting and completing the research

The senior PI devotes 15% of his time to this project. Additionally, the BetterBirth director and co-PI is working full-time on this project.

7.3. Are there research staff members, in addition to the Principal Investigator?
☐**No:**
☒**Yes: If yes; outline training plans to ensure that research staff members are adequately informed about the protocol and study-related duties**

In Boston, about 20 individuals support BetterBirth research and have been trained on our protocol and study design.

In India, there are over 250 research staff members on the ground; all have received extensive study-related training. One module of their training is specifically devoted to understanding the BetterBirth study design; separate modules of training focus on consent processes and ethics.

7.4. Describe the minimum qualifications for each research role (e.g., RN, social worker) their experience in conducting research, and their knowledge of local study sites and culture

Those doing direct observation (FADAs and FADA TLs), as well as our program coaches, typically have a nursing background. Field-based data collectors and call-center operators generally have previous on-the-ground program implementation or research experience.

7.5. Briefly describe how the research facilities and equipment at the research site(s) support the protocol's aims, e.g., private rooms available for interviews, etc.

The study has two major areas of data collection. One is observation of essential birth practices, which takes place in the admission, labor/delivery, and discharge rooms in accordance with the design of the WHO Safe Childbirth Checklist.

Data on outcomes will be collected from the BetterBirth call center allowing the participant to answer questions about maternal and neonatal mortality and morbidity from the privacy of their home.

7.6. Are there provisions for medical and/or psychological support resources (e.g., in the event of incidental findings, research-related stress)?
☒No ☐Yes: If yes; describe the provisions and their availability

8. Vulnerable Populations

8.1. Are there any potentially vulnerable populations (e.g., children, pregnant women, human fetuses, neonates, prisoners, elderly, economically disadvantaged, employees or students of the investigator or sponsor, undocumented, terminally ill, cognitively impaired or mentally ill, etc.)?
☐No: If no, skip to 9.1
☒Yes: If yes; identify all vulnerable populations
Vulnerable populations include pregnant women and their neonates.

8.2. Describe safeguards to protect their rights and welfare
Please see Risk (section 10) and Participant Privacy (section 14) below.

9. Consent Process

9.1. Will consent to participate be obtained?
☐No: If no, skip to 9.5
☒Yes: If yes; describe the setting, role of individuals involved, timeframe(s), and steps to minimize coercion/undue influence during the consent process (at the time of initial consent and throughout the study)

The study is of a quality improvement intervention designed to improve the delivery of essential birth practices as defined by the national guidelines. The risk of the proposed data collection is minimal and so informed consent procedures are designed to reflect this low risk and to not increase risk for any participants**.**

In our BetterBirth Protocol, surrogate consent refers to consent that is given by a family member (such as the husband, mother, or mother-in-law) in the case that a woman is unable to consent for herself.

There are two situations where surrogate consent is used, namely: (1) at the time of labor and delivery for observation of care provided by birth attendant; and (2) at discharge/referral out for follow-up of the mother-infant pair. At observation, surrogate consent is taken if the woman is in advanced labor and cannot carry a conversation. At discharge or referral out, the defined scenarios in which we consider a woman unable to consent for herself include when (1) the mother has died at the facility; (2) when the woman is referred out and unable to consent for herself as she is too ill; or (3) when the woman is unable to consent for herself (i.e. unable to carry out a conversation), but not referred out.

Facility and HCW
Agreement for participation including randomization of facilities in the each district will be obtained from the District Chief Medical Officer (CMO). He will be asked to provide a letter of support and agreement for the district to participate and to endeavor to obtain essential supplies. Agreement will also be obtained from the facility Medical Officer in Charge (MOIC) for participation of the facility in the study. The staff will be oriented to the study and study procedures by the study team leader and an informational sheet shared tailored to whether the site is a control or intervention facility. (See HCW Info Sheet Intervention and Control)
In the smaller sample of birth events that will be observed for process data during delivery, birth attendants will be asked for consent for observation of their delivery activities by the observers (FADAs) in facilities where this observation activity occurs. These health care workers will be free to refuse participation and opt-out at any point without notification of the MOIC or any impact on their employment at the facility.

The FADA will use the following script (in Hindi): "We have permission from the MOIC to watch the delivery services here. Would it be OK to watch you today if your patient(s) agree to let us watch?"

A waiver of documentation of consent is being requested from birth attendants for a number of reasons:

(1) Because some of the healthcare workers may not be officially on staff, there may be a risk to them to document that they are providing healthcare in the facility. The only record linking the HCW and the research would be the consent document and the principal risk would be potential harm resulting from an expected breach of confidentiality, which would identify a birth attendant/HCW by name.

(2) Low risk of the data collection

(3) Consent here is not for any new or experimental treatment, but only data collection with minimal risk.

Mother: Observation
In the smaller sample of birth events that will be observed for process data during delivery, written informed consent will be obtained from the mother. Consent will be documented by signature or equivalent mark such as fingerprint depending on mother's ability. If a woman is unable to provide written consent for observation because she is in distress or she finds it difficult to speak because she is in advanced in her labor when she reaches the facility, consent will be obtained from her spouse or the birth companion who accompanied her to the facility. While verbal consent would be acceptable from a standard ethics perspective, based on discussions with local stakeholders, written consent is preferred by facilities directors for activities that occur in their facilities.
Participation in the study will be totally voluntary and no monetary incentives will be provided. Mothers are free to opt out of the study at entry. Participants, who consent to be a part of the study, are also free to opt out of the study at any time they wish. In case a patient opts out of the study, the care provided to the mother (and the baby), during the admission and after discharge, will not be any different from what she, and the baby, would have received as a study participant.

Surrogate consent is proposed if needed because of:

(1) Low risk of the data collection (the observers do not interact with the HCWs or patients)

(2) Consent is not for any new or experimental treatment, but only data collection with minimal risk.

Mother: Follow-up Facility health care workers will obtain and document informed verbal consent for follow-up after delivery from women who present for delivery at study facilities for childbirth in both IHF and CHF facilities or surrogate consent from a birth companion. This will occur after delivery but before discharge; a non-related witness will observe the giving of verbal consent. The information sheet in Hindi will be reviewed with them (see follow-up information sheet). Mothers who agree will receive a follow-up call to them at their identified contact information or by a home visit starting after 7 days post-delivery to inquire about the health status of the mother and the baby. Eligible respondents are described above. Verbal consent for data collection will be reconfirmed and documented at the time of the call or visit.

Obtaining verbal consent is preferred in this situation for several reasons:

(1) Low risk of the data collection

(2) Consent here is not for any new or experimental treatment, but only data collection with minimal risk.

Surrogate consent is proposed if needed because of:

(1) Low risk of the data collection

(2) Consent is not for any new or experimental treatment, but only data collection with minimal risk.

(3) Surrogate consent will only be used at the time of discharge when the woman is deceased, when the woman has been referred out of the facility and is unable to provide consent herself, or when the mother is in severe distress (i.e. unable to hold a conversation) and is unable to provide consent herself. .

(4) Consent will be re-confirmed by the mother before data collectors proceed to ask outcome questions. Consent to ask outcomes questions about the mother and her baby at the time of follow-up may be obtained by husband, mother-in-law, or other family member when the mother is deceased or in severe distress, or when the mother herself had previously provided consent at the time of discharge.

Patient satisfaction
At the end of the follow-up call or visit, the respondents will be asked three questions around the care received. Prior to these questions, the data collector will ask for verbal consent and only proceed if given. (See Patient satisfaction survey)

HCW Surveys
Health care workers will be asked to complete a survey on safety culture (IHFs and CHFs at baseline, after 6 months of implementation at both CHFs and IHFs, and after about 12 months of implementation at both CHFs and IHFs (near the end of outcomes data collection in the site)) and checklist acceptability (IHFs only at baseline, after at least 6 months following introduction, and again about 12 months after following introduction (near the end of outcomes data collection in the site)). Further, Cost-effectiveness surveys will be conducted.

HCWs who are involved in the delivery process and literate in Hindi will be given the survey. Documentation of informed consent is asked to be waived, but the HCW will still read the explanation of the study and then can choose to either complete or not complete the survey. No identifying information will be collected and the survey will be collected by the research staff or placed in a secure container for pick-up by the staff. Thus, documentation of consent would be the only identifiable information collected on the health care worker. We are requesting a waiver of documentation of consent in order to protect privacy and confidentiality of the health care worker. (See HW safety attitude survey questionnaire, Cost-effectiveness survey, and Checklist utilization survey).

Medical officers in charge (MOIC) interview
The facility leaders (MOICs) of a sample of intervention health facilities will be asked for written consent to participate in semi structured interviews to capture facility-wide system changes which may be related to the intervention.

9.2. Are there any special populations?
☒No ☐Yes: If yes; describe the process to obtain consent, permission or assent

9.3. Will consent of the participants be documented in writing?
☒Yes ☐No: If no; describe the rationale for requesting a waiver or alteration of documentation of consent (and/or parental permission)

9.4. Will participants be provided with a copy of their signed consent form or information sheet (when a consent form is not signed)?
☒Yes ☐No: If no; explain any extenuating circumstances that make it impossible or inappropriate to meet this requirement, i.e., doing so may place participants at increased risk, if inadvertently disclosed

9.5. Is a waiver or alteration of consent (and/or parental permission) being requested?
☐No ☒Yes: If yes; describe the rationale for the request. If the alteration is because of deception or incomplete disclosure, explain whether and how participants will be debriefed (include any debriefing materials with the application)

We request a waiver of consent for our Health Care Worker during FADA observations as well as for the surveys; please see 9.1 above for detailed information on our consent processes for our data collection.

10. Risks

10.1. Are there any <u>reasonably foreseeable</u> risks, discomforts, and inconveniences to participants and/or groups/communities?
☒No ☐Yes: If yes; indicate probability, magnitude, and duration of each (note that risks may be physical, psychological, social, legal, and/or economic)

The proposed study intervention poses minimal (if any) risk to study participants. The WHO SCC program involves checkpoints and guidelines consistent with international and in-country standards. Checklist use is anticipated to enable birth attendants to remember to perform, as per established guidelines, critical activities that promote safe childbirth.

10.2. Identify whether any of the information collected, if it were to be disclosed outside of the research, could <u>reasonably</u> place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability or reputation.

If information were disclosed outside of the research, to our knowledge, it would not reasonably place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability or reputation.

10.3. Outline provisions in place to minimize risk

Data collected during the study will be obtained through three sources: BetterBirth register, telephonic interview or follow-up by the FIDAs, and/ or direct observation of health care worker practice by the FADAs. Direct observation of births is a possible inconvenience to mothers undergoing childbirth. Moreover, birth attendants might not feel comfortable having external observers in the childbirth environment. These risks will be mitigated through deploying female newly trained nurses as observers, obtaining prior written informed consent from both the mothers and health workers, and obtaining approval from the facility leaders to observe the processes.

11. Benefits

11.1. Describe potential benefits of study participation (indicate if there is no direct benefit)

Subjects and patients may experience improved adherence to accepted standards for safe childbirth. Also, by implementing the Safe Childbirth Checklist, safety around the time of childbirth may be sustained in the site in which the study is performed.

11.2. Describe potential benefits of the research to the local community and/or society

The Safe Childbirth Checklist has been adopted by the Government of India; however, it is not regularly utilized. This research may help the local community and society see that the SCC is being used and may improve adherence to safe birth practices in the area. There is also potential to reduce maternal and perinatal mortality.

12. Reportable Events

12.1. Outline plans for communicating reportable events (e.g., adverse events, unanticipated problems involving risks to participants or others, breach of confidentiality)

The checklist program is a quality improvement intervention and does not subject mothers and newborns to any new clinical practice that is beyond the routine care they are expected to receive. Moreover, the intervention is based entirely on widely accepted guidelines and evidence, and in previous studies of the SCC, no safety concerns of adverse events related to checklist used were observed. Hence, significant adverse events related to the checklist implementation are unlikely. However, if an adverse event directly related to the checklist implementation occurs, the health workers at the facility will immediately notify the BetterBirth Deputy Chief of Party (Research) who will escalate the information to the Principal Investigators in India and at the Harvard Chan School. The adverse event will be notified to the data safety and monitoring board (DSMB) by the investigators.

13. Research Related Injuries (this section must be completed for any greater than minimal risk research)

13.1 Are there provisions for medical care and compensation for research-related injuries?

☒No ☐Yes: If yes; outline these provisions (Please note that although Harvard's policy is not to provide compensation for physical injuries that result from study participation, medical treatment should be available including first aid, emergency

treatment and follow-up care as needed. If the research plan deviates from this policy, provide appropriate justification.)

14. Participant Privacy

14.1. Describe provisions to protect participants' privacy (their desire to control access of others to themselves, e.g., the use of a private interview room) and to minimize any sense of intrusiveness that may be caused by study questions or procedures

Health outcomes data
Every birth event will be allotted a unique identity code (UIC), which will be a combination of a facility code, date and the serial number of the mother as listed in the facility register.

Only the BetterBirth register and follow-up database will contain identifying information such as name and contact details, and the study data will be stored in a HIPAA-compliant encrypted database (using industry standard 256-bit AES encryption) accessible only on the CEL server (in India) and shared with Dimagi and key technical members of Ariadne Labs' informatics team. Only de-identified data exports from the database will be made accessible to investigators. Under no circumstances will identifiable data be provided to investigators.
Process measures data
No identifiers will be assigned to health workers observed in the formal observation data collection part of the study (FADA data). These data collection forms will be anonymous and no identifiers (i.e., name of the health worker) will be listed on data collection forms.

A UIC for each birth event observation, similar to that generated for health outcomes will be generated for process records. The UIC in process records will be used for cross checking the consistency of the processes data with health outcome data, as a quality assurance measure. Similar to the outcome data management, the registration and study data for process measures will also be stored in a HIPAA-compliant encrypted database (using industry standard 256-bit AES encryption) accessible only on the CEL Servicer (in India) and shared with Dimagi and key technical members of Ariadne Labs' informatics team. Only de-identified data exports from the database will be made accessible to investigators for secure download from the server. Under no circumstances will identifiable data be provided to investigators. (See next section "Methods used to protect the confidentiality of data collected" for further detail.)

Health worker Surveys (safety attitude and checklist utilization)
No personal level identifying information for the health worker or medical officer in-charge will be collected on the questionnaires. All responses will be anonymous and only aggregate information will be presented. The MOIC semi-structured interviews will be coded and no identifying information or statements will be used.

15. Data Confidentiality

15.1. Will the information that is obtained be recorded in such a manner that participants can be identified, directly or through identifiers linked to the participants?
☐ **No: If no, skip to 16.1**
☒ **Yes: If yes; either state that participants will be told that their data will be public or describe provisions to maintain the confidentiality of identifiable data, e.g., use of password protections (please refer to the Harvard Research Data Security Policy (HRDSP), at http://vpr.harvard.edu/pages/harvard-research-data-security-policy, for additional information about required data security measures) [NOTE: The**

HRDSP does not always apply if data are not being stored at Harvard facilities. Please consult the HRDSP for additional information.]

See Section 14.1 for details on the provisions to maintain the confidentiality of identifiable data.

15.2. Describe i) whether data will be transmitted, and if so how; ii) how long it will be stored; and iii) plans for the data at the end of the storage period (how will it be destroyed, or will it be returned to data provider)

Data management and technology partners

Dimagi is a technology company that specializes in assisting organizations with data management. Dimagi has a long track record in supporting organizations to collect data with mobile technology and working with international development, implementation and research organizations in 20 countries. Dimagi has specific expertise using mobile technology to collect clinical trials data in low resources settings. The data management system that Dimagi will use for this project will be fully HIPAA compliant.

Dimagi Inc.'s US office is located at 585 Massachusetts Ave, Suite 3, Cambridge, MA 02139. Their primary India office is at Dimagi-India, D - 1/28 Vasant Vihar, New Delhi 110057.

Overview

Mobile phones or tablets will be used to enter data obtained from the BetterBirth register, data obtained from home visit follow-up, and process measures data. The BetterBirth register will be retained by the facility at the end of the study. The birth event registration, health outcomes and processes data will be hosted by the CEL server and shared with Dimagi on a HIPAA-compliant server and by Ariadne Labs of Harvard School of Public Health for long term storage and appropriate dissemination of data. The minimal set of registration data i.e. name, address and telephone numbers will be accessed by the CATI at a call center, using a web interface and by the FIDA during home visits when locating the patient's residence.

Any requests for outcome or process data will be routed through a partnership between CEL and the Ariadne Labs Informatics Team. No physical records will be created and only information de-identified from any patient identifiers will be provided to the Investigators. Original paper forms for process outcomes, health worker user impressions survey, checklist utilization feed back survey and notes of the interview for operational changes with medical officer in-charge will be kept in a locked file cabinet in PSI-India office at Lucknow only accessible to study staff.

The following technical specifications and processes will be used to safeguard the confidentiality of data during recoding, storage and transmission between mobile devices, CEL/Dimagi server and Investigators.

Recording and storing the data on mobile phones

Each phone or tablet will be enabled with password protection to restrict unauthorized access. Password of the specific device will be available only to the data collector to whom the device is allocated. Data stored locally will be encrypted using AES 256-Bit Symmetric Encryption and will be fully HIPAA compliant. After submission to the server all data on the mobile device will be erased except (for FIDAs) the subset of registration data required for future home visits by data collectors is retained. These data will be removed after follow up with patient is concluded.

Data transfer to servers

All data transfers between the mobile devices, CEL server, Dimagi servers, and Ariadne Labs servers will be secured and encrypted using industry standard HTTPS transmission protocol. Data transfers will be monitored by intrusion monitoring systems.

Data storage on Dimagi server

CEL will host the primary data set in India and share data with the Dimagi server, which is fully secured and compliant with the privacy provisions of US federal regulations as defined in the Health Insurance Portability and Accountability Act (HIPAA) of 1996. All data is stored encrypted at rest using AES 256-bit Symmetric Encryption. The Dimagi server is protected from intrusion at all times using Network Intrusion Detection System (NIDS), Web Application Firewall (WAF), Host Intrusion Detection System (HIDS). The infrastructure is housed in an ISO 27001 certified facility with biometric security. Data is backed up every 24 hours both on-site and off-site.

Data storage by Investigators

Investigators will only have access to process and outcome data de-identified from any patient identifiers. Key technical members of CEL and Ariadne Labs' informatics team will be designated with access to the full data sets.. Process and outcome data will be transmitted from servers to the investigators using a secure transfer system. All data transfers will be performed using encrypted industry standards such as HTTPS transmission protocol, secure FTP, or similar encrypted mechanisms. All data files will be stored on servers compliant with Harvard University's Enterprise Information Security Policies (HEISP) and The Harvard Research Data Security Policy (HRDSP) accessible only to PI-designated study staff as well as key technical personnel at Ariadne Labs.

Storage of study documents

During the trial, all physical study documents will be kept in a locked file cabinet in the PSI India office in Lucknow. The exception is consent forms, which will periodically transferred to CEL and kept in locked file cabinets at a storage site in Lucknow, India which CEL maintains. At the study's end, study documents will be stored for seven years in accordance with the regulations set out by the Harvard Institutional Review Board and the Indian Counsel of Medical Research (ICMR). The plan for storing study documents at the study's end is summarized in the table below.

Study Document	**Storage Plan**
Electronic Storage	
Resource availability (facility) survey	Scans of paper tools and the database to which these data will be entered will be maintained on a secure server at Ariadne Labs.
Health worker user impressions survey	Scans of paper tools and the database to which these data will be entered will be maintained on a secure server at Ariadne Labs.
Checklist utilization	Scans of paper tools and the database to which these data will be entered will

feedback survey	be maintained on a secure server at Ariadne Labs.
Cost effectiveness analysis tools	Scans of paper tools and the database to which these data will be entered will be maintained on a secure server at Ariadne Labs.
Medical officer in charge interview transcripts	Audio files of recorded interviews will be maintained on a secure server at Ariadne Labs.
Transcripts and notes from the medical officer in charge interview	Interview transcripts and notes will be maintained on a secure server at Ariadne Labs.
Database Storage	
FIDA SBR	The database to which these data have been entered will be maintained on a secure server at Ariadne Labs. Paper tools remain at the study sites.
Physical Storage	
Consent forms	Physical copies of all consent forms (Mother Observation and Mother Follow-Up) will be kept in locked file cabinets at a storage facility Uttar Pradesh in maintained by CEL.
FADA observation tool	Paper tools will be stored in locked file cabinets at storage facility in Uttar Pradesh. The database to which these data have been entered will be maintained on a secure server at Ariadne Labs.
Follow-up questions (outcomes and patient satisfaction)	Call recordings will be maintained on a hard drive at CEL. The database to which these data have been entered will be maintained on a secure server at Ariadne Labs.

15.3. Indicate how research team members and/or other collaborators are permitted access to information about study participants

Access to data on Dimagi server

Access to the servers is restricted only to key technical personnel at CEL, Dimagi and key technical members of Ariadne Labs' informatics team and is password protected. All interactions with the server are audited and are logged by username, date, time and location.

Access to registration information required for follow-up/home visit will be password protected. Access to monitoring and evaluation reports and progress monitoring reports will be provided to key study personnel and will be password protected. All passwords and account user IDs will be managed by CEL, Dimagi and authorized Ariadne Labs Informatics Team.

Registration tables contain patient identify information will only be accessible to a senior technician at CEL/Dimagi Inc. and will not be shared with investigators.

All requests for outcome and process data will be routed through CEL and Dimagi. Requests only from personnel authorized by the PIs will be honored. No physical records of any data requested will be generated. Any code linking patient registration information to process and outcome data will be destroyed when the trial is complete.

15.4. If future use of data, data sharing, i.e., required of NIH-funded studies using/generating large-scale human genomic data, or future open access, i.e., free availability and unrestricted use, of data is planned or likely, indicate how data will be shared/released.

N/A

16. Costs and Payments

16.1. Identify any costs that participants may incur during the study, including transportation costs, childcare, or other out-of-pocket expenses

There are no anticipated costs that participants may incur during the study.

16.2. Is there any payment or reimbursement that participants may receive during the study?

☒No ☐Yes: If yes; specify the amount, method and timing of disbursement. (Please refer to Harvard University Financial Policy on Human Subject Payments at http://policies.fad.harvard.edu/pages/human-subject-payments)

17. Multi-site Study Management

17.1. Is this a multi-site study?

☐No ☒Yes: If yes; describe plans for communication among sites regarding adverse events, interim results, protocol modifications, monitoring of data, etc.

BetterBirth holds weekly management-level meetings to inform staff across our sites regarding adverse events, interim results analysis planning (as interim results are accessible only by the Data Safety Monitoring Board), protocol modifications, monitoring of data, etc.

18. Investigational Drug/Biologic/Device

18.1. Does this study involve an Investigational Drug/Biologic/Device?

☒No: If no; skip to 19.1

☐Yes: If yes; identify and describe the drug/biologic/device (e.g., marketing status: Is there an IND/IDE, classification of a device as significant vs. non-significant risk)

18.2. Describe its administration or use

18.3. Compare the research drug/biologic/device to the local standard of care

18.4. Describe plans for receiving, storage, dispensing and return (to ensure that they will be used only for participants and only by authorized investigators)

18.5. If proven beneficial, describe anticipated availability and cost to participants post-study; plans (if applicable) to make available

19. HIPAA Privacy Protections

19.1. Are HIPAA privacy protections required? Please note that only Harvard University Health Services and Harvard School of Dental Medicine are covered entities at Harvard. Harvard is otherwise not a HIPAA covered entity. If, however, data is derived from a Covered Entity (e.g. a hospital or community health center), mark 'yes' and address the items below.

☒**No: If no; skip to 20.1**

☐**Yes: If yes; include at least one of the following:**

Describe plans for obtaining authorization to access protected health information

Provide the rationale for a waiver of authorization or limited waiver of authorization request

20. Data and Specimen Banking

20.1. Does the study include Data and Specimen Banking?

☐**No: If no; skip to 21.1**

☒**Yes: If yes; identify what will be collected and stored, and what information will be associated with the specimens**

See Section 15 on Data Confidentiality for information on data banking.

20.2. Describe where and how long the data/specimens will be stored and whether participants' permission will be obtained to use the data/specimens in other future research projects

See Section 15 on Data Confidentiality for information on data banking.

20.3. Identify who may access data/specimens and how

See Section 15 on Data Confidentiality for information on data banking.

20.4. Will specimens and/or data be sent to research collaborators outside of Harvard?

☐**No** ☒**Yes: If yes; describe the plan**

See Section 15 on Data Confidentiality for information on data banking.

20.5 Will specimens and/or data be received from collaborators outside of Harvard?

☐**No** ☒**Yes: If yes; describe the plan**

See Section 15 on Data Confidentiality for information on data banking.

21. Sharing Study Results

21.1. Is there a plan to share study results with individual participants?

☒**No** ☐**Yes: If yes; describe the plan**

21.2. Is there a plan to disseminate aggregate results to the community where the research is conducted?

☐**No** ☒**Yes: If yes; describe the plan**

Since this is a randomized controlled trial with blinded results, those results will be shared, in collaboration with the Government of Uttar Pradesh, with the community after research data collection and analysis has been completed.

22. Regulatory Compliance

22.1. Describe plan for monitoring regulatory compliance, in order to ensure proper record keeping and retention of required regulatory documents

We report updates to our regulatory documents to our five regulatory boards on a regular basis as required.