Protocol for a cluster randomised trial in Madhya Pradesh, India: Community health promotion and medical provision and impact on neonates (CHAMPION2); and support to rural India's public education system and impact on numeracy and literacy scores (STRIPES2)

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Study protocol

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Abstract

Background

Rural areas of India exhibit high neonatal mortality, and low literacy and numeracy. We assess the effect of a complex package of health interventions on neonatal survival, and the effect of out-of-school-hours teaching on children's literacy and numeracy, in rural Madhya Pradesh.

Methods/Design

This is a cluster-randomised controlled trial with villages (clusters) receiving either a health (CHAMPION2) or education (STRIPES2) intervention. Building on the design of the earlier CHAMPION/STRIPES trial villages receiving the health intervention are controls for the education intervention, and vice versa.Clusters 196 villages in Satna district, Madhya Pradesh, India: each at least five kilometres from a Community Health Centre, a population below 2,500, and at least 15 children eligible for the education intervention. Participants CHAMPION2 - resident married women under 50 without a family planning operation, provided they are enumerated pre-randomisation, or marry a man enumerated pre-randomisation. STRIPES2 - resident children born 16June 2010-15June 2013, not in school before the 2018-2019 school year and intending to enrol in first grade in 2018-2019 or 2019-2020.

Administrative Information

Note: the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/).

Title {1}	Protocol for a cluster randomised trial in Madhya Pradesh, India: Community health promotion and medical provision and impact on neonates (CHAMPION2); and support to rural India's public education system and impact on numeracy and literacy scores (STRIPES2)
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Role of sponsor {5c}	The research manager of Effective Intervention has participated in the study design and writing of the protocol

Introduction

Background and rationale {6a}

CHAMPION 2

It is estimated that 2.6 million neonatal deaths occur annually, of which 24% (640, 000) are in India [1]. In 2015, the major determinants of neonatal deaths in India were prematurity and low birth weight (44%), birth asphyxia and birth trauma (19%), and neonatal infections (19%) [2].

Despite India's rapid economic growth, there has been little progress in improving neonatal survival [2]. According to Sample Registration System Statistical Report 2017, India's neonatal mortality rate (NMR) is 23 per 1000 live births [3]. Estimates vary widely between the different states i.e. NMR is 5 per 1000 live births in Kerala and 33 per 1000 live births in Madhya Pradesh [3]. There are large disparities in health, with NMRs 50% higher in rural areas compared to urban areas (14 and 27 in urban and rural respectively) [3]. The state of Madhya Pradesh is characterised by a marginalised, tribal population, where less than 30% of mothers in rural villages have four or more antenatal care visits and the proportion of illiterate women is about 50% [4]. Within the state, NMR fluctuates between 24 per 1000 live births in Indore district, and 57 per 1000 live births in Satna district [5].

India, like other South Asian countries, has national programmes aimed at improving maternal and newborn health. In 2005, India's National Rural Health Mission (NRHM, now a component of National Health Mission) launched *Janani Suraksha Yojana* (JSY), a major safe motherhood intervention to reduce maternal and neonatal mortality [6]. JSY is a conditional cash transfer scheme targeting poor pregnant women who deliver in health facilities and receive postnatal care [6].

The JSY is responsible for increasing the proportion of deliveries occurring in health facilities from 26% in 2005 to 81% in 2015 in Madhya Pradesh [4, 6]. Despite the above initiative, there has not been a corresponding reduction in neonatal mortality Madhya Pradesh [7]. There is also evidence suggesting that the quality of care in some facilities is substandard [7, 8].

Another key element of the NRHM is the Accredited Social Health Activist (ASHA). The ASHA acts as an effective link between the government and community by facilitating pregnant women in accessing antenatal care, delivery in health facility, postnatal care, and other available health services. The ASHA receives performance-based incentives for her various services including referral and escort services for pregnant women under NRHM [6,9]. ASHAs have also been trained to provide home-based neonatal care through postnatal home visits and providing health education through community mobilisation [9]. Evaluations have shown that the NRHM has had a positive impact on increasing attendance at antenatal care and institutional deliveries, and on immunisation rates [8].

Scaling up community programs worldwide to improve neonatal health has the potential for reducing neonatal mortality by 24% [10]. Community support, community mobilisation, home visits by trained community health workers, and strengthening referral systems are the most effective community-based interventions [10]. Evidence based research has also prompted the World Health Organisation (WHO) and UNICEF's Every Newborn Action Plan to recommend these approaches [11].

Over the past 15 years, there have been several trials aiming to improve maternal and newborn health through home visits; some of these trials took place in India [12–14]. A study in Uttar Pradesh, India, found an intervention that included home visits and community meetings led to improved care practices and neonatal survival [13]. Another study evaluated the effectiveness of scaling-up India's Integrated Management of Neonatal and Childhood Illness (IMNCI) strategy that included postnatal home visits and treating sick neonates in accordance to pre-defined guidelines. Findings suggested that IMNCI strategy has the potential of reducing neonatal mortality by 12% when brought to scale [14].

Community mobilisation is the other main approach to community health, in particular, community mobilisation through participatory learning and action (PLA) [15]. PLA includes women's groups operated by women identifying problems relevant to their own health needs, coming with culturally acceptable solutions, and implementing these solutions [15]. A meta-analysis and systematic review testing the impact of community mobilisation using PLA with women's groups that also included five studies from South Asia, suggested this to be a highly effective and low-cost intervention in reducing neonatal and maternal mortality [15]. A recent cluster randomised controlled trial (cRCT) demonstrated that ASHAs can reduce neonatal mortality using the PLA approach with women's groups [16]. The Indian government has now mandated ASHAs to deliver PLA through women's groups in 18 separate states in India, beginning with Odisha and Jharkhand [17].

The original CHAMPION trial randomised 464 villages in Telangana, India. Villages were randomised to an intervention aimed at reducing neonatal mortality or to a control arm offering the usual ongoing health services. The health intervention included a package comprising community health promotion (i.e. health education through village health worker-led participatory discussion groups), outreach (i.e. mobile teams providing antenatal and postnatal care in the home or through fixed day health services), and provision of facility-based care (i.e. subsidised access to non-public health centres) [18]. The primary outcome of neonatal mortality was significantly lower in the intervention arm compared to the control arm (52 neonatal deaths per 1000 live births vs. 69 per 1000 live births), a reduction of 24% (Relative Risk 0.76; 95% CI 0.64 to 0.90; p = 0.0018). The authors concluded that the CHAMPION intervention was strongly justified in this setting, but the trial needed adaptation and further development for evaluation in other areas [18].

The objective of the CHAMPION2 trial is to assess whether an adapted intervention is also able to improve the neonatal survival, albeit in a different region of India. The original study design will be further developed using lessons learned from the original CHAMPION trial, as well as relevant evidence generated since the conception of the original trial. The CHAMPION2 trial will also be contextualised to socio-cultural patterns and behaviours relating to neonatal and maternal health in Madhya Pradesh, India.

STRIPES2

India has made steady progress in improving rates of primary school enrolment. In rural areas, about 97% of children between 6 and 14 years are now in school [19]. The levels of learning achievement, however, remain low. The 2018 Annual Status of Education Report (ASER) survey shows that proficiency in reading and mathematics is worryingly low and Indian children may spend several years in school without learning even the basic skills in language and maths [19].

Several strategies have been proposed to address the low quality of education, but many of these approaches fail to improve children's learning as they tend to exclusively address the provision of facilities, materials and access to school rather than improve the child's experience in the learning process [20–25].

Few studies have systematically measured the impact of supplementary teaching on learning outcomes. Evidence from Chile and India agree that providing extra teaching with tutors hired from the local community successfully raise the scores of low-performing children [26–28]. A three-month tutoring program targeting fourth grade low-performing students in Chile significantly increased pupils' reading skills [28].(29) In India, a program that provided remedial classes for third and fourth grade pupils in public schools of Mumbai and Vadodara increased the overall test scores of language and maths by 0.28 SD in the second year of the programme [26]. Another study in Uttar Pradesh, India showed positive impact on children's reading skills who had a high attendance in reading camps lead by community volunteers [25].

In Telangana, the STRIPES trial intervention that included children attending public primary schools, demonstrated important results in improving maths and language scores [27]. This trial evaluated the effectiveness of an intervention that provided 18 months supplementary, remedial teaching and learning materials (and an additional 'kit' of materials for girls). The primary outcome was a composite of language and mathematics test scores. These scores were significantly higher in the intervention group (107 villages; 2364 children) than in the control group (106 villages; 2014 children) at the end of the trial (mean difference on a percentage scale 15.8; 95% CI 13.1 to 18.6; p = 0.001; 0.75 Standard Deviation (SD) difference). Composite test scores were not significantly different in the 54 villages (614 girls) with the additional kits for girls compared to the 53 villages (636 girls) without these kits at the end of the trial (mean difference on a percentage scale 0.5; 95% CI –4.34 to 5.4; p = 0.84). The STRIPES trial provided strong evidence that supplementary, implemented in remote rural areas, has a strong impact in improving math and language skills. Given the little evidence found in previous trials, it would be beneficial to adapt and further develop the STRIPES trial to determine whether the study findings are generalizable to different settings.

Taking into consideration the above evidence, the primary aim of STRIPES2 is to assess whether an intervention adapted from Pratham's current model of working with early grades has a similar effect on the literacy and numeracy of primary school-aged children in Madhya Pradesh, using a design developed from the STRIPES trial.

Objectives {7}

Our main research question is whether the success of the CHAMPION and STRIPES trial interventions can be further generalised, after appropriate adaptations and developments, in Madhya Pradesh. This new cluster-randomised trial therefore combines the further developed versions of the previous CHAMPION (addressing neonatal survival) and STRIPES (addressing learning levels among primary-school-age children) interventions. Participants in the control arm of the health intervention will receive the education intervention, whereas participants in the control arm of the education intervention will receive the health intervention.

This protocol has been written taking into account the SPIRIT guidelines [29].

Trial design {8}

This study is a cluster-randomised controlled trial with villages receiving either a health (CHAMPION2) or education (STRIPES2) intervention.

Methods: Participants, Interventions, And Outcomes

Study setting {9}

The trial will take place in Satna district, Madhya Pradesh, with a population of 2.23 million, of which 79% live in a rural setting with a predominantly agrarian economy [30, 31].

In terms of education, between 2006 and 2018, Madhya Pradesh has experienced an increase in school enrolment rates [19]. In rural villages, 96% of children between 6 and 14, and 94% between 11 and 14 years old were enrolled in school in 2018 [19]. However, the achievement in basic reading was very low with only about 18% of children in grade three being able to read a short story (7–10 sentences) in the local language [19].

In terms of neonatal health, Satna has one of the highest NMR in Madhya Pradesh, with higher NMR in rural areas compared to urban areas (61 per 1000 live births in rural areas, and 43 per 1000 live births in urban areas) [5]. Satna is also the second worst performing district in terms of neonatal, infant and child mortality in Madhya Pradesh [4], which is the state with the highest NMR in India [3].

The Government delivers healthcare through Sub-Centres, Primary Health Centres (PHCs), Community Health Centres (CHCs) and Civil Hospitals (CH), and one District Hospital (DH), which has a Special Newborn Care Unit (SNCU).

In Satna district, only 23.1% of the pregnant women had four or more antenatal care visits, 85.8% receive tetanus toxoid vaccination, 17.1% consume iron folic acid (IFA) for 100 days or more, 7.6% received full antenatal care (i.e. at least four or more antenatal care visits, at least one Tetanus Toxoid injection, and IFA for 100 days or more) [4]. Overall in the district 80% of deliveries occur in health facilities [4]. Approximately 56.2% of mothers received a postnatal check-up within 48 hours of delivery [4]. Satna district has an ambulance system (the *108* and *Janani Surakhsa Express (JE)),* responsible for

transporting pregnant women and babies with serious health complications to the district hospital [32]. Whereas JE was considered relatively accessible to even the most marginalised populations, anecdotal evidence suggests that in practice there may be long delays, especially in areas that are difficult to access [32, 33]. Recently these two systems have been merged, and a single transport system (108) addresses all kinds of medical needs, not just pregnancy and newborn. Hence, transport may not always be speedily available.

Emergency obstetric care (EmOC) is a package of medical interventions required to treat seven obstetric complications [34, 35]. The medical interventions included in this package include parenteral antibiotics, oxytocic drugs and anticonvulsants, manual removal of placenta, removal of retained products, and assisted vaginal deliveries [35]. Evidence suggests that birth attendants in JSY facilities in Madhya Pradesh are often not able to perform EmOC adequately [6, 36]. These findings may help to explain why there has not been a corresponding improvement in neonatal survival despite increased rates of facility-based deliveries.

Eligibility criteria {10}

The trial will be conducted in Satna district, Madhya Pradesh, India. Satna district is further divided into 10 *tehsils* (sub-districts). Three *tehsils* (Birsinghpur, Majhgawan and Raghurajnagar) were excluded due to difficult access (forest area); violent robbery; and urban sub-district. The remaining seven *tehsils* potentially eligible for the trial comprise 1263 villages (68% of all villages in Satna), with a population of 1,441,930 [30].

In these seven *tehsils,* villages were included if they:

- Were considered rural, with less than 2,500 population and with more than 120 children under the age of 6 [30] (villages where we did not find at least 15 children eligible for STRIPES2 were excluded after enumeration);
- Were accessible by road;
- Were not within a 5 kilometres radius of the Community Health Centres (as such villages are already well served by the local health services);
- Had a minimum of 3 kilometres between the centres of the villages (to avoid ‘contamination’, though even with that buffer we may have some contamination as villages are very spread out).

From July 2017 to January 2018, we conducted a baseline enumeration to enlist the eligible women and children.

For CHAMPION2, a woman was eligible if during enumeration she satisfied all the following criteria:

- She is married;
- Neither she nor her husband have had a family planning operation (i.e. tubectomy or vasectomy);
- She is less than 50 years old;

- She is resident of one of the trial villages at the time of the baseline survey;
- She gives her consent after getting a complete explanation of the study.

In addition, a woman was considered eligible if she married a man who was enumerated and unmarried at the time of enumeration, resident of the village, and aged between 13 and 50 years.

If an eligible woman died, her widowed husband was added to the list of unmarried men. If this widowed man married again then his wife was considered as eligible.

The woman had to fulfil the usual criteria for eligibility including she was less than 50 years old, resident of the village, gave her consent, and neither she nor her husband have had a family planning operation.

Women (and their babies) who moved to a trial village for other reasons (e.g. their mother's residence for delivery of their baby), were not included in the study, and will not have access to the antenatal and postnatal care provided by the intervention team (unless they were enumerated in another CHAMPION2 intervention village).

For the primary trial analysis, we will start counting births and deaths 12 months after the randomisation. This lag in measurement is necessary to ensure adequate exposure to the intervention taking into account both the time interval between conception and birth, and the fact that training and establishment of services in intervention villages will take around six months.

For STRIPES2, a child was considered eligible if:

- S/he was born between 16th June 2010 and 15th June 2013a;
- S/he is not yet enrolled in primary school;
- S/he is expected to be resident in the village and be enrolled in school for the first time, in the first grade in the academic year of 2018–2019;
- Her/his parents agree that s/he participates after hearing the explanation about the programme and its evaluation tests.

For STRIPES2, only children enumerated during the baseline and present for the test will be considered in the final analysis. Children who move into the trial villages will not be included after the enumeration.

Women and the parents of the children enumerated were informed that they may withdraw from the trial at any time.

Catch-up enumeration: Before randomization of villages, from April-June 2019, we conducted a catch-up enumeration in all the selected villages to enlist the eligible women and children who were missed during baseline enumeration and to update the marital status of previously enlisted unmarried men. If a man who was unmarried during baseline enumeration was discovered to have since married, then his name was removed from the unmarried men list and his wife was considered as eligible.

For STRIPES2, a child was considered eligible at the catch-up enumeration if:

- S/he was born between 16th June 2010 and 15th June 20133;
- S/he was enrolled in grade 1 in primary school in the 2018–19 school year or was planning to enter grade 1 in 2019–20;
- S/he is expected to be resident in the village in 2019–2020;
- Her/his parents agree that s/he participates after hearing the explanation about the programme and its evaluation tests.

Knowledge, Attitudes, and Practices (KAP) survey: Before randomization of villages, from November 2018-January 2019, we conducted a KAP survey on women who had delivered a live baby within two years of the interview, in 50 randomly selected villages. We assessed health service utilisation, beneficial and harmful behaviours, and knowledge. This KAP survey will guide the need and topics of further formative research for CHAMPION2 intervention.

Who will take informed consent? {26a}

All women and the main responsible for children who have been enumerated were informed about the trial and gave their consent to participate. During the trial, all women who are eligible to participate will be informed and asked to give a consent.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Participants may withdraw their consent at any time during the trial.

No biological specimen will be collected during the trial.

Women and caregivers will be free to accept or not any interview during the trial.

Interventions

Intervention description {11a}

CHAMPION2

Formative research (quantitative and/or qualitative) may be carried out to help identify key areas (e.g. knowledge, attitudes, behaviour, care, etc) in need of improvement through interviews and focus groups with local women, healthcare providers and village elders.

The intervention in the CHAMPION2 trial will build on the knowledge acquired in the original CHAMPION trial as well as evidence published since the inception of the original trial. The intervention will work with the existing healthcare infrastructure and government services including *Anganwadis,* NICE Nurse Midwives (NMW) and ASHAs who will be tracking women and their babies in the antenatal period, at birth

and in the postnatal period. New services aimed at improving health knowledge and increasing the uptake of services will be created using ASHAs, VHWs (recruited as part of the intervention when required as described below), and midwives. These community health workers will endeavour to ensure uniformity in quality of care across services in the intervention arm.

A survey on the services and related infrastructure of the health facilities was conducted according to the Indian Public Health Standards (IPHS) [37]. Based on this survey, NICE may facilitate modest improvements to services provided at some CHCs. A small percentage of high risk or emergency cases will be referred to tertiary level care.

The place of delivery will be discussed during birth planning sessions and the intervention team will direct pregnant women to plan for deliveries at designated CHCs, CHs or other hospitals. However, the final choice of where they wish to deliver will be with the family. Transportation to health facilities is currently provided by the government (108 ambulance). If government transport services are not available, the intervention team may arrange alternative transport for urgent cases.

The intervention will include the following key elements:

Health promotion

A health awareness campaign will be launched in the different communities to promote knowledge relating to maternal and neonatal health.

Examples of the different promotional strategies include focus groups and *Nukkad Natak's* (Village level Street Plays). These will be adapted based on local customs to convey important messages to communities. There will also be discussion groups surrounding any concerns the communities have regarding the intervention. All members of the community, and not just women eligible for the trial, will be the focus of these campaigns.

Community mobilisation with women's groups

Community mobilisation with women's groups used in previous trials will be adapted to suit the context of the local population [15]. All the women of the village, not just the women eligible for the trial, will be allowed to participate. The ASHA (VHW) with PLA teams will lead the groups for sessions involving issues related to maternal and newborn health. Discussions about the risk factors in pregnancy, delivery, and the postnatal period will be facilitated, and solutions will be derived to tackle these issues. The objective of these meetings is to improve mothers' health knowledge, encourage greater use of fixed day service (see below), promote safe delivery, encourage delivery of high-risk pregnancies at an appropriate health centre, and to provide women a forum to discuss solutions to important issues in maternal and newborn health.

Fixed day services (FDS) provided by ASHAs, VHWs, and NICE nurse midwives

Approximately every two weeks, teams of two midwives will visit the intervention villages offering a package of antenatal and postnatal care, and other services relating to the mother and her newborn baby. The midwives will offer these services after the women's group session, assisted by an ASHA (VHW) based in the village. If a woman is unable to attend the services, the midwives and ASHA (VHW) will visit her at home. These services will be given only to pregnant women identified by NICE who have been enumerated and confirmed to be eligible for the trial.

Examples of the different components of antenatal care include the following: checking for anaemia (haemoglobin levels), weight, monitoring for pre-eclampsia (blood pressure, protein in urine), monitoring for infections and gestational diabetes. Examples of services provided in the delivery period include the following: promotion of a clean delivery and other essential newborn care practices, assisting a delivery where access to a health facility is not possible. Postnatal services can include the following: advice on breastfeeding (i.e. the importance of colostrum, initiating breastfeeding within an hour of delivery, exclusive breastfeeding for six months), care of the newborn (appropriate thermal care), and how to recognise danger signs in mothers and newborns.

To access these services, pregnant women will receive the NICE ANC card for tracking immunisations, participation in health groups, hospitalisations, and regular check-ups (antenatal, postnatal and newborn). The midwives will keep a record of visits to the village, women seen, emergency deliveries assisted, and cases referred. The ASHAs (VHWs) and midwives will also keep a detailed record of all their cases and meet regularly to share information regarding their work and problems encountered.

Referrals

ASHAs (VHWs), and midwives will be responsible for facilitating and monitoring the referrals of mothers and newborns to the nearest CHC or CH that has adequate human resources, equipment, medicines and disposables available.

ASHA (Community health workers)

At the community level, ASHAs will have a critical role in delivering the intervention. A Village Health Worker (VHW) may be appointed by the trial when the ASHA is: not consistently available, not resident in the village, working in both intervention and control villages, not supporting the trial, or not performing well. The trial team will recruit VHWs from the local community based on their literacy, communication proficiency, previous knowledge and experience in pregnancy and childbirth (usually she will be from the same village, educated until at least the 5^{th} class, married, previously given birth, and recommended by the community).

The ASHAs (VHWs) will receive a combination of theoretical and practical training by midwives and doctors, on the following topics: monitoring pregnancies, identification of risk factors in both the expectant woman and the newborn, clean delivery practices, appropriate thermal care, breast feeding, appropriate care-seeking, arranging the logistics of referrals in case of emergencies, trust-building, and case management.

NICE Nurse Midwife

Nurse Midwife (NMW) employed by NICE will provide the antenatal and postnatal care services after the women's group discussions. They will also offer guidance to supervise ASHAs (VHWs). Midwives may conduct emergency deliveries if they occur during their visits to the villages, and monitor referrals to health facilities. In case of complications, the NMW will be responsible for referring the mother or neonate in distress to the next level of care. Midwives will be trained by doctors to deliver clear information related to pregnancy, childbirth and neonatal care, and the use of communication tools to address deeply rooted superstitions and practices that may have negative impacts on the health of both mother and neonate.

Community Consultant

Conflicts have arisen in previous community trials with women who are not eligible to receive the intervention, unfavourable pregnancy outcomes, expectation mismatch. To help resolve these issues, a consultant who is an expert in handling conflicts in community trials will facilitate discussions to resolve these disputes. The consultant will also train and support ASHAs (VHWs) and supervisors in conducting community level activities of interpersonal communication and support them on the basic principles for interacting effectively with the communities.

STRIPES2

The education intervention comprises of before/after school teaching lessons for two hours, typically six days a week given by a "Pratham Instructor" (PI). Each PI will be trained and paid to conduct teaching learning activities in Hindi for a group of up to about 30 eligible children in the village. Thus, for the period of about 17 months the same cohort of children would receive the intervention. Pratham Cluster Leaders (CLs) will support, coordinate, and monitor PIs work.

The initial two-three weeks will be a warm up phase. During this period, the PIs will carry out a series of activities to enable children to interact comfortably with the instructors such as playing, singing, colouring, and drawing. Thereafter, activities will be conducted to help PIs understand what children can do easily and what they are struggling with. After this period, the PI will commence providing the instructional classes. The subject matter covered in these sessions will reinforce the curriculum covered in school and will develop literacy and numeracy skills of children in pace with their cognitive abilities.

Pratham has seen promising results when efforts are made to engage with mothers of young children, to demonstrate and orient them on activities that they can do with their children at home. [38]. PIs will thus have frequent contact with mothers through door-to-door meetings, community events and creation of

mothers' groups. Mothers will be oriented to engage in activities with their children to promote their attendance and learning.

The activities in communities will thus build on Pratham's past experience; not only building a strong foundation, but also trying to create a sustainable learning environment that supports children's development.

Material kits

Pratham will develop material kits to be used during the before/after school activities and at home. The material for the classes will include the instructor's manual, as well as teaching learning material such as story-books, activity booklets and more. In addition, Pratham teams will orient mothers on use of the home materials. Orientations may be done in groups for easy comprehension of mothers or one by one. Videos may also be shown for this purpose

Outcomes {12}

CHAMPION2

Primary outcome: neonatal mortality [39]

Secondary outcomes will include: maternal mortality [39]; stillbirths and perinatal deaths [39]; causes of death [39]; antenatal care; delivery care; immediate newborn care; postnatal care; health knowledge; hospital admissions of enrolled women during pregnancy or afterwards, or their babies (during neonatal period); maternal blood transfusions; cost effectiveness of intervention.

STRIPES2

Primary outcome: composite literacy and numeracy test score using Early Grade Reading Assessment (EGRA) and Early Grade Mathematics Assessment (EGMA), respectively [41–43].

Secondary outcomes include: separate scores for literacy and numeracy; parents' engagement on child's learning; enrolment in school; parent's report of school attendance; cost effectiveness of the intervention

Participant timeline {13}

Duration

Randomisation was done in June 2019. STRIPES2 will run for about 17 months and CHAMPION2 will run for three and half years.

Timeline

December 2015Protocol submitted to the L V PRASAD EYE Institute (LVPEI) and London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committees

January to October 2016Permits sought and obtained from the Departments of Health and Education in Madhya Pradesh (Mission Director from the National Health Mission, Director of the Child Health for Madhya Pradesh, Additional Mission and Director of the Education Department)

February 2017Resubmission of protocol and short report to LVPEI and LSHTM Ethics Committees and MP government

March to May 2017Village consent, village mapping and piloting of enumeration forms

June 2017Training for enumeration

July 2017 to January 2018Enumeration of the participants and data entry

September 2018 to April 2019ICMR application and approval

April to June 2019 Catch-up enumeration

19 June 2019Randomisation

June to December 2019 Intervention design, village sensitisation and trainings

October 2019STRIPES2 intervention starts

December 2019CHAMPION2 intervention starts

19 June 2020Neonatal and maternal survival start to count to final analysis

August 2020First survey of children's enrolment and attendance in school

February 2021Second survey of children's enrolment and attendance in school

March/April 2021Final numeracy and literacy tests for children (STRIPES2)

November 2021Statistical analysis of STRIPES2 completed

December 2022Final data collection for CHAMPION2

May 2023Statistical analysis of CHAMPION2 completed

Sample size {14}

The process by which clusters (villages) were selected is described in the following section entitled Recruitment. Following the use of the first three criteria to identify clusters (steps 1 to 3), there are 484 villages that are potentially eligible for the trial. Originally it had been the intention to randomise 300

villages, because this gave over 90% statistical power to detect i) a 20% reduction in neonatal mortality in CHAMPION2 and ii) a difference of 0.25 standard deviations in mean standardised test scores in STRIPES2. However, incorporating the buffer zones described in the village selection procedure above meant that only 204 villages could be selected. These 204 villages have a mean population of 1487 (minimum 558, maximum 2490) and a standard deviation of 505 (equating to a coefficient of variation of 0.34). Estimating the number of children in each school year from the number under the age of six (divided by 6), the mean number of children in each school year is 38.3 (minimum 20, maximum 71) with a standard deviation of 13.3 (a coefficient of variation of 0.35). Assuming that 25% of the children will not satisfy the eligibility criteria this gives an estimated mean number of eligible children per village of 28.7 with a minimum of 15.

In CHAMPION the design effect for neonatal mortality was 1.306, equating to an intra-cluster correlation coefficient (ICC) of 0.011 (with allowance for variability in cluster size, assumed coefficient of variation = 0.34). For CHAMPION2, allowing for the fact that each village has an average population of 1487 and estimated crude birth rate of 30.7 per 1000 population per year in rural areas of Satna district [3], 114 births per village over a thirty-month follow-up period are expected. Assuming i) an ICC of 0.011 for the primary outcome, ii) an assumed coefficient of variation for village size variability of 0.34, iii) that 5% of villages will be excluded for reasons such as withholding consent and iv) that there will be 10% loss to follow-up, a trial with 194 villages (95% of 204) has 75% power (5% 2-sided significance) to detect a 20% reduction in neonatal mortality from 6.7% to 5.36% and 91% power (5% 2-sided significance) to detect a 25% reduction in neonatal mortality from 6.7% to 5.0%. Since the reduction in neonatal mortality seen in CHAMPION was 25%, proceeding with 204 villages seems reasonable given the requirement for buffer zones in order to avoid contamination.

We estimated that the 204 villages will include an average of 28.7 eligible students (5,740 students in total). In the STRIPES trial the estimated effect was a 0.75 SD increase in mean score: however, effects of smaller magnitude than this would still be important to detect. Conservatively assuming that 60% of the eligible children (4,860 students) will take the test at the end of the trial and an intra-cluster correlation coefficient of 0.23 (as seen in the STRIPES trial) then a trial with 194 villages (i.e. assuming that 5% of the 204 villages will not take part) will give 88% power to detect a difference of 0.25 SD in mean standardised scores between intervention and control villages using a conventional 2-sided significance level of 5% (assuming a coefficient of variation in numbers taking the test by village of 0.35). If the treatment effect is of the order of that seen in the STRIPES trial then there will be reasonable statistical power to explore interactions by ethnicity, gender, wealth and geographic location.

As described above, in the sample size calculation we anticipated that 194 of the 204 villages would be randomised. In fact, 196 were randomised with six being removed since they were found to be too close to urban areas to be considered rural, and two removed because insufficient eligible children were found.

Recruitment {15}

Following discussion with the *Sarpanch* (the head of a *Panchayat* which is a group of villages), all eligible children and women were enumerated in all villages in which we got village consent. These villages were selected from all villages in Satna district that satisfy the criteria of eligibility.

Cluster identification

The pathway to select villages (clusters) was the following:

- From the census 2011 data we selected Satna district;
- The tehsils of Birsinghpur, Majhgawan and Raghurajnagar were excluded (difficult access, violent robbery and urban sub-district);
- Villages with a population larger than 2500 and fewer than 120 children under the age of 6 (suggesting fewer than 20 children in each school year) were excluded;
- Villages within five km of a CHC or CH were excluded;
- Using a program developed in the statistical package Stata, villages were selected using an algorithm that attempts to maximise both i) the total number of villages selected and ii) the population of selected villages, whilst ensuring that there is a distance of at least three kilometres between the centre of each pair of selected villages (buffer zones to reduce contamination).
- During the enumeration period, we will identify the eligible children, women and men in each selected village;
- If a selected village cannot be included (if, for example, consent is refused or there are insufficient eligible children) then this village should be dropped from the selected list and can be replaced by one or more substitute villages not originally selected, provided that there is a distance of at least three kilometres between each pair of selected villages.

Randomisation

Randomisation was done at the village (cluster) level with stratification by village size and distance to the nearest Community Health Centre (CHC) or Civil Hospital (CH).

Control groups

CHAMPION2 control villages will receive the STRIPES2 intervention as well as the usual health services provided by the government, private, and other Non-Governmental Organisations (NGOs). STRIPES2 control villages will receive the CHAMPION2 intervention as well as the usual education services provided by the government and other NGOs.

It is anticipated that the CHAMPION2 intervention will have negligible impact on children's learning scores, and the STRIPES2 intervention will have negligible impact on neonatal mortality. The fact that

these interventions are being carried out may improve the extent and quality of the data collected in the control villages. The relevant interventions will be expanded into the controls if proven to be successful.

Randomisation flowchart

The process from village selection to inclusion in final analysis is shown in Figure 1.

Assignment of interventions

Sequence generation {16a}

The trial statistician based in London carried out the randomisation of clusters using a random number generator. Randomisation was stratified by population size, and distance to the nearest CHC or CH.

Assignment of interventions: Blinding

Who will be blinded {17a}

Due to the nature of the interventions, it will not be possible to have a blinded study. Participants will be aware as to whether they are in the CHAMPION2 or STRIPES2 intervention or control. Nevertheless, the teams who will be assessing the children and all doctors who will be assigning a cause of death using the World Health Organisation's verbal autopsy toolkit [44] will be blinded to whether a child/woman belongs to a control or intervention cluster.

Data collection and management

Plans for assessment and collection of outcomes {18a}

An independent research team based in Satna will manage the enumeration, monitoring, surveys and tests. Except for the list of eligible participants in the trial, no further data will be shared by the research team during the trial. A set of procedures will be established to recruit, train and monitor the research staff, preserving the segregation from the intervention group.

It will be possible to locate enumerated participants including women, unmarried men, children and parent, by assigning an ID number that is a combination of the village identifier, and household identifier.

For CHAMPION2, during enumeration, women were interviewed about their previous obstetric and pregnancy-related history. Neonatal deaths were assessed for the year before enumeration through recall based on a truncated pregnancy history. Once the intervention starts, participating women will be continuously monitored. Unmarried men will also be enumerated and monitored to determine if they get married. If an unmarried man gets married, his wife becomes resident of the village, and gives consent to participate in the trial, then she will be followed-up in cycles of 30–33 days.

Research teams will visit all the trial villages in a cycle of 30–33 days to register new pregnancies, follow-up those already recorded, interview for pregnancy outcomes and follow-up the newborn status until the baby is aged 29 days. Research teams will also monitor enumerated unmarried men to determine if they have recently been married. If a woman is recorded to be pregnant and leaves the village, the research team should attempt to ascertain her pregnancy outcome from her as part of the cycle of household visits, or by calling her over the phone or interviewing her family (if she does not come back to the village)

Cases of death (neonates up to and including the 28^{th} day of life, women who died pregnant or within 42 days after the delivery) will be investigated to ascertain the possible cause of death using verbal autopsies developed by WHO and adapted for local understanding. Stillbirths will be defined as the death of a fetus from the 28^{th} week of gestation and before birth [45]. To ascertain the weeks of gestation we will use the Last Menstrual Period (LMP) recorded when research teams first become aware that a woman is pregnant. Two doctors, blinded to allocation, will independently assign the cause of death. In case of disagreement on one main cause of death, a third doctor will be recruited to resolve the disagreement.

In STRIPES2, a follow-up survey will be conducted two times during the trial to update the status (residence, school enrolment, and attendance) of those children enlisted. In one of these surveys, we will also record information to generate a wealth index.

Literacy and numeracy tests will be administered by the end of the intervention to all children enumerated who are available in the village on the test day. Both the tests will be designed to measure a student's foundation skills in literacy and numeracy in the early grades.

Data management {19}

All data related to pregnancies, births, deaths, children's school enrolment, parent's engagement in child's education and the final EGRA and EGMA (literacy and numeracy) tests will be double-entered in the main office of the research team in Satna. The database has been developed by Sealed Envelope (https://www.sealedenvelope.com), an independent company contracted to construct and maintain a bespoke database for the trial, who will also keep a periodical backup of the data. Paper forms will be stored there in a secure location and destroyed after the statutory period expires.

Confidentiality {27}

All data will be kept strictly confidential—names will be removed from the database before analysis and the paper data collection instruments will be kept in a secure location in Satna, Madhya Pradesh, and destroyed after the statutory period expires.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Prior to commencing statistical analysis, a detailed statistical analysis plan will be written by the trial statistician. This will be considered by the trial Steering and Data Monitoring Committees and signed off by the Principal Investigator before statistical analysis is carried out.

CHAMPION2

Analysis of outcomes will follow the intention to treat principle. As this trial has a complex hierarchical structure, with multiple women per cluster, potentially multiple pregnancies per women, and potentially multiple births per pregnancy, we will use a generalised estimating equations (GEE) analysis approach [46]. This assumes non-independence of all observations from the same cluster, and accounts for non-independence of multiple outcomes from the same woman.

For the primary outcome, the relative risk with a 95% confidence interval will be obtained from a GEE model with a binary outcome, a log link, a 'working' assumption of independence with robust standard errors to take account of clustering. The model will include the stratifying variables [47, 48]. The risk difference and hence the estimated number of lives saved will be estimated using a similar model, but with an identity rather than a log link.

For secondary binary outcomes, relative risks will be estimated using the same approach as for the primary outcome.

STRIPES2

The primary analysis will also follow the intention to treat principle. Mean child-specific composite test scores at the end of the final academic year will be compared using analysis of covariance regression models with adjustment for stratification factors and with robust standard errors to allow for clustering by village. Bootstrap confidence intervals will be reported for non-normally distributed continuous outcomes. Intervention-gender interactions will be tested.

ECONOMICS

We will measure the cost effectiveness from the provider point of view. Project cost will be collected prospectively and converted to economic cost. Cost data will be adjusted for inflation, using the Indian consumer price index and reported in Indian Rupees and US dollars equivalent period. Incremental cost effectiveness will be measured relative to the status quo alternative as defined by outcomes in the control arms.

Methods for additional analysis {20b}

For both CHAMPION2 and STRIPES2 secondary analyses will extend the models described above for the respective primary outcomes to (separately) investigate interactions by the two stratification factors (village size and distance to the nearest Community Health Centre or Civil Hospital).

Methods in analysis to handle protocol non-adherence and missing data {20c}

For both CHAMPION2 and STRIPES2 a per-protocol analysis will be carried out. This will exclude participants in the respective intervention arms deemed not to have satisfied adherence criteria that will be pre-specified in the statistical analysis plan.

In the event of substantial missing data, secondary analysis using techniques such as multiple imputation will be considered, with details pre-specified in a supplementary statistical analysis plan.

Interim analyses {21b}

CHAMPION2 interim analyses will be pre-specified and provided confidentially by the trial statisticians to an independent Data Monitoring Committee (DMC), which will be guided by the Peto-Haybittle rule [49]. The DMC will report to the Trial Steering Committee (TSC).

As in STRIPES2 there are no concerns about the safety of the intervention, and there is only one assessment of the primary efficacy outcome, there will be no such interim analysis for STRIPES2.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

Trial Management Group

The trial will have independent implementation and research teams. A Trial Steering Committee (TSC), with independent membership (an obstetrician, a paediatrician and an education researcher) will supervise the trial.

Implementation team

The team in charge of implementing and managing the CHAMPION2 intervention will be composed of:

- The Programme Officer (PO) who will oversee the implementation of the whole programme assisted by junior program officers (JPOs);
- ASHAs (VHWs) who will be responsible for the following: mobilising the community for FDS, facilitating the community mobilisation with women's groups, monitoring pregnant women, imparting health education, helping to conduct home deliveries in emergency situations, and facilitating referrals.
- Nurse midwives who will provide services in the FDS, supervise the ASHAs (VHWs) conduct deliveries if needed, and give logistical support in the villages.
- Field Monitors who will supervise ASHAs (VHWs), facilitate FDS, and monitor referrals to health facilities.

- Consultants in maternal and newborn health, community mobilisation and support, and liaison who will: monitor patient care logistics and outcomes, build capacity of the team in community sensitisation and support in resolving community level issues.
- A team lead by JPO will be conducting and managing the Participatory Learning and Action (PLA).

The STRIPES2intervention team will consist of:

- National and state team members who will provide ongoing guidance and support to the program.
- A Programme Head (PH) who will liaison with the local government officers, and with internal state, and central teams. S/he will oversee the teams' operations on the ground and be responsible for implementation of the education intervention.
- Two Content Associates who will provide content support to the teams. They will work with members from Pratham's central content team to design/develop teaching and learning materials for the intervention.
- A Monitoring, Measurement and Evaluation Associate who will be responsible for training teams on and analysing internal measurements.
- Cluster leaders (CLs)—each CL will be responsible for about 10 villages. They will provide training and supervision to the Pratham instructors, while also facilitating engagement with the community.
- Pratham instructors (PIs) who will lead the classes, monitor every child's learning progress, liaise with mothers.

The research team responsible for enumerating all the participants, monitoring pregnant women and newborns, conducting the tests and collecting the data that will be used to evaluate the impact of the interventions is composed of:

- One Project Coordinator who will be responsible for leading the research teams (health and education), organising trainings, liaising with other Coordinators and Database team
- Survey Enumerators who will visit households and conduct interviews during enumeration and for the annual survey (STRIPES2).
- Village Enumerators (VE) who will be monitoring whether the enumerated women are alive, pregnant and present in the village during the 30–33-days cycle (CHAMPION2).
- Data Supervisors (DS) who will lead the field research teams, supervise and facilitate the work of all enumerators. They will: verify the completed forms and conduct quality checks to validate them; monitor newborns; complete pregnancy outcome questionnaires, verbal autopsies and interviews to enrol women married into the trial villages.
- Training Coordinator who will organise induction and teams' monthly meetings; liaise the Database Manager and field teams for data related issues.
- Data Supervisors for Verbal Autopsies (DSVA) are the ones responsible for conducting the verbal autopsy interviews (MVA and NVA)

- Cluster Coordinators (CC) who will coordinate the work of the data supervisors; lead meetings; organise the distribution of forms; and engage in community interaction along with supervisors.
- One Field Manager who will be in charge of the monitoring cycle data (CHAMPION2). S/he will: select the field staff, organise the forms distribution, verify the quality and validate the data collected.
- A Database Manager who will be responsible for coordinating the data entry operators; correcting double entry inconsistencies; coordinate the printing and distribution of forms; liaise with the Database programmer in London; manage the database and assure its integrity.
- Data Entry Operators who will do the double entry of all the data.
- Doctors who will attribute the cause of death in maternal and neonatal verbal autopsies.
- Test Administrators who will conduct the final tests for STRIPES' evaluation.

Composition of the data monitoring committee (DMC), its role and reporting structure {21a}

The CHAMPION2 DMC includes a statistician and a clinician, both independent of the trial and the sponsor. The primary role of the DMC is to safeguard the interests of the study participants and to enhance the integrity and credibility of the trial. The DMC will report to the Trial Steering Committee (TSC).

Adverse event reporting and harms {22}

Information will be collected about harms - Serious Adverse Events (SAEs). An SAE is formally defined as any untoward occurrence that results in death; is life-threatening; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; or is a congenital anomaly/birth defect [40]

For this trial, SAEs are defined as deaths (stillbirths, neonatal and maternal), maternal blood transfusions, hospital admissions other than for labour, and prolongation of existing hospitalisation (beyond 48 hours). Information about persistent or significant disability/incapacity or congenital anomaly/birth defect will not be collected due to the difficulty of ascertaining this in routine data collection in this trial but, if a child dies, information about birth defects will be collected within the verbal autopsy process. Information about SAEs will be collected as part of routine outcome data collection in the villages by the research team.

In addition, if any other serious but unexpected adverse event is seen which might be related to a trial intervention, this should be logged by calling the trial coordinator (TC) and a written SAE report submitted. The TC will coordinate the reporting of all such events within 7 days to the L V PRASAD EYE Institute and London School of Hygiene and Tropical Medicine Ethics Committees. This expedited reporting will be limited to those outcomes not already listed as primary or secondary outcomes, yet which might reasonably occur as a consequence of the trial intervention.

Dissemination plans {31a}

We will attempt to disseminate the results of the trial in international, National, State and District level conferences, and to villages participating in the trial, and publish the findings in peer-reviewed journals following the CONSORT guidance for cluster RCTs [51]. All publications must be approved by the Trial Steering Committee.

Trial Status

MP trial protocol Version X 18th November 2019.

Recruitment of participants started on 1st of June 2017 and will continue till approximately December 2021 for eligible women (CHAMPION2). For STRIPES2, no more children will be added to the list of participants.

Randomisation was done in June 2019. The trial interventions are scheduled to start from October-December 2019.

Abbreviations

ANC - antenatal care

ASCs - academic support classes

ASER - Annual Status of Education Report

ASHA - Accredited Social Health Activist

CH - Civil Hospital

CHC - Community Health Centre

CL - Cluster Leader

CRA—Cooperative Reflective Approach

cRCT—Cluster Randomised Trial

CE - Community Educator

DMC- Data Monitoring Committee

EDD - Expected Delivery Date

EGRA - Early Grade Reading Assessment

EGMA - Early Grade Mathematics Assessment

EI - Effective Intervention

EmOC - Emergency Obstetric Care

FDS - Fixed Day Services

GCP - Good Clinical Practice

GEE - generalised estimating equations

ICC - intra-cluster correlation coefficient

ICH - International Conference on Harmonisation

ICMR - Indian Medical Council of Research

IMNCI - India’s Integrated Management of Childhood Illness

IPHS - Indian Public Health Standards

JE - Janani Surakhsa Express

KAP—Knowledge Attitudes Practice

LMP - last menstrual period

LSHTM - London School of Hygiene and Tropical Medicine

LVPEI - L V PRASAD EYE Institute

NCERT - National Council Educational Research and Training

NGO - Non-Governmental Organisation

NMR - Neonatal Mortality Rate

NMW—Nurse Midwife

PI - Pratham Instructor

PLA - Participatory Learning and Action

PNC - postnatal care

SCERT - State Council Educational Research and Training

SNCU - Special Newborn Care Unit

TSC- Trial Steering Committee

VHW - Village Health Worker

Definitions

Early neonatal deaths: deaths of newborns within seven days of delivery (i.e. 0–7 days) [39].

Emergency Obstetric Care (EmOC): a package of medical interventions required to treat seven obstetric complications [34]. The medical interventions include parenteral antibiotics, oxytocic drugs and anticonvulsants, manual removal of placenta, removal of retained products, and assisted vaginal deliveries [35].

Late neonatal deaths: neonatal deaths occurred between the 8th and 29th day of life [39].

Maternal death: defined by the World Health Organisation as death of a women while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes [39].

Maternal mortality ratio: the ratio of maternal deaths per 100000 live births [52].

Neonatal mortality rate: the number of deaths of a newborn infant during the first 28 completed days of life per 1000 live births [39].

Perinatal deaths: Refers to pregnancy loss at or beyond 28 weeks gestation and early neonatal dates within 7 days of delivery [39].

Perinatal mortality rate: the number of perinatal deaths per 1000 total births in a given year. The perinatal period starts at the beginning of fetal viability (28 weeks of gestation) and ends at end of the 7th completed day after delivery. Perinatal deaths are the sum of stillbirths plus early neonatal deaths [42].

Sarpanch: an elected head of a village-level statutory institution of local self-government called the panchayat (village government) in India, Pakistan and Bangladesh. The Sarpanch is the focal point of contact between government officers and the village community.

Stillbirth: refers to pregnancy loss at or beyond 28 weeks' gestation without any signs of life [42].

Declarations

Acknowledgements

We would like to acknowledge the work of A. Jaipal Reddy designing the research activities. All the teams of supervisors and enumerators who arduously mapped and registered women and children. The data entry team who processed all the paper forms. Sealed Envelope team: Tony Brady and Piotr Gawron for designing the database. Jitendra Ahirwar for helping develop the content and Nikhil Swaminathan for helping develop the internal measurement systems and processes for STRIPES2. All NICE team for their contribution to the programme's design and implementation plan.

Authors' contributions {31b}

All authors contributed extensively to the design of the study, and have contributed to, commented on and approved the final manuscript. In addition, CF and DE prepared the statistical analysis plan. The package of interventions for CHAMPION2 was designed by PR, RN, MG and the NICE Foundation team. The STRIPES2 intervention was designed by RB, AA, DS, SS, and the Pratham Education Foundation team. SK and HR provided field and data support for designing the research component. PB designed the economic analysis. IF prepared the first version of the protocol. SiS revised the protocol.

Funding {4}

Effective Intervention NGO

Effective Intervention, Centre for Economic Performance, London School of Economics, UK. Email: admin@effint.org

Availability of data and materials {29}

Data sharing is not applicable to this article (a protocol) as no datasets will be generated or analysed during this stage of the study. After publication of the initial results, the anonymised datasets used and/or analysed during the trial with relevant statistical code will be available from the corresponding author on reasonable request.

Ethics approval and consent to participate {24}

Ethics committees of L V PRASAD Eye Institute, Hyderabad, India (LEC 02–16–008) and London School of Hygiene and Tropical Medicine (LSHTM Ethics Ref: 10482) have approved the trial protocol. We have obtained the necessary approvals from Indian Council of Medical Research, New Delhi and Government of Madhya Pradesh to conduct this trial in Satna district. The trial complies with the Declaration of Helsinki, local laws, and the International Conference on Harmonisation Good Clinical Practice (ICH-GCP). Any protocol modifications will be communicated to both the Ethics Committees, and consent will be re-obtained at the village and individual (woman or parents) level at that point if deemed necessary.

For this trial, we received approval from the Indian Medical Council of Research (ICMR), New Delhi, India. At the state level, approval of the protocol was obtained from the Department of Health & Family Welfare of the government of Madhya Pradesh.

This trial employs multiple tiers of consent: village, individual, and individual on behalf of the child. Agreement to approach eligible villages was first obtained from the Sarpanch. In the trial villages, consent was obtained from the village after the trial has been presented in a meeting with village elders representing all the castes and village residents. Consent was given in oral form during a village meeting with written documentation (or thumbprint) of the approval given by the Sarpanch. This process of obtaining consent through meetings with approval of the 'guardians' of the clusters is common in trials in which the intervention is delivered at the level of a cluster and it is not possible to obtain informed consent for randomisation from individuals within the cluster before a baseline survey.

Once the trial was accepted at the village meeting, the villages were considered eligible for baseline enumeration. During the process of baseline interview, each head of household, each potentially eligible women and one parent or care-giver of each potentially eligible child was informed in the local language (Hindi) about the trial and their participation and asked for a signature or thumbprint to indicate their consent to join the trial. Only people who agree to participate were enumerated. Women and parents of enumerated children have the right to withdraw consent at any time during the trial. This process of consent is compatible with current standards for Cluster Randomised Trials [50].

Consent for publication {32}

Participants (household heads, women and caregivers on behalf of children) were informed that we would revisit the households to interview them about pregnancies, babies and children's school enrolment so we could understand to the impact of CHAMPION2 and STRIPES2 programmes. All participants agreed that all individual information collected during interviews will be used only for research purposes and in ways that will not reveal their identity.

Competing interests {28}

PB is the Executive Chair of EI; IF is a paid employee of EI but has no competing interests. DE and CF received research grants funding from EI but have no competing interests. SS is employed in these research grants but have no competing interests. SK and HR receive research funding from EI but have no competing interests. PR, RN and MG declare a potential competing interest due to the involvement of the NICE Foundation (an independent organization) which is involved in programs intervening with women and children in rural and urban Telangana (previously AP) and Rajasthan. RB, AA, DS and SS declare a potential competing interest due to the involvement of Pratham Education Foundation (an independent organization) which currently works with programmes to improve the quality of education in India.

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References

1. UN Inter-agency Group for Child Mortality Estimation Levels and trends in child mortality: Report 2015. New York: UNICEF; 2015.
2. Liu L, Chu Y, Oza S, Hogan D, Perin J, Bassani DG, et al. National, regional, and state-level all-cause and cause-specific under-5 mortality in India in 2000–15: a systematic analysis with implications for the Sustainable Development Goals. Lancet Glob Heal 2019;7:e721–34.
3. Office of the Registrar General & Census Commissioner, India. Sample Registration System Statistical Report 2017. New Delhi: Ministry of Home Affairs, Government of India; 2017. http://www.censusindia.gov.in/vital_statistics/SRS_Statistical_Report.html. Accessed 1 October 2019.
4. International Institute for Population Sciences (IIPS) and ICF. 2017. National Family Health Survey (NFHS-4), India, 2015-16: Madhya Pradesh. Mumbai: IIPS.
5. Office of the Registrar General & Census Commissioner, India. Annual Health Survey 2012-13 Fact Sheet Madhya Pradesh. New Delhi: Ministry of Home Affairs, Government of India; 2013.
6. Government of India, Ministry of Health and Family Welfare, Maternal Health Division, New Delhi. Janani Suraksha Yojana. 2019. https://nhm.gov.in/index1.php?lang=1&level=3&sublinkid=841&lid=309. Accessed 1 October 2019.
7. Sabde Y, Diwan V, Randive B, Chaturvedi S, Sidney K, Salazar M, et al. The availability of emergency obstetric care in the context of the JSY cash transfer programme in Madhya Pradesh, India. BMC

Pregnancy and Childbirth. 2016;16(1):1-13.

8. Lim SS, Dandona L, Hoisington JA, James SL, Hogan MC, Gakidou E. India's Janani Suraksha Yojana, a conditional cash transfer programme to increase births in health facilities: an impact evaluation. Lancet. 2010;375(9730):2009-23.
9. Government of India, Ministry of Health and Family Welfare. About Accredited Social Health Activist (ASHA. 2019. http://164.100.154.238/communitisation/asha/about-asha.html. Accessed 1 October 2019.
10. Lassi ZS, Bhutta SA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. Cochrane Database Syst Rev. 2015(3):CD007754.
11. World Health Organization. Every newborn : an action plan to end preventable deaths. World Health Organization; 2014. 53 p.
12. Bang AT, Reddy HM, Deshmukh MD, Baitule SB, Bang RA.. Neonatal and infant mortality in the ten years (1993 to 2003) of the Gadchiroli field trial: Effect of home-based neonatal care. J Perinatol. 2005;25(SUPPL. 1):S92-S107.
13. Kumar V, Mohanty S, Kumar A, Misra RP, Santosham M. Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial. Lancet. 2008;372(9644):1151–62.
14. Bhandari N, Mazumder S, Taneja S, Sommerfelt H, Strand TA. Effect of implementation of Integrated Management of Neonatal and Childhood Illness (IMNCI) programme on neonatal and infant mortality: cluster randomised controlled trial. BMJ. 2012;344:e1634.
15. Prost A, Colbourn T, Seward N, Azad K, Coomarasamy A, Copas A, et al. Women's groups practising participatory learning and action to improve maternal and newborn health in low-resource settings: a systematic review and meta-analysis. Lancet. 2013;381(9879):1736-46.
16. Tripathy P, Nair N, Sinha R, Rath S, Gope RK, Rath S, et al. Effect of participatory women's groups facilitated by Accredited Social Health Activists on birth outcomes in rural eastern India: a cluster-randomised controlled trial. Lancet Glob Heal.4(2):e119-e28.
17. Government of India, Ministry of Health and Family Welfare. Participatory Learning and Action (PLA) Module for ASHA Facilitator/ASHA. http://nhsrcindia.org/sites/default/files/PLA%20Module%20for%20ASHA_English.pdf . Accessed 1 October 2019.
18. Boone P, Mann V, Eble A, Mendiratta T, Mukherjee R, Figueiredo R, et al. Community health and medical provision: impact on neonates (the CHAMPION trial). BMC Pediatr. 2007;7(26).
19. Annual Status of Education Report (Rural) 2018. New Delhi: ASER Centre; 2019. http://img.asercentre.org/docs/ASER%202018/Release%20Material/aserreport2018.pdf. Accessed 1 October 2019.
20. McEwan PJ. Improving Learning in Primary Schools of Developing Countries. Rev Educ Res. 2015;85(3):353-94.

21. Evans DK, Popova A. What Really Works to Improve Learning in Developing Countries? An Analysis of Divergent Findings in Systematic Reviews. World Bank Res Obs. 2016;31(2):242-70.
22. Masino S, Niño-Zarazúa M. What works to improve the quality of student learning in developing countries? Int J Educ Dev. 2016;48:53-65.
23. Ganimian AJ, Murnane RJ. Improving Educational Outcomes in Developing Countries: Lessons from Rigorous Evaluations. Working Paper 20284 National Bureau of Economic Research. 2014.
24. Glewwe P, Muralidharan K. Improving Education Outcomes in Developing Countries. In: Machin S, Woessmann L, Hanushek EA, editors. Handbook of the Economics of Education.Elsevier; 2016. P. 653–743.
25. Banerjee AV, Banerjee R, Duflo E, Glennerster R, Khemani S. Pitfalls of participatory programs: evidence from a randomised evaluation in eduation in India. Am Econ J Econ Policy.2010;2(1):1-30.
26. Banerjee AV, Cole S, Duflo E, Linden L. Remedying Education: Evidence from two Randomized Experiments in India. Q J Econ. 2007;122(3):1235-64.
27. Lakshminarayana R, Eble A, Bhakta P, Frost C, Boone P, Elbourne D, et al. The Support to Rural India's Public Education System (STRIPES) Trial: A Cluster Randomised Controlled Trial of Supplementary Teaching, Learning Material and Material Support. PLoS One. 2013;8(7):e65775.
28. Cabezas V, Cuesta J, Gallego F. Effects of short-term tutoring on cognitive and non-cognitive skills: Evidence from a randomized evaluation in Chile. Unpublished manuscript, Pontificia Universidad Católica de Chile, Santiago. 2011.
29. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586.
30. Census of India Website: Office of the Registrar General & Census Commissioner, India [Internet]. http://www.censusindia.gov.in/2011census/c-01.html . Accessed 1 October 2019.
31. Ministry of Micro, Small and Medium Enterprises, Government of India. Industrial Profile of Madhya Pradesh 2014-15. Indore: MSME-Development Institute; 2015.
32. Sidney K, Ryan K, Diwan V, De Costa A. Utilization of a State Run Public Private Emergency Transportation Service Exclusively for Childbirth: The Janani (Maternal) Express Program in Madhya Pradesh, India. PLoS ONE. 2014;9(5):e96287.
33. Sabde Y, De Costa A, Diwan V. A spatial analysis to study access to emergency obstetric transport services under the public private "Janani Express Yojana" program in two districts of Madhya Pradesh, India. Reprod Health. 2014;11:57.
34. World Health Organization, UNFPA, UNICEF, AMDD. Monitoring Emergency Obstetric Care: a Handbook. France: World Health Organization, UNFPA, UNICEF and AMDD; 2009. 161 p. UNICEF W, UNFPA. Guidelines for Monitoring the Availability and Use of Obstetric Services. 1997.
35. Paxton A, Maine D, Freedman L, Fry D, Lobis S. The evidence for emergency obstetric care. Int J Gynaecol Obstet. 2005;88(2):181-93.

36. Chaturvedi S, Upadhyay S, De Costa A. Competence of birth attendants at providing emergency obstetric care under India's JSY conditional cash transfer program for institutional delivery: an assessment using case vignettes in Madhya Pradesh province. BMC Pregnancy Childbirth. 2014;14(1):174.
37. Directorate General of Health Services Ministry of Health & Family Welfare Government of India. Indian Public Health Standards (IPHS): Guidelines for Community Health Centres Revised 2012. http://164.100.154.238/images/pdf/guidelines/iphs/iphs-revised-guidlines-2012/community-health-centres.pdf. Accessed 1 October 2019.
38. Banerji R, Berry J, Shotland M. The Impact of Maternal Literacy and Participation Programs: Evidence from a Randomized Evaluation in India. Am Econ J Appl Econ. 2017;9(4): 303–37.
39. World Health Organisation. International Classification of Diseases, Tenth Revision (ICD-10). Geneva: World Health Organisation, 2007.
40. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceutical for Human Use: ICH Harmonised Guideline. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). 11 June 2015
41. Dubeck M GA. The early grade reading assessment (EGRA): its theoretical foundation, purpose, and limitations. International Journal of Educational Development. 2015. https://www.sciencedirect.com/science/article/pii/S0738059314001126?via%3Dihub Accessed 8 November 2019.
42. Reubens A. Early grade mathematics assessment: A conceptual framework based on mathematics skills development in children. RTI International, Research Triangle Park, NC 27709-2194, Tech. Rep.2009. https://pdf.usaid.gov/pdf_docs/Pnads439.pdf Accessed 8 November 2019.
43. Platas L K-GL, Sitabkhan Y,. Using an assessment of early methematical knowledge and skills to inform policy and practice: examples from the early grade mathematics assesment. International Journal of Education in Mathematics, Science and Technology. 2016;4(3)(163-173). https://files.eric.ed.gov/fulltext/EJ1102189.pdf Accessed 8 November 2019.
44. World Health Organisation 2017. Verbal autopsy standards: the 2016 WHO verbal autopsy instrument https://www.who.int/healthinfo/statistics/verbalautopsystandards/en/ Accessed 1 October 2019.
45. Lawn J BH, Waiswa P. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet. 2016;387(10018):587-603.
46. Liang K, Zeger S. Longitudinal data analysis using generalized linear models. Biometrika. 1986;73(1):13-22.
47. Sackett DL, Deeks JJ, Altman DG. Down with odds ratios! Evidence-Based Med. 1996;1:164–6.
48. Lee Y, Nelder JA. Conditional and Marginal Models: Another View. Stat Sci. 2004;19(2):219–38.
49. Peto R, Pike M, Armitage P, Breslow N, Cox D, Howard S, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. Br J Cancer. 1977;35(1):1-39.

50. Weijer C, Grimshaw JM, Eccles MP, McRae AD, White A, Brehaut JC, et al. The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials. PLoS Med. 2012;9(11):e1001346.
51. Campbell MK, Piaggio G, Elbourne DR, Altman DG, CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. BMJ. 2012;345: e5661.
52. World Health Organization, UNICEF, United Nations Fund for Population Activities, World Bank, United Nations. Department of Economic and Social Affairs. Population Division. Trends in maternal mortality, 1990 to 2013: estimates by WHO, UNICEF, UNFPA, the World Bank estimates, and the United Nations Population Division. 2014.56 p.

Figures

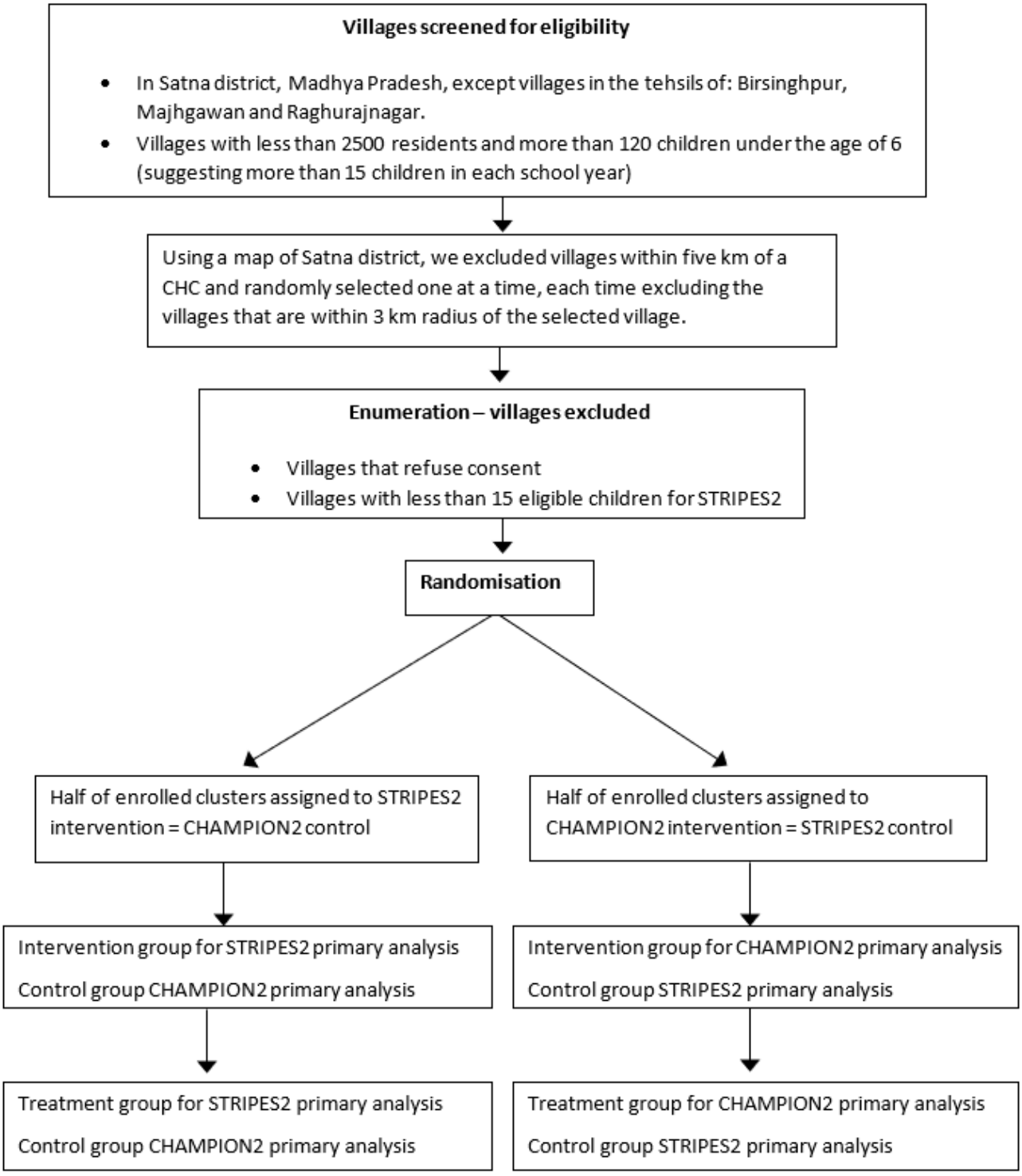

Figure 1

Flowchart of villages through trial

Supplementary Files

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