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TITLE

Interventions to increase immunisation coverage among children 12-23 months of age in India through participatory learning and community mobilisation: pilot study for a cluster randomised trial

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ABSTRACT (300 words)

Objective: With the aim of conducting a future cluster randomised trial to assess intervention impact on child vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

Trial Design: Cluster-randomised design with a 1:1 allocation ratio

Methods: Clusters were 12 villages in rural Uttar Pradesh. All women residing in a selected village who were mothers of a child 0 to 23 months of age were eligible; participants were chosen at random. Over 4 months, intervention group (IG) villages received: (1) home visits by volunteers; (2) community mobilisation events to promote immunisation. Control group (CG) villages received community mobilisation to promote nutrition. A toll-free number for immunisation was offered to all IG and CG village residents. Primary outcomes were ex-ante criteria for feasibility of the main study related to processes for recruitment and randomisation (50% of villages would agree to participate and accept randomisation; 30 women could be recruited in 70% of villages) and retention of participants (50% of women retained from baseline to end line). Clusters were assigned to IG or CG using a computer-generated randomisation schedule. Neither participants nor those delivering interventions were blinded, but those assessing outcomes were blinded to group assignment.

Results: All villages contacted agreed to participate and accepted randomisation. Thirty six women were recruited per village; 432 participants were randomised (IG *n*=216; CG *n*=216). No clusters were lost to follow up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

Conclusions: Criteria related to feasibility were satisfied, giving us confidence that we can successfully conduct a larger cluster randomised trial. Methodological lessons will inform design of the main study.

Trial Registration: None

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ARTICLE SUMMARY

Strengths and limitations of this study

- This feasibility study for a cluster randomised trial of participatory, community-based interventions to improve child vaccination coverage closely replicated the methods of the planned main study, and enabled us to conclude with confidence that we could successfully carry out the main study.
- Field experience enabled us to identify key potential barriers to success of the larger trial and to develop strategies to address them in the main study.
- This pilot study also considered a range of secondary outcomes using appropriate statistical methods, including cluster- and individual-level proxy endpoints indicative of intervention effectiveness.
- Analyses revealed an important positive effect of interventions on several proxy endpoints; however, the relationship of proxy to final endpoints is unknown, multiple proxy endpoints were considered, and results were not fully consistent. The number of study clusters was small.
- A definitive judgment concerning intervention impact on child vaccine coverage must await the larger study.

INTRODUCTION

Background

Immunisation has been instrumental in global progress towards the UN Millennium Development Goal to reduce under-5 mortality (MDG 4).[1] The potential for future impact is even greater: partly due to highly effective new vaccines offering protection against some forms of diarrhoea and pneumonia, the World Health Organization and UNICEF estimate that 29% of deaths among children 1 to 59 months are now vaccine-preventable.[2]

To realise their potential, antigens must reach all children; yet, one in five children worldwide still does not have access to basic vaccines.[3 4] In May 2012, the World Health Assembly approved the Global Vaccine Action Plan (GVAP) to ensure that the full benefits of vaccines are extended to all people.[4]

Interventions to improve vaccination outcomes are commonly categorised either as targeting health services delivery or supply (e.g. improving human resources training and supervision, logistics, cold chain maintenance and vaccine storage), or demand for vaccines. Common approaches to increase demand involve offering incentives for vaccination, or knowledge translation and education (KTE) to promote and sustain vaccine uptake.[5] Mixed strategies combine features of supply and demand approaches.

Demand-side interventions may be particularly promising as equity-based strategies to reach underserved populations. A recent systematic review and meta-analysis by our group found that demand-side interventions lead to substantial gains in child vaccination coverage in diverse developing country settings.[6] KTE and incentives strategies were both effective.[6] The review highlighted the

need for additional research to clarify which types of interventions are most effective in specific health and social contexts, and to advance knowledge concerning delivery of interventions at scale, including financial and programmatic sustainability over time.[6]

For children less than 12 months, India's Universal Immunisation Programme (UIP) now provides free vaccination against 8 vaccine-preventable diseases: tuberculosis, diphtheria, tetanus, pertussis, polio, measles, hepatitis, and rotavirus.[7] Notwithstanding, in 2012, India accounted for the largest share among all countries (30%) of the world's 22.6 million under-vaccinated (defined as failure to receive three doses of diphtheria-tetanus-pertussis (DTP) vaccine) children, underscoring the need to strengthen uptake of routine immunisation (RI) in this context.[8] Only one study has evaluated use of demand-side interventions to strengthen RI in India. Banerjee and colleagues tested the use of food incentives to promote immunisation uptake in rural Rajasthan and found an important positive effect.[9] No published study has as yet evaluated use of KTE to promote vaccine uptake in India. KTE interventions have demonstrated considerable success in increasing vaccination coverage in similar contexts,[6 10-14] and may be particularly important where levels of formal education are low.

Objectives and hypotheses

With the ultimate aim of conducting a future cluster randomised trial to assess intervention impact on vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

Objectives of the planned future cluster randomised trial to study effectiveness (main study)

Purpose: To evaluate the impact, cost-effectiveness, scalability and sustainability of participatory, community-based KTE interventions to improve coverage of UIP-recommended vaccines among children less than 24 months from underserved communities in India.

Hypothesis: We postulated that participatory, community-based KTE interventions could increase vaccination coverage in these populations.

Primary objective

1. To evaluate the impact of the KTE interventions on vaccination coverage of children 12-23 months of age

Secondary objectives

2. To evaluate the impact of the KTE interventions on equity of vaccination coverage. Analyses will study potential disparities in vaccination coverage among population subgroups reflecting differences in living standards, parental education, and religion.
3. To evaluate the impact of the interventions on routine immunization (RI) (as compared to campaign) coverage, overall and among equity strata
4. To document the costs of offering the interventions and, if successful, assess the costs, effectiveness, and cost-effectiveness of offering the interventions at larger scale
5. To document the process and delivery context to draw lessons for potential scale up and sustainability within the Indian health system.

Objectives of the current pilot study

We conducted a four-month pilot study to inform development of the main study.[15] Pilot study methods closely replicated those of the planned main study, including use of a cluster randomised and controlled design. A cluster design is required as interventions are structured around communities rather than individuals. The pilot study was not designed to determine effectiveness[15] as the time period was too short to permit interventions to affect child vaccination status. We studied intervention effect on several proxy outcomes to evaluate proof of concept.

Primary Objective:

1. To assess the feasibility of processes key to success of the main study.[15] These included ability to recruit the desired number of villages and participants per village, the acceptability of randomisation procedures and interventions, ability to deliver interventions as planned, the value of incorporating a control intervention, and subjects' understanding of intervention materials and data collection tools.

Secondary Objectives:

2. To study intervention impact on several proxy indicators of immunisation uptake at cluster and individual levels.
3. To identify shortcomings and potential barriers to success for the larger trial, and to take steps to allay them.[15]

We estimated the intra-cluster correlation for the main trial outcome using a larger, representative sample of 60 villages.[16]

METHODS

Trial design

Consonant with the planned main study, this pilot employed a cluster-randomised design with a 1:1 allocation ratio. Clusters were rural villages of 2000 to 5000 inhabitants in Bawan Block, an administrative division of Hardoi district, Uttar Pradesh (UP). Villages were randomly assigned to either the intervention or control group. A survey to assess knowledge, understanding, and practices concerning immunisation, diarrhoea and child health was administered to participants at baseline prior to randomisation, and four months later at end line.

Participants

Setting & Location

India's estimated under-5 mortality was 57.3 per 1000 live births in 2012; progress is insufficient to achieve the MDG4 target of 38 deaths per 1000 by 2015.[17] According to the latest national survey data, only 61% of India's children 12-23 months were fully immunized.[18] In 2012, Uttar Pradesh had the largest share among all states (28%) of India's child mortality and an under-5 mortality rate of 74.9 per 1000 live births.[17] In 2011, 45.3% of UP's children were fully immunised.[19]

Among UP districts, Hardoi has poorer than average performance. With a population of 4 million[20], Hardoi figures among the 81 (of 640) districts accounting for 1/3 of India's 2012 child mortality[17], and receives development funds targeted to India's most backwards districts.[21] Estimated under-5

mortality was 89.6 per 1000 in 2012,[17] and full immunisation coverage was 49.9%.[19] Bawan is one of Hardoi's 19 administrative blocks. Bawan was chosen as the pilot study site for reasons related to logistics and feasibility, and because it consistently performs below district averages on development indicators.5-89-1215-16

Eligibility criteria for clusters

Villages were eligible for inclusion if they had 2000 to 5000 inhabitants and were located in Bawan Block. Census data showed that 23 of Bawan's 126 villages were candidates for inclusion. We eliminated 1 village with which we had had previous contact. Twelve of the remaining 22 villages were selected to ensure maximum geographical distance between clusters.

Eligibility criteria for participants

All women residing in a selected village who were mothers of a child 0 to 2 years of age were eligible to participate. We excluded those not able to understand and speak Hindi or Urdu, cognitively impaired, or who did not intend to reside in the village for the study duration (4 months). Eligibility criteria applied only to scientific data collection and inclusion in the main analysis.

The sampling unit was the household. We selected 36 households containing one or more eligible mothers within each village using sampling procedures designed to provide near random selection of households spread over the community.[22]

Interventions

India's Integrated Child Development Services (ICDS) scheme offers nationwide nutrition and health promotion. In addition to the regular ICDS services, women residing in intervention group (IG) villages received: (1) home visits by volunteers using "engagement packages" designed to improve knowledge, awareness, and attitudes towards immunisation; (2) community mobilisation through activities, events, and discussion groups to identify problems related to immunisation in their communities, discuss possible causes and solutions, and give feedback on the project. Control group (CG) villages received community mobilisation through activities, events, and discussion groups to raise awareness on issues related to nutrition, diarrhoea prevention and treatment in their communities, and give feedback on the project. A toll-free number for immunisation enabling anonymous queries and feedback was offered to all residents of IG and CG villages. Table 1 summarises study interventions.

Table 1. Study interventions

Activity	Intervention Group (IG) [2]	Control Group (CG)
Baseline survey[1]		
Randomisation[1]		
Home visit 0	Rapport formation; information	Rapport formation; information
Community Discussion 1	Project introduction; sharing district report card; skit (vaccination); toll-free number (vaccination)	Project introduction; sharing district report card; skit (ORS); toll-free number (vaccination)
Home visit 1	Story 1 (Key messages) • Timely vaccination can save children from life threatening illnesses (polio) • In case of queries, one should ask a local CHW (or toll free number) Activity: immunisation schedule	
Home visit 2	Story 2 (New messages) • Vaccination is free of charge and available at the local Anganwadi centre Activity: protect immunisation card	
Home visit 3	Story 3 (New messages) • Every vaccine has a specific purpose and all doses are required • Challenges occur in daily life, but one should avoid missing a vaccination dose • Even if the child has a minor illness, she or he can be vaccinated Activity: immunisation schedule	
Community Discussion 2	Discussion of barriers to immunisation and local solutions; toll-free number (vaccination); Activities: immunisation calendar; immunisation card; skit (vaccination)	Discussion of barriers to early child nutrition and local solutions; toll-free number (vaccination); Activities: skit
Home visit 4	Story 4 (New messages) • Place the right priority on vaccination – if one's child falls ill, one can incur expense and health risk Activity: immunisation card	
Home visit 5	Story 5 (New messages) • In case of service delivery problems, tell a responsible person (or toll-free number) • If a child's vaccine dose is missed, obtain it at the next opportunity Activity: immunisation card	
Home visit 6	Story 6 (New messages) • Vaccination benefits everyone (herd immunity). Activity: immunisation schedule	
Community Discussion 3	Feedback on project components (home visits, community discussions, toll-free number); suggestions for improvement	Feedback on project components (home visits, community discussions, toll-free number); suggestions for improvement
End line survey[1]		

[1] Identical for intervention and control groups

[2] Key messages were repeated for reinforcement; only new content is described

Interventions addressed individuals, households, and communities. While home visits were directed in the first instance to the mothers of young children enrolled in the study, activities were open to friends, neighbours, and other members of the household. Community events were open to all.

Outcomes

Primary outcomes

We established ex-ante criteria for feasibility of the main study related to processes for participant recruitment, randomisation, and retention. Specifically, we viewed the study as feasible if (i) 50% of villages approached would agree to participate and accept randomisation; (ii) 30 women per village could be recruited in 70% of villages; (iii) 50% of women were retained from baseline to end line. Below these thresholds, we judged that the study would not be feasible without major modifications.

Secondary outcomes

We studied process indicators related to implementation fidelity (ability to delivery interventions as planned) and two indicators of community response ((i) participation in community events; (ii) additional participants who joined the endline survey (as a measure of the indirect effect of interventions)). We also studied three proxy indicators of intervention impact on immunisation uptake. We described differences between IG and CG villages for two cluster-level outcomes: (i) use of the toll-free number; and (ii) monthly immunisation day footfall. (iii) We compared performance of individuals belonging to the IG versus CG on the change from baseline to endline survey on key indicators related to information

conveyed through the engagement packages and community events. There were no changes to outcomes after commencement of the trial.

Sample size

For a feasibility study, sample size is not established based on power to detect an anticipated intervention impact. We set the number of clusters at 12 as six clusters per study arm is a minimum for cluster comparisons using a t-test,[23] and for logistical and budgetary reasons. To facilitate statistical testing within clusters we fixed the number of households per village to be 30, but inflated this to 36 to account for potential non-response and missing values. We therefore sought to recruit 432 individual participants allocated equally between intervention and control villages. In all 12 villages, community discussions and the toll-free number were open to the entire community.

Randomisation

Sequence generation and allocation concealment

Villages were assigned to either intervention or control groups using simple randomisation with a 1:1 allocation following a computer-generated randomisation schedule. The random allocation sequence was generated at the CRCHUM by a professional statistician (MPS) using the R package blockrand[24] and kept in a password-protected computer. The statistician was not involved in study implementation. Prior to release of the randomisation code only the statistician had access to the allocation sequence. Randomisation code was released all at once and treatment groups assigned only after completion of all recruitment procedures and baseline measurements.

Implementation

Field team leaders enrolled clusters by contacting village officials in person to explain study aims and activities and request consent to participate. Subsequently, in each participating village, field team members directly approached a random sample of households to request their consent to participate in the baseline survey and pilot study. Enrolment occurred prior to randomisation. No advertisements were used for recruitment, and no incentives or rewards were offered for participation. Field team members informed households personally of their study group assignments.

Blinding

Due to the nature of the interventions, neither participants nor those involved in intervention delivery were blinded to group assignment. Data analysis was not masked. We took two measures to reduce the potential impact of knowledge of group assignment on study outcomes. (1) The study used a control intervention to enhance acceptability of randomisation and to conceal the true study hypothesis. (2) We hired independent surveyors for the end line survey to assess study outcomes. These surveyors were not informed of group assignment.

Statistical methods

We used descriptive statistics (counts, frequencies, proportions) to assess study feasibility and processes. Descriptive statistics were also used to compare the IG and CG on cluster-level outcomes. We compared the IG and CG on individual-level outcomes reflecting change from baseline to end line survey on

selected indicators using generalised estimating equations (GEE) regressions adjusted for village-level clustering using an exchangeable correlation structure. Additional analyses considered GEE models adjusted simultaneously for village-level clustering, maternal education and wealth quintile. These analyses included participants with complete data; complementary analyses explored results for participants with incomplete data.

The Pratham (New Delhi, India) and CRCHUM (Montreal, Canada) research ethics committees approved this study. The study will be prospectively registered in an international trial registry before starting the main trial.

RESULTS

Primary Outcomes

Village recruitment and the baseline survey occurred between January 12th and February 3rd, 2014. Four villages were replaced prior to randomisation, one due to failure to meet inclusion criteria, and three due to surveyor error during the baseline survey. A surveyor administered components of the baseline survey in the wrong order. Randomisation assignments were released to the core study team on February 4th, 2014 and communicated in person to all 12 villages on February 7th and 8th, 2014. The intervention began immediately thereafter and ran for four months as planned. The endline survey was initiated on May 27th and completed by June 30th, 2014.

Feasibility criteria related to recruitment, randomisation and retention were satisfied. [Figure 1] All villages contacted (100%, 16/16) agreed to participate and accepted randomisation. Thirty six women were recruited in 100% (12/12) of villages randomised. No clusters were lost to follow up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

[Figure 1 approximately here]

Baseline data

Table 2 presents characteristics of the study sample. There were clear baseline imbalances between intervention and control groups, with the CG having higher living standards, maternal education, and

proportions of children vaccinated. The 12 study villages had better access to electricity and health services and somewhat higher living standards than Hardoi district as a whole. Notwithstanding, the IG had lower proportions of children vaccinated as compared to the CG and to district averages.

Table 2. Characteristics of 12 villages and 432 households, mothers and children included in the pilot study

	Characteristics of participating villages						District[1]	
	Control *n*=6		Intervention *n*=6		Total N=12		N=60	
Village electrification	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
None	0	(0)	0	(0)	0	(0)	8	(13)
Less than 6 hours	0	(0)	2	(33)	2	(17)	30	(50)
More than 6 hours	6	(100)	4	(67)	10	(83)	22	(37)
Number of health centres								
0	0	(0)	0	(0)	0	(0)	2	(3)
1	3	(50)	5	(83)	8	(67)	25	(42)
2	2	(33)	1	(17)	3	(25)	16	(27)
3	0	(0)	0	(0)	0	(0)	13	(22)
4	1	(17)	0	(0)	1	(8)	4	(7)
Proportion in poorest 20%[2]								
Mean (SD) in %	14 (1)		26 (10)		20(11)		24	(15)
	Characteristics of participating households, mothers and children							
	Control *n*=216		Intervention *n*=216		Total N=432		N=1192	
Dwelling materials (floor, walls, roof)[3]	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Natural (kachcha)	31	(14)	59	(27)	90	(21)	389	(33)
Intermediate (Semi pucca)	154	(71)	129	(60)	283	(65)	720	(60)
Solid (Pucca)	31	(14)	28	(13)	59	(14)	83	(7)
Mother's education (years)								
None (0)	83	(38)	120	(56)	203	(47)	696	(58)
Some primary (1 to 5)	24	(11)	18	(8)	42	(10)	86	(7)
Some upper primary (6 to 8)	8	(4)	2	(1)	10	(2)	218	(18)
Some secondary (9 to 12)	101	(47)	76	(35)	177	(41)	192	(16)
Child immunisation card?								
No	249	(57)	337	(67)	586	(62)	680	(57)
Yes	188	(43)	170	(34)	358	(38)	512	(42)
Child Vaccination[4]								
None	12	(6)	14	(7)	26	(6)	58	(5)
Partial	161	(75)	178	(82)	339	(79)	794	(67)
Full	43	(20)	24	(11)	67	(16)	340	(29)

[1.] Data for Hardoi district are from a representative sample of 60 villages (1192 households) collected in 2013 and included for purposes of comparison[16]

[2.] This is the proportion in the poorest wealth quintile. Wealth quintiles for this 12 village pilot study were calculated using items and methods similar to those for India's major national surveys. See [16]

[3.] Dwelling characteristics were assessed by observation using definitions drawn from India's major national surveys. See [16]

[4.] "Full immunisation" among children 12-23 months is defined as 1 dose of Bacille Camille Guerette (BCG) vaccine, 3 doses of polio vaccine, 3 doses of diphtheria-pertussis-tetanus (DPT) vaccine, and 1 dose of measles vaccine.

Secondary Outcomes

Intervention fidelity: Of the six planned immunisation KTE home visits, an average of 5.9 visits were delivered to the 216 IG participants. Three rounds of community discussions were held as planned in all 12 villages.

Community response: (i) Community discussions: Community discussion 1 included 1210 adult participants (752 from IG villages and 458 from CG villages). Community discussion 2 involved 1140 participants (593 IG and 547 CG). Community discussion 3 involved 946 participants (604 IG and 342 CG). (ii) Additional participants in the endline survey: 139 additional community members (96 (69%) IG; 43 (31%) CG) volunteered to take the endline survey.[Figure 1]

Toll-free number

IG and CG villages differed in use of the toll-free number, with more calls originating from IG villages (n=11) versus CG villages (n=3). Monthly call volume was lower than anticipated; there were 14 calls from the 12 villages over four months.

Immunisation day footfall

Inspection of monthly immunisation day footfall from April 2013 to May 2014 revealed no clear differences between IG and CG villages.[Supplementary Figure 1] Quality of administrative data was poor. One of six IG villages and one of six CG villages had no immunisation records. Four months of data were missing for the IG including two months during the intervention period. Two months of data were

missing for the CG, but none in the intervention period. Records were incomplete and often related to only one immunisation centre rather than to the entire village. The precise number of children eligible for vaccination in the catchment area was not known in any village.

Analysis of individual responses to baseline and end line surveys

Table 3 describes proportions of correct responses given by the 373 mothers who completed both baseline and endline surveys for selected indicators of knowledge and understanding about vaccination. Results were heterogeneous; regression analyses modelled the change from baseline to endline to clarify patterns of variation.[Table 4, Supplementary Table 1] General knowledge about vaccination improved in the IG (OR 2.38 [95% CI: 1.60 to 3.58], p-value <0.001) but not the CG (OR 1.29 [95% CI: 0.56 to 2.99], p-value 0.545). Ability to interpret the child's immunisation card did not improve in either study group. Knowledge of the vaccination calendar increased markedly in the IG but not the CG, for all doses except the birth dose.[Table 4] For these indicators, odds ratios for the intervention effect ranged from 7.55 to 18.25; adjustment for maternal education and wealth quintile resulted in larger IG effect sizes. [Table 4] Maternal education (ever having attended school) confounded the intervention effect in several analyses. Wealth quintile was not an important confounder in any analysis. [Table 4, Supplementary Table 1]

Table 3: Proportions of correct responses given by 373 participating mothers on selected indicators of knowledge and understanding about vaccination, by study group (*n* (%))

Indicator	Control (N=178)		Intervention (N=195)	
	Baseline *n*=178	End line *n*=178	Baseline *n*=195	End line *n*=195
General knowledge of vaccination[1]				
Vaccination protects against how many diseases?	102 (57)	113 (63)	90 (46)	131 (67)
Questions related to the immunisation card[2]				
What is the child's date of birth?	42 (23)	47 (27)	32 (16)	36 (18)
Why does the immunisation card have multiple boxes?	114 (64)	72 (40)	85 (43)	86 (44)
How many doses has the child received?	31 (17)	27 (15)	30 (15)	16 (8)
Which vaccine has the child received?	34 (19)	30 (17)	26 (13)	21 (11)
Questions related to the immunisation schedule[3, 4]				
Do you know the immunization schedule of your child? (yes)	20 (11)	111 (62)	21(11)	182 (93)
At birth	11 (6)	93 (52)	15 (8)	170 (87)
Dose at 1.5 months	4 (2)	31 (17)	7 (4)	148 (76)
Dose at 2.5 months	4(2)	22 (12)	5 (3)	156 (80)
Dose at 3.5 months	5 (3)	15 (8)	3 (2)	148(76)
Dose at 9 months	11 (6)	47 (26)	12 (6)	172 (88)

[1] Surveyors informed participants of the correct answer directly prior to asking the question. See [16]
[2] A sample filled vaccination card was used to elicit responses to these four questions. See [16]
[3] These are spontaneous responses to the question "Do you know the immunization schedule of your child?" If yes, please name all the doses." See [16]
[4] We recorded as correct all responses recommended in the Indian immunisation schedule; however, this table presents only doses for children less than 12 months.

Table 4. Univariate regression models describing knowledge of the vaccination schedule at end line versus baseline for 373 participating mothers, by dose and study group

Vaccine Dose[1]	Model 1[2]			Model 2[3]		
	OR	(95%CI)	p-value	OR	(95%CI)	p-value
Birth						
IG	5.23	(0.57 - 48.29)	0.145	5.52	(0.53 - 57.38)	0.152
CG	4.17	(1.51 - 11.57)	0.006	4.34	(1.62 - 11.61)	0.003
1.5 months						
IG	7.55	(3.25 - 17.29)	0.000	10.01	(3.51 - 28.58)	0.000
CG	1.45	(0.49 - 4.37)	0.500	1.35	(0.42 - 4.41)	0.614
2.5 months						
IG	14.11	(5.90 - 33.78)	0.000	18.56	(8.08 - 42.65)	0.000
CG	0.76	(0.27 - 2.11)	0.598	0.70	(0.21 - 2.29)	0.558
3.5 months						
IG	18.25	(7.43 - 44.83)	0.000	25.04	(8.79 - 71.3)	0.000
CG	0.43	(0.13 - 1.44)	0.170	0.38	(0.08 - 1.73)	0.209
9 months						
IG	11.30	(3.42 - 37.31)	0.000	15.37	(5.12 - 46.17)	0.000
CG	0.60	(0.34 - 1.05)	0.073	0.53	(0.27 - 1.03)	0.061

IG - intervention group; CG - control group

[1] These are spontaneous responses to the question "Do you know the immunization schedule of your child? If yes, please name all the doses."

[2] Models adjusted for village-level clustering.

[3] Models adjusted for village-level clustering, mother's education (mother attended school yes/ no), and wealth quintile.

Analysis of the 59 mothers lost to follow up revealed no significant differences with respect to the 373 mothers remaining in the study in terms of household characteristics, personal characteristics, or baseline survey responses.[Supplementary Tables 2-4] The proportion of correct responses was generally higher among the 139 additional community participants who volunteered to take the end line survey, as compared to the 373 participating mothers. The child's father had the highest proportion of correct responses among all categories of participants.[Supplementary Tables 5-7; Supplementary Figure 2]

DISCUSSION

Key findings from the pilot study

We highlight six findings from the pilot study: (1) Pre-established criteria for feasibility of the planned main study related to recruitment, randomisation and retention were fully satisfied for clusters and individuals; (2) Intervention fidelity was excellent; (3) Community participation was high but weaker in the CG; (4) As hypothesised, use of a toll-free number was higher in the IG than in the CG. Notwithstanding, call volumes were low overall; (5) No clear conclusions could be drawn concerning trends in immunisation centre footfall; (6) Multiple analyses revealed a very strong effect of the immunisation intervention on individual participant learning, but results were variable across indicators.

Methodological lessons for the planned main study

Reflection on pilot findings and experiences suggests several lessons for the future study.

1. Study groups were unbalanced on characteristics likely to be related to study participation and child vaccination status, with IG participants systematically disadvantaged as compared to controls. (i) During the pilot, we adopted two strategies to enhance community partnership and ensure participation of households and individuals. First, we learned to cultivate support from influential members of the community and to seek their help in motivating others to join the study. Second, we diversified our field teams to include underrepresented groups. We view these strategies as essential to successful recruitment, randomisation, and retention. (ii)

Randomisation failed to achieve balance between study arms due to the small number of clusters involved in this pilot study. The future study should consider design options to improve balance and increase study power and precision, such as inclusion of a larger number of clusters, stratification,[23] and restricted randomisation using balancing criteria.[25] (iii) Substantively, pilot results show that the intervention was successful on many measures in a very disadvantaged population.

2. Although intervention fidelity was excellent, the value of a parallel control intervention was unclear. Through discussion with our study teams, we learned that that active presence of field staff in control villages lead to opportunities for contamination as villagers requested field team members to share information and advice on child health themes raised by the baseline survey. All content for the main study should likely be delivered through an intervention arm.
3. The first round of community discussions were delivered as one large gathering per village. In the control group, the first community discussion coincided with local religious festivals in two of the six control villages, while in one control village, people were reluctant to meet together due to caste and class divisions. The second and third community discussions were delivered in rounds of three to six smaller meetings per village, and groups were more homogeneous with respect to age, sex, and status. This strategy was more effective.
4. Use of a toll-free number was lower than anticipated. To our surprise, in endline discussions with the community we learned that the toll-free service was extremely valued. However, active presence of our field teams meant that questions were addressed preferentially to them. Toll-free and KTE intervention components should not be evaluated together.
5. Administrative data on immunisation was inadequate for scientific use. The Government of India is investing to improve vital statistics using biometric and digital technologies. Until this process

reaches maturity, the future main study should consider undertaking a census of participating villages at baseline to determine target population denominators.

6. Analysis of individual participant survey responses showed a compelling effect for some but not all components of the main vaccine intervention on proxy outcomes. (i) These results provide an evidence base to improve aspects of the main intervention prior to fielding the larger study. Different communications methods were used for the different components. (ii) Results also encourage us to consider the adequacy of our questionnaires. We used a previously developed survey with only marginal modifications.[16] Questions were only distantly related to the study interventions to ensure that both study groups had a reasonable chance to reply correctly. Questions related to the immunisation card may have been difficult to interpret. The main endpoint of the future study will be immunisation status rather than knowledge or health literacy, avoiding some of these difficulties. (iii) The intervention had an indirect effect. In our sample, community participants had higher scores than the mothers who were the target participants, with fathers having the highest scores on average. This likely reflects how gender biases shape ability to learn over the life course in this context. The community sample was not randomly selected.

Conclusions

This pilot study provided rich lessons to inform design of a future trial and to refine interventions. Criteria related to feasibility of the main study were satisfied. Based on our extensive knoweldge of the district,[16 26] we believe that evidence of feasibility can be generalised to other settings in Hardoi, Uttar Pradesh. In addition, cluster-randomised trials of participatory learning interventions have been

conducted in similar locations,[27 28] lending support to our assessment that the study is feasible. Findings from this pilot study give us confidence that we can successfully conduct a cluster randomised trial to assess the effectiveness of KTE interventions to improve vaccination coverage among children less than 24 months of age in rural northern India.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no conflicts of interest in relation to this work.

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AUTHOR CONTRIBUTIONS

MJ had principal responsibility for conception and design of the study, interpretation of data, and drafting of the manuscript; DC contributed to data acquisition and revision of the manuscript for important intellectual content; GKK had principal responsibility for statistical analysis and revised the manuscript for important intellectual content; SD contributed to data acquisition and revision of the manuscript for important intellectual content; MPS contributed to conception and design of the study, analysis and interpretation of the data, and revision of the manuscript for important intellectual content; JKS contributed to conception and design of the study and revision of the manuscript for important intellectual content; SP contributed to conception and design of the study and revision of the manuscript for important intellectual content.

All authors approved the final version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA SHARING STATEMENT

Statistical code and data are available from the corresponding author.

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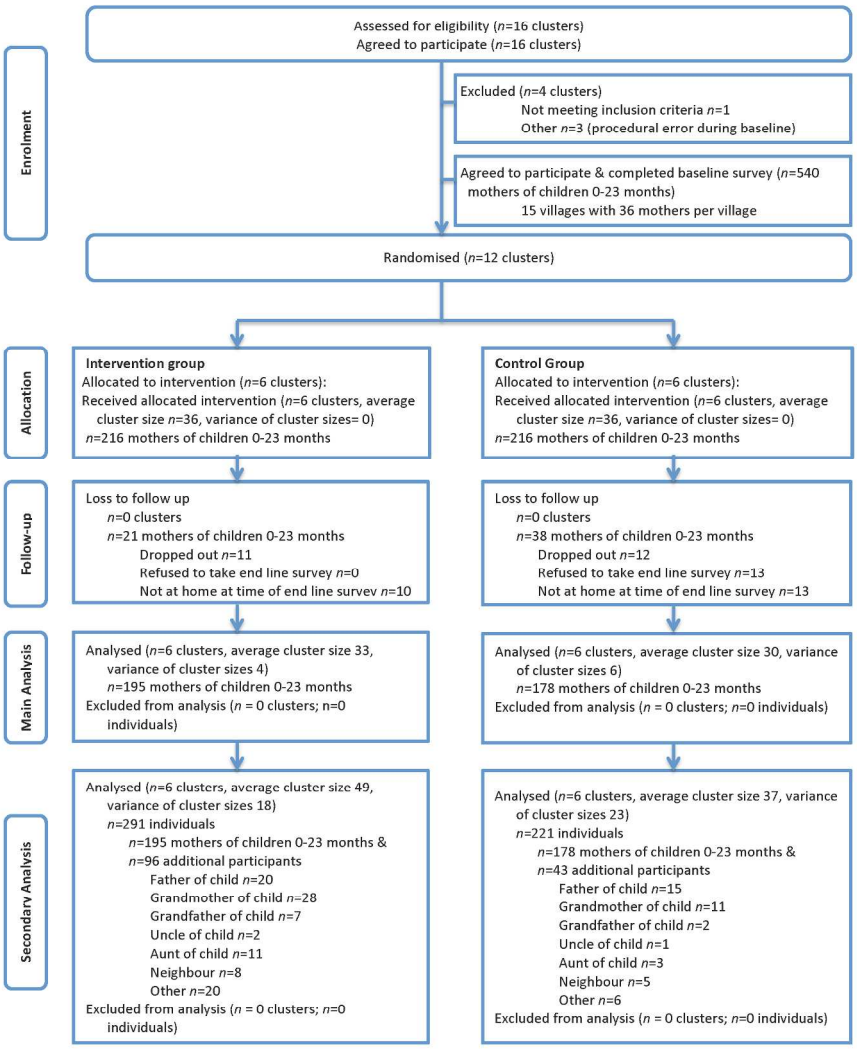
Figure 1. Flow diagram of progress of clusters and individuals through the study



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APPENDIX FOR THE STUDY: INTERVENTIONS TO INCREASE IMMUNISATION COVERAGE AMONG CHILDREN 12-23 MONTHS OF AGE IN INDIA THROUGH PARTICIPATORY LEARNING AND COMMUNITY MOBILISATION: PILOT STUDY FOR A CLUSTER RANDOMISED TRIAL (JOHRI ET AL., 2015)

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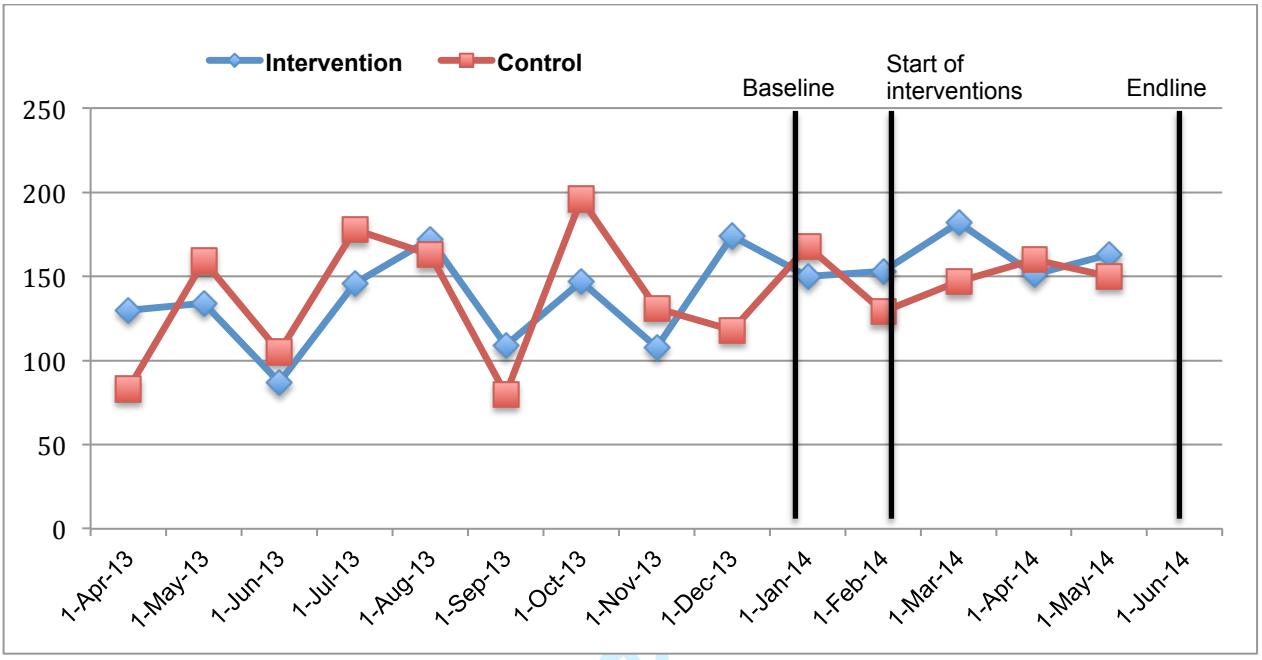
Secondary outcomes

Supplementary Figure 1. Total number of children vaccinated in intervention and control villages, April 1st, 2013 to May 1st, 2014[1]



[1] A total of 12 villages participated in the pilot study, 6 villages in the intervention group and 6 in the control group

Supplementary Table 1: Full results of univariate regression models for selected indicators of immunisation intervention performance at end line versus baseline for 373 participating mothers, by dose and study group

General information about vaccination

Vaccination protects against how many diseases?	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	2.38	(1.60 - 3.58)	0.000	2.80	(1.72 - 4.56)	0.000
CG (end line vs. baseline)	1.29	(0.56 - 2.99)	0.545	1.36	(0.50 - 3.72)	0.543
Mother attended school				4.53	(3.01 - 6.81)	0.000
Quintile of wealth index						
Q1 (poorest)				Ref.		
Q2				1.03	(0.56 - 1.90)	0.924
Q3				0.95	(0.58 - 1.57)	0.853
Q4				1.53	(0.94 - 2.49)	0.085
Q5				2.14	(0.89 - 5.15)	0.091

Knowledge of the immunisation card

What is the child's date of birth? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	1.15	(0.95 - 1.40)	0.148	1.20	(0.94 - 1.53)	0.137
CG (end line vs. baseline)	1.16	(0.99 - 1.36)	0.075	1.21	(0.99 - 1.48)	0.061
Mother attended school				20.89	(8.35 - 52.28)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.71	(0.66 - 4.46)	0.272
Q3				1.54	(0.71 - 3.33)	0.27
Q4				2.14	(0.93 - 4.91)	0.073
Q5				3.58	(1.66 - 7.72)	0.001

Why does the immunisation card have multiple boxes? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value

IG (end line vs. baseline)	1.02	(0.54 - 1.92)	0.948	1.02	(0.52 - 2.03)	0.948
CG (end line vs. baseline)	0.38	(0.14 - 1.07)	0.066	0.34	(0.11 - 1.04)	0.059
Mother attended school				2.38	(1.89 - 3.01)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.67	(0.47 - 0.95)	0.024
Q3				0.87	(0.51 - 1.51)	0.632
Q4				1.07	(0.65 - 1.74)	0.799
Q5				1.78	(1.08 - 2.94)	0.024

How many doses has the child received? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	0.49	(0.26 - 0.94)	0.031	0.43	(0.21 - 0.88)	0.02
CG (end line vs. baseline)	0.85	(0.66 - 1.09)	0.193	0.82	(0.61 - 1.11)	0.206
Mother attended school				24.73	(8.90 - 68.73)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.19	(0.47 - 3.01)	0.716
Q3				1.52	(0.50 - 4.60)	0.457
Q4				1.28	(0.48 - 3.44)	0.618
Q5				3.11	(1.49 - 6.49)	0.002

Which vaccine has the child received? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	0.79	(0.47 - 1.30)	0.349	0.75	(0.41 - 1.38)	0.357
CG (end line vs. baseline)	0.86	(0.67 - 1.10)	0.229	0.84	(0.62 - 1.12)	0.233
Mother attended school				8.76	(3.97 - 19.36)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.43	(0.61 - 3.36)	0.416

Q3	1.62	(0.78 - 3.32)	0.193
Q4	1.36	(0.48 - 3.84)	0.558
Q5	4.00	(1.60 - 10.00)	0.003

Knowledge of the immunisation schedule (by dose)

	Model 1			Model 2		
Birth Dose	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	5.23	(0.57 - 48.29)	0.145	5.52	(0.53 - 57.38)	0.152
CG (end line vs. baseline)	4.17	(1.51 - 11.57)	0.006	4.34	(1.62 - 11.61)	0.003
Mother attended school				1.37	(0.79 - 2.36)	0.258
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.45	(0.19 - 1.10)	0.080
Q3				0.48	(0.18 - 1.25)	0.131
Q4				0.36	(0.12 - 1.03)	0.057
Q5				0.63	(0.16 - 2.59)	0.527

	Model 1			Model 2		
Dose at 1.5 months	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	7.55	(3.25 - 17.29)	0.000	10.01	(3.51 - 28.58)	0.000
CG (end line vs. baseline)	1.45	(0.49 - 4.37)	0.500	1.35	(0.42 - 4.41)	0.614
Mother attended school				2.74	(1.66 - 4.53)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.69	(0.36 - 1.33)	0.270
Q3				0.59	(0.24 - 1.46)	0.257
Q4				0.53	(0.25 - 1.12)	0.096
Q5				0.83	(0.46 - 1.52)	0.553

	Model 1			Model 2		
Dose at 2.5 months	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	14.11	(5.90 - 33.78)	0.000	18.56	(8.08 - 42.65)	0.000
CG (end line vs. baseline)	0.76	(0.27 - 2.11)	0.598	0.70	(0.21 - 2.29)	0.558

Mother attended school				2.26	(1.12 - 4.53)	0.022
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.81	(0.47 - 1.39)	0.436
Q3				1.02	(0.47 - 2.22)	0.964
Q4				0.48	(0.22 - 1.07)	0.073
Q5				0.89	(0.44 - 1.82)	0.756

Dose at 3.5 months	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	18.25	(7.43 - 44.83)	0.000	25.04	(8.79 - 71.3)	0.000
CG (end line vs. baseline)	0.43	(0.13 - 1.44)	0.170	0.38	(0.08 - 1.73)	0.209
Mother attended school				2.17	(0.93 - 5.06)	0.074
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.69	(0.34 - 1.42)	0.316
Q3				0.75	(0.33 - 1.70)	0.491
Q4				0.42	(0.17 - 1.03)	0.058
Q5				1.01	(0.27 - 3.86)	0.983

Dose at 9 months	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	11.30	(3.42 - 37.31)	0.000	15.37	(5.12 - 46.17)	0.000
CG (end line vs. baseline)	0.60	(0.34 - 1.05)	0.073	0.53	(0.27 - 1.03)	0.061
Mother attended school				2.41	(1.03 - 5.62)	0.041
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.67	(0.22 - 2.08)	0.488
Q3				0.58	(0.17 - 2.01)	0.386
Q4				0.93	(0.33 - 2.60)	0.891
Q5				0.90	(0.22 - 3.63)	0.886

Model 1 adjusted for village-level clustering.
Model 2 adjusted for village-level clustering, mother's education (mother attended school yes/ no), and wealth quintile.

Analysis of loss to follow up (Supplementary Tables 2 – 4)

Supplementary Table 2: Household characteristics of 59 women lost to follow up (A) with 373 women who participated in the pilot study (B)

		Baseline survey only (A)		Baseline & Endline surveys (B)		
Caracteristics of household		n	mean(sd)	n	mean(sd)	T test (B-A)
Number of people living in the household (mean (sd))		59	6.2 (2.7)	373	6.9 (2.9)	0.1280
Number of rooms in the house (mean (sd))		59	1.9(1.4)	373	1.8 (1.5)	0.7595
Type of family		n	%	n	%	P-value
	Nuclear	29	49.2	187	50.1	0.889
	Joint	30	50.8	186	49.9	
Religion of head of household						
	Hindu	49	83.0	330	88.5	0.238
	Muslim	10	17.0	43	11.5	
Education level of father (years)						
	None(0)	11	18.6	99	26.5	0.573
	Some Primary (1 to 5)	13	22.0	81	21.7	
	Some upper primary (6 to 8)	2	3.4	8	2.1	
	Some secondary (9 to 12)	33	55.9	185	49.6	
Father's employment status						
	Daily wages	21	35.6	155	41.5	0.211
	Work on own land	15	25.4	111	29.8	
	Fixed Income	13	22.0	41	11.0	
	Self employed	8	13.6	50	13.4	
	Unemployed	2	3.4	16	4.3	
Type of Dwelling						
	Natural (kachcha)	10	17.0	80	21.5	0.594
	Intermediate (Semi pucca)	39	66.1	244	65.4	
	Solid (Pucca)	10	16.9	49	13.1	
Type of flooring						
	Sand/dung	50	84.7	328	87.9	0.762
	Cement/stone/brick	5	8.5	23	6.2	
	Other	4	6.8	22	5.9	
Wealth index of household						
	Poorest (quintile 1)	8	13.6	80	21.4	0.733
	Second	14	23.7	81	21.7	
	Middle	12	20.3	65	17.4	
	Fourth	13	22.0	75	20.1	
	Richest (quintile 5)	12	20.3	72	19.3	
Possess child's immunisation card?						
	No	38	64.4	409	54.8	0.154
	Yes	21	35.6	337	45.2	

Vaccine coverage (0 to 8 doses)					
None (0)	4	6.8	22	5.9	0.965
Partially vaccinated (1 to 7)	46	78.0	293	78.5	
Fully vaccinated (8)	9	15.2	58	15.5	

Supplementary Table 3: Characteristics of 59 women lost to follow up (A) and 373 women who participated in the pilot study (B)

	Baseline survey only (A)		Baseline & Endline (B)		
Participant Characteristics	n	Mean (sd)	n	Mean (sd)	p- value
Mother's age (mean (sd))	59	26.0 (3.6)	371	26.1(4.5)	0.8164
Education level of mother (years)	n	%	n	%	
None (0)	24	40.7	179	48.0	0.255
Some Primary (1 to 5)	3	5.1	39	10.5	
Some upper primary (6 to 8)	2	3.4	8	2.1	
Some secondary (9 to 12)	30	50.8	147	39.4	
Mother's employment status					
Daily wages	1	1.7	0	0.0	0.052
Work on own land	0	0.0	2	0.5	
Self employed	0	0.0	3	0.8	
Housewife	58	98.3	368	98.5	
Place of delivery of child					
Government hospital	36	61.0	205	55.0	0.895
Private hospital	2	3.4	18	4.8	
At home	21	35.6	148	39.7	
On the way to hospital	0	0.0	1	0.3	
Other	0	0.0	1	0.2	

Supplementary Table 4: Comparison of number of correct responses to selected questions for 59 women lost to follow up (A) and 373 women who participated in the pilot study (B)

Indicator	Baseline only (A)		Baseline & Endline (B)		
	n	%	n	%	p- value
Vaccination protects against how many diseases?	36	61.0	192	51.5	0.172
What kind of water to prepare ORS?	47	79.7	298	80.5	0.874
What is first step in preparing ORS?	49	83.0	293	79.2	0.493
What is the child's date of birth?	12	20.3	74	20.1	0.960
Why does the immunisation card have multiple boxes?	37	62.7	199	53.8	0.200
How many doses has the child received?	10	17.0	61	16.5	0.929
Which vaccine has the child received?	10	17.0	60	16.2	0.887

Analysis of additional community participants who joined the end line survey (Supplementary Tables 5-7; Figure 2)

Supplementary Table 5: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by study group (*n* (%))

	Main analysis: 373 mothers present at baseline and end line						Secondary Analysis: 139 participants					
	Control n=178		Intervention n=195		Total N=373		Control n=43		Intervention n=96		Total N=139	
	n	%	n	%	n	%	n	%	n	%	n	%
Vaccination protects against how many diseases?	113	63.5	131	67.2	244	65.4	32	74.4	79	82.3	111	79.9
What kind of water to prepare ORS?	164	92.1	163	84.0	327	87.9	40	95.2	85	89.5	125	91.2
What is first step in preparing ORS?	162	91.0	168	86.6	330	88.7	40	93.0	80	84.2	120	87.0
What is the child's date of birth?	47	26.4	36	18.6	83	22.3	17	39.5	37	38.9	54	39.1
Why does the immunisation card have multiple boxes?	72	40.5	86	44.3	158	42.5	24	55.8	52	54.2	76	54.7
How many doses has the child received?	27	15.2	16	8.3	43	11.6	10	23.3	18	18.8	28	20.1
Which vaccine has the child received?	30	16.9	21	10.8	51	13.7	13	30.3	29	30.2	42	30.2
Do you know the immunization schedule of your child?[1]	111	62.4	182	93.3	293	78.5	19	44.2	68	70.8	87	62.6

[1] As declared by the respondent (not necessarily correct)

Supplementary Table 6: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by study group[1]

	Community, N=139		Mothers, N=373		P- value
	n	%	n	%	(B-A)
Vaccination protects against how many diseases?	111	79.9	244	65.4	0.002
What kind of water to prepare ORS?	125	91.2	327	87.9	0.290
What is first step in preparing ORS?	120	87.0	330	88.7	0.585
What is the child's date of birth?	54	39.1	83	22.3	0.000
Why does the immunisation card have multiple boxes?	76	54.7	158	42.5	0.014
How many doses has the child received?	28	20.1	43	11.6	0.013
Which vaccine has the child received?	42	30.2	51	13.7	0.000
Do you know the immunization schedule of your child?[2]	87	62.6	293	78.5	0.000

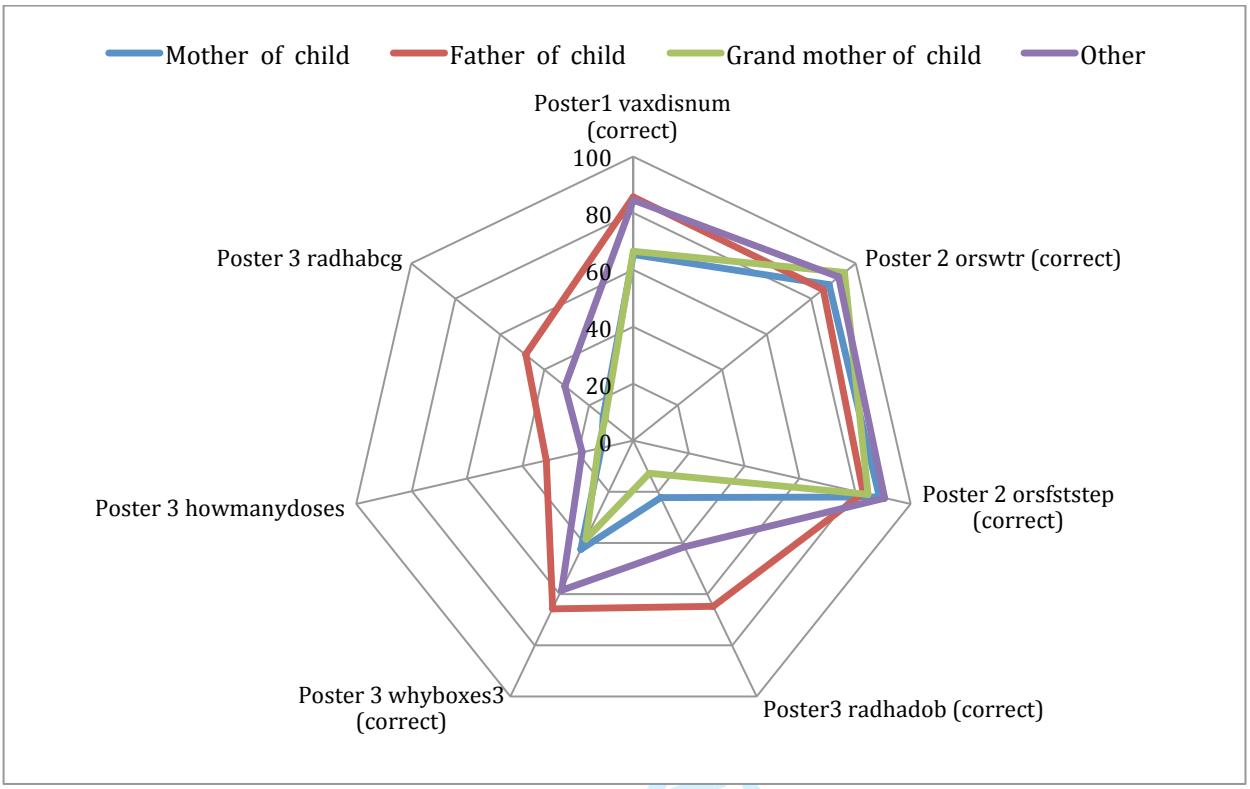
[1] We used the χ^2 test to compare results between groups
[2] As declared by the respondent (not necessarily correct)

Supplementary Table 7: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by type of participant

	Total additional community participants (B), N=139		Father of child, N=35		Grand mother of child,N=39		Other , N=65		Mother of child (A), N=373	
	n	%	n	%	n	%	n	%	n	%
Vaccination protects against how many diseases?	111	79.9	30	85.7	26	66.7	55	84.6	244	65.4
What kind of water to prepare ORS?	125	91.2	29	85.3	37	94.9	59	92.2	327	87.9
What is first step in preparing ORS?	120	87.0	29	82.9	33	84.6	58	90.6	330	88.7
What is the child's date of birth?	54	39.1	22	64.7	5	12.8	27	41.5	83	22.3
Why does the immunisation card have multiple boxes?	76	54.7	23	65.7	15	38.5	38	58.5	158	42.5
How many doses has the child received?	28	20.1	11	31.4	5	12.8	12	18.5	43	11.6
Which vaccine has the child received?	42	30.2	17	48.6	5	12.8	20	30.8	51	13.7
Do you know the immunization schedule of your child?[1]	87	62.6	13	37.1	28	71.8	46	70.8	293	78.5

[1] As declared by the respondent (not necessarily correct)

Supplementary Figure 2: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by type of participant



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Interventions to increase immunisation coverage among children 12-23 months of age in India through participatory learning and community engagement: pilot study for a cluster randomised trial

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TITLE

Interventions to increase immunisation coverage among children 12-23 months of age in India through participatory learning and community engagement: pilot study for a cluster randomised trial

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ABSTRACT (300 words)

Objective: With the aim of conducting a future cluster randomised trial to assess intervention impact on child vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

Trial Design: Cluster-randomised design with a 1:1 allocation ratio

Methods: Clusters were 12 villages in rural Uttar Pradesh. All women residing in a selected village who were mothers of a child 0 to 23 months of age were eligible; participants were chosen at random. Over 4 months, intervention group (IG) villages received: (1) home visits by volunteers; (2) community mobilisation events to promote immunisation. Control group (CG) villages received community mobilisation to promote nutrition. A toll-free number for immunisation was offered to all IG and CG village residents. Primary outcomes were ex-ante criteria for feasibility of the main study related to processes for recruitment and randomisation (50% of villages would agree to participate and accept randomisation; 30 women could be recruited in 70% of villages) and retention of participants (50% of women retained from baseline to end line). Clusters were assigned to IG or CG using a computer-generated randomisation schedule. Neither participants nor those delivering interventions were blinded, but those assessing outcomes were blinded to group assignment.

Results: All villages contacted agreed to participate and accepted randomisation. Thirty six women were recruited per village; 432 participants were randomised (IG *n*=216; CG *n*=216). No clusters were lost to follow up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

Conclusions: Criteria related to feasibility were satisfied, giving us confidence that we can successfully conduct a larger cluster randomised trial. Methodological lessons will inform design of the main study.

Trial Registration: ISRCTN16703097

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ARTICLE SUMMARY

Strengths and limitations of this study

- This feasibility study for a cluster randomised trial of participatory, community-based interventions to improve child vaccination coverage closely replicated the methods of the planned main study, and enabled us to conclude with confidence that we could successfully carry out the main study.
- Field experience enabled us to identify key potential barriers to success of the larger trial related to quality of administrative data on immunisation, baseline covariate imbalances following randomisation, measurement and information biases, and contamination, and to develop strategies to address them in the main study.
- This pilot study also considered a range of secondary outcomes using appropriate statistical methods, including cluster- and individual-level proxy endpoints indicative of intervention effectiveness.
- Analyses revealed an important positive effect of interventions on several proxy endpoints; however, the relationship of proxy to final endpoints is unknown, multiple proxy endpoints were considered, and results were not fully consistent. The number of study clusters was small.
- A definitive judgment concerning intervention impact on child vaccine coverage must await the larger study.

INTRODUCTION

Background

Immunisation has been instrumental in global progress towards the UN Millennium Development Goal to reduce under-5 mortality (MDG 4).[1] The potential for future impact is even greater: due in part to highly effective new vaccines that can protect against some forms of diarrhoea and pneumonia, the World Health Organization and UNICEF estimate that 29% of deaths among children 1 to 59 months are now vaccine-preventable.[2]

To realise their potential, antigens must reach all children; yet, one in five children worldwide still **do** not have access to basic vaccines.[3 4] In May 2012, the World Health Assembly approved the Global Vaccine Action Plan (GVAP) to ensure that the full benefits of vaccines are extended to all people.[4]

Interventions to improve vaccination outcomes are commonly categorised either as targeting health services delivery or supply (e.g. improving human resources training and supervision, logistics, cold chain maintenance and vaccine storage), or demand for vaccines. Common approaches to increase demand involve offering incentives for vaccination, or knowledge translation and education (KTE) to promote and sustain vaccine uptake.[5] Mixed strategies combine features of supply and demand approaches.

Demand-side interventions may be particularly promising as equity-based strategies to reach underserved populations. A recent systematic review and meta-analysis by our group found that demand-side interventions lead to substantial gains in child vaccination coverage in diverse developing country settings.[6] KTE and incentives strategies were both effective.[6]

For children less than 12 months, India's Universal Immunisation Programme (UIP) now provides free vaccination against 8 vaccine-preventable diseases: tuberculosis, diphtheria, tetanus, pertussis, polio, measles, hepatitis, and rotavirus.[7] Notwithstanding, in 2012, India accounted for the largest share among all countries (30%) of the world's 22.6 million under-vaccinated (defined as failure to receive three doses of diphtheria-tetanus-pertussis (DTP) vaccine) children, underscoring the need to strengthen uptake of routine immunisation (RI) in this context.[8] Only one study has evaluated use of demand-side interventions to strengthen RI in India. Banerjee and colleagues tested the use of food incentives to promote immunisation uptake in rural Rajasthan and found an important positive effect.[9] No published study has as yet evaluated use of KTE to promote vaccine uptake in India. KTE interventions have demonstrated considerable success in increasing vaccination coverage in similar contexts,[6 10-14] and may be particularly important where levels of formal education are low.

Our research will make three key contributions to knowledge and practice concerning community-based interventions to increase vaccination coverage. (1) We are designing the first trial of KTE interventions in India. The proposed study location has especially weak health services and poor governance, as well as very low rates of education and health literacy.[15] Immunisation coverage is low and there has been little progress over the last two decades. Through formative and evaluative research, we will develop and test a locally appropriate KTE model. (2) The trial will assess scientific issues of global significance related to KTE intervention delivery, including equity impact, cost-effectiveness, and financial and programmatic sustainability over time.[6] (3) Through our NGO partners, it will contribute to development of a scalable implementation model for India.

Objectives and hypotheses

With the ultimate aim of conducting a future cluster randomised trial to assess intervention impact on vaccination coverage, we designed a pilot study to assess feasibility and aid in refining methods for the larger study.

Objectives of the planned future cluster randomised trial to study effectiveness (main study)

Purpose: To evaluate the impact, cost-effectiveness, scalability and sustainability of participatory, community-based KTE interventions to improve coverage of UIP-recommended vaccines among children less than 24 months from underserved communities in India.

Hypothesis: We postulated that participatory, community-based KTE interventions could increase vaccination coverage in these populations.

Primary objective

1. To evaluate the impact of the KTE interventions on vaccination coverage of children 12-23 months of age

Secondary objectives

2. To evaluate the impact of the KTE interventions on equity of vaccination coverage. Analyses will study potential disparities in vaccination coverage among population subgroups reflecting differences in living standards, parental education, and religion.
3. To evaluate the impact of the interventions on routine immunization (RI) (as compared to campaign) coverage, overall and among equity strata

4. To document the costs of offering the interventions and, if successful, assess the costs, effectiveness, and cost-effectiveness of offering the interventions at larger scale
5. To document the process and delivery context to draw lessons for potential scale up and sustainability within the Indian health system.

Objectives of the current pilot study

We conducted a four-month pilot study to inform development of the main study.[16] Pilot study methods closely replicated those of the planned main study, including use of a cluster randomised and controlled design. A cluster design is required as interventions are structured around communities rather than individuals. The pilot study was not designed to determine effectiveness[16] as the time period was too short to permit interventions to affect child vaccination status. We studied intervention effect on several proxy outcomes to evaluate proof of concept.

Primary Objective:

1. To assess the feasibility of processes key to success of the main study.[16] These included ability to recruit the desired number of villages and participants per village, the acceptability of randomisation procedures and interventions, ability to deliver interventions as planned, the value of incorporating a control intervention, and subjects' understanding of intervention materials and data collection tools.

Secondary Objectives:

2. To study intervention impact on several proxy indicators of immunisation uptake at cluster and individual levels.

3. To identify shortcomings and potential barriers to success for the larger trial, and to take steps to allay them.[16]

We estimated the intra-cluster correlation for the main trial outcome using a larger, representative sample of 60 villages.[15]

METHODS

Trial design

Consonant with the planned main study, this pilot employed a cluster-randomised design with a 1:1 allocation ratio. Clusters were rural villages of 2000 to 5000 inhabitants in Bawan Block, an administrative division of Hardoi district, Uttar Pradesh (UP). Villages were randomly assigned to either the intervention or control group. A survey to assess knowledge, understanding, and practices concerning immunisation, diarrhoea and child health was administered to participants at baseline prior to randomisation, and four months later at end line.

Participants

Setting & Location

The trial location is rural Hardoi district, Uttar Pradesh (UP), India. UP is India's most populous state with more than 200 million inhabitants and the largest share (28% in 2012) among all states of India's child mortality.[17] UP is also home to India's greatest number of unimmunised children.[18] With a population of 4 million subdivided into 5 Tehsils (19 blocks)[19], Hardoi figures among 81 (of 640) districts accounting for 1/3 of India's 2012 child mortality[17], and receives development funds targeted to India's most backwards districts. In Hardoi district, estimated under-5 mortality was 89.6 per 1000 (UP 74.9; India 57.3) in 2012[20], coverage of DTP3 (a standard measure of routine immunisation system performance used by international agencies such as WHO, UNICEF and GAVI [21-23]) was 41.9%[15] (UP 55.9%[20]; India71.5%[18]), and full immunisation was 49.9% (UP 45.3%; India 61.0%).[18] Bawan is one

of Hardoi's 19 administrative blocks. Bawan was chosen as the pilot study site for reasons related to logistics and feasibility, and because it consistently performs below district averages on development indicators.

Eligibility criteria for clusters

Villages were eligible for inclusion if they had 2000 to 5000 inhabitants and were located in Bawan Block. Census data showed that 23 of Bawan's 126 villages were candidates for inclusion. We eliminated 1 village with which we had had previous contact. Twelve of the remaining 22 villages were selected to ensure maximum geographical distance between clusters.

Eligibility criteria for participants

All women residing in a selected village who were mothers of a child 0 to 2 years of age were eligible to participate. We excluded those not able to understand and speak Hindi or Urdu, cognitively impaired, or who did not intend to reside in the village for the study duration (4 months). Eligibility criteria applied only to scientific data collection and inclusion in the main analysis.

The sampling unit was the household. We selected 36 households containing one or more eligible mothers within each village using sampling procedures designed to provide near random selection of households spread over the community.[24]

Interventions

Interventions employed a variety of individual, small group and community-wide approaches that can eventually be delivered by volunteers. The target populations reside in rural areas with weak health services. Our focus on community-based KTE is grounded in two findings from our 2013 district survey: (1) Social factors structuring access, opportunities, and empowerment also shape immunization coverage. (2) Mothers are considered the primary caregivers for their children but are often not empowered to fulfil this role.[15] Study interventions contribute to learning and empowerment and forging of links across social groups, thereby reinforcing the resilience of individuals and communities and creating conditions for positive change. Interventions aim to increase the effectiveness of local immunisation services without substantial added public investment, and are designed as a support to local health workers. Interventions took place over 4 months and will be standardised in future to facilitate delivery at scale.

India's Integrated Child Development Services (ICDS) scheme offers nationwide nutrition and health promotion. In addition to the regular ICDS services, women residing in intervention group (IG) villages received: (1) six home visits by volunteers (one visit every three weeks) using "engagement packages" designed to improve knowledge, awareness, and attitudes towards immunisation. Engagement packages consist of visually appealing story cards, discussions, games and activities, delivered one-on-one or in small groups with friends, fathers, and other family members. Together, these activities help to cultivate confidence, raise awareness and create a space wherein the mother's capacity to make decisions on immunisation is recognised and supported; (2) three community mobilisation events involving activities, theatre, and discussion groups to identify problems related to immunisation in their communities, discuss possible causes and solutions, and give feedback on the project. Control group (CG) villages received community mobilisation through activities, events, and discussion groups to raise awareness on issues related to nutrition, diarrhoea prevention and treatment in their communities, and

give feedback on the project. A toll-free number for immunisation enabling anonymous queries and feedback was offered to all residents of IG and CG villages. Table 1 summarises study interventions.

Table 1. Study interventions

Activity	Intervention Group (IG) [2]	Control Group (CG)
Baseline survey[1]		
Randomisation[1]		
Home visit 0	Rapport formation; information	Rapport formation; information
Community Discussion 1	Project introduction; sharing district report card; skit (vaccination); toll-free number (vaccination)	Project introduction; sharing district report card; skit (ORS); toll-free number (vaccination)
Home visit 1	Story 1 (Key messages) • Timely vaccination can save children from life threatening illnesses (polio) • In case of queries, one should ask a local CHW (or toll free number) Activity: immunisation schedule	
Home visit 2	Story 2 (New messages) • Vaccination is free of charge and available at the local Anganwadi centre Activity: protect immunisation card	
Home visit 3	Story 3 (New messages) • Every vaccine has a specific purpose and all doses are required • Challenges occur in daily life, but one should avoid missing a vaccination dose • Even if the child has a minor illness, she or he can be vaccinated Activity: immunisation schedule	
Community Discussion 2	Discussion of barriers to immunisation and local solutions; toll-free number (vaccination); Activities: immunisation calendar; immunisation card; skit (vaccination)	Discussion of barriers to early child nutrition and local solutions; toll-free number (vaccination); Activities: skit
Home visit 4	Story 4 (New messages) • Place the right priority on vaccination – if one's child falls ill, one can incur expense and health risk Activity: immunisation card	
Home visit 5	Story 5 (New messages) • In case of service delivery problems, tell a responsible person (or toll-free number) • If a child's vaccine dose is missed, obtain it at the next opportunity Activity: immunisation card	
Home visit 6	Story 6 (New messages) • Vaccination benefits everyone (herd immunity). Activity: immunisation schedule	
Community Discussion 3	Feedback on project components (home visits, community discussions, toll-free number); suggestions for improvement	Feedback on project components (home visits, community discussions, toll-free number); suggestions for improvement
End line survey[1]		

[1] Identical for intervention and control groups

[2] Key messages were repeated for reinforcement; only new content is described

Interventions addressed individuals, households, and communities. While home visits were directed in the first instance to the mothers of young children enrolled in the study, activities were open to friends, neighbours, and other members of the household. Community events were open to all.

Outcomes

Primary outcomes

We established ex-ante criteria for feasibility of the main study related to processes for participant recruitment, randomisation, and retention. Specifically, we viewed the study as feasible if (i) 50% of villages approached would agree to participate and accept randomisation; (ii) 30 women per village could be recruited in 70% of villages; (iii) 50% of women were retained from baseline to end line. Below these thresholds, we judged that the study would not be feasible without major modifications.

Secondary outcomes

We studied process indicators related to implementation fidelity (ability to delivery interventions as planned) and two indicators of community response ((i) participation in community events; (ii) additional participants who joined the endline survey (as a measure of the indirect effect of interventions)). We also studied three proxy indicators of intervention impact on immunisation uptake. We described differences between IG and CG villages for two cluster-level outcomes: (i) use of the toll-free number; and (ii) monthly immunisation day footfall. (iii) We compared performance of individuals belonging to the IG versus CG on the change from baseline to endline survey on key indicators related to information

conveyed through the engagement packages and community events. There were no changes to outcomes after commencement of the trial.

Sample size

For a feasibility study, sample size is not established based on power to detect an anticipated intervention impact. We set the number of clusters at 12 as six clusters per study arm is a minimum for cluster comparisons using a t-test,[25] and for logistical and budgetary reasons. To facilitate statistical testing within clusters we fixed the number of households per village to be 30, but inflated this to 36 to account for potential non-response and missing values. We therefore sought to recruit 432 individual participants allocated equally between intervention and control villages. In all 12 villages, community discussions and the toll-free number were open to the entire community.

Randomisation

Sequence generation and allocation concealment

Villages were assigned to either intervention or control groups using simple randomisation with a 1:1 allocation following a computer-generated randomisation schedule. The random allocation sequence was generated at the CRCHUM by a professional statistician (MPS) using the R package blockrand[26] and kept in a password-protected computer. The statistician was not involved in study implementation. Prior to release of the randomisation code only the statistician had access to the allocation sequence. Randomisation code was released all at once and treatment groups assigned only after completion of all recruitment procedures and baseline measurements.

Implementation

Field team leaders enrolled clusters by contacting village officials in person to explain study aims and activities and request consent to participate. Subsequently, in each participating village, field team members directly approached a random sample of households to request their consent to participate in the baseline survey and pilot study. Enrolment occurred prior to randomisation. No advertisements were used for recruitment, and no incentives or rewards were offered for participation. Field team members informed households personally of their study group assignments.

Blinding

Due to the nature of the interventions, neither participants nor those involved in intervention delivery were blinded to group assignment. Data analysis was not masked. We took two measures to reduce the potential impact of knowledge of group assignment on study outcomes. (1) The study used a control intervention to enhance acceptability of randomisation and to conceal the true study hypothesis. (2) We hired independent surveyors for the end line survey to assess study outcomes. These surveyors were not informed of group assignment. They were told that our goal was to understand how mother's knowledge affects child health. Baseline and end line questionnaires encompassed immunisation, diarrhoea, and other aspects of child health.

Statistical methods

We used descriptive statistics (counts, frequencies, proportions) to assess study feasibility and processes. Descriptive statistics were also used to compare the IG and CG on cluster-level outcomes. We compared the IG and CG on individual-level outcomes reflecting change from baseline to end line survey on selected indicators using generalised estimating equations (GEE) regressions adjusted for village-level clustering using an exchangeable correlation structure. Additional analyses considered GEE models adjusted simultaneously for village-level clustering, maternal education and wealth quintile. These analyses included participants with complete data; complementary analyses explored results for participants with incomplete data.

The Pratham (New Delhi, India; approval date December 10, 2013) and CRCHUM (Montreal, Canada; approval number CE 12.391) research ethics committees granted permission for this study. The study will be prospectively registered in an international trial registry before starting the main trial.

RESULTS

Primary Outcomes

Village recruitment and the baseline survey occurred between January 12th and February 3rd, 2014. Four villages were replaced prior to randomisation, one due to failure to meet inclusion criteria, and three due to surveyor error during the baseline survey. A surveyor administered components of the baseline survey in the wrong order. Randomisation assignments were released to the core study team on February 4th, 2014 and communicated in person to all 12 villages on February 7th and 8th, 2014. The intervention began immediately thereafter and ran for four months as planned. The endline survey was initiated on May 27th and completed by June 30th, 2014.

Feasibility criteria related to recruitment, randomisation and retention were satisfied. [Figure 1] All villages contacted (100%, 16/16) agreed to participate and accepted randomisation. Thirty six women were recruited in 100% (12/12) of villages randomised. No clusters were lost to follow up. The main analysis included 86% (373/432) of participants, 90% (195/216) from the IG and 82% (178/216) from the CG.

[Figure 1 approximately here]

Baseline data

Table 2 presents characteristics of the study sample. There were clear baseline imbalances between intervention and control groups, with the CG having higher living standards, maternal education, and

proportions of children vaccinated. The 12 study villages had better access to electricity and health services and somewhat higher living standards than Hardoi district as a whole. Notwithstanding, the IG had lower proportions of children vaccinated as compared to the CG and to district averages.

Table 2. Characteristics of 12 villages and 432 households, mothers and children included in the pilot study

	Characteristics of participating villages						District[1]	
	Control *n*=6		Intervention *n*=6		Total N=12		N=60	
Village electrification	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
None	0	(0)	0	(0)	0	(0)	8	(13)
Less than 6 hours	0	(0)	2	(33)	2	(17)	30	(50)
More than 6 hours	6	(100)	4	(67)	10	(83)	22	(37)
Number of health centres								
0	0	(0)	0	(0)	0	(0)	2	(3)
1	3	(50)	5	(83)	8	(67)	25	(42)
2	2	(33)	1	(17)	3	(25)	16	(27)
3	0	(0)	0	(0)	0	(0)	13	(22)
4	1	(17)	0	(0)	1	(8)	4	(7)
Proportion in poorest 20%[2]								
Mean (SD) in %	14 (1)		26 (10)		20(11)		24	(15)
	Characteristics of participating households, mothers and children							
	Control *n*=216		Intervention *n*=216		Total N=432		N=1192	
Dwelling materials (floor, walls, roof) [3]	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Natural (kachcha)	31	(14)	59	(27)	90	(21)	389	(33)
Intermediate (Semi pucca)	154	(71)	129	(60)	283	(65)	720	(60)
Solid (Pucca)	31	(14)	28	(13)	59	(14)	83	(7)
Mother's education (years)								
None (0)	83	(38)	120	(56)	203	(47)	696	(58)
Some primary (1 to 5)	24	(11)	18	(8)	42	(10)	86	(7)
Some upper primary (6 to 8)	8	(4)	2	(1)	10	(2)	218	(18)
Some secondary (9 to 12)	101	(47)	76	(35)	177	(41)	192	(16)
Child immunisation card?								
No	249	(57)	337	(67)	586	(62)	680	(57)
Yes	188	(43)	170	(34)	358	(38)	512	(42)
Child Vaccination[4]								
None	12	(6)	14	(7)	26	(6)	58	(5)
Partial	161	(75)	178	(82)	339	(79)	794	(67)
DTP3	78	(36)	61	(28)	139	(32)	497	(42)
Full	43	(20)	24	(11)	67	(16)	340	(29)

[1.] Data for Hardoi district are from a representative sample of 60 villages (1192 households) collected in 2013 and included for purposes of comparison[15]

[2.] This is the proportion in the poorest wealth quintile. Wealth quintiles for this 12 village pilot study were calculated using items and methods similar to those for India's major national surveys. See [15]

[3.] Dwelling characteristics were assessed by observation using definitions drawn from India's major national surveys. See [15]

[4.] "Full immunisation" among children 12-23 months is defined as 1 dose of Bacillus Calmette-Guérin (BCG) vaccine, 3 doses of polio vaccine, 3 doses of diphtheria-pertussis-tetanus (DPT) vaccine, and 1 dose of measles vaccine.

Secondary Outcomes

Intervention fidelity: Of the six planned immunisation KTE home visits, an average of 5.9 visits were delivered to the 216 IG participants. Three rounds of community discussions were held as planned in all 12 villages.

Community response: (i) Community discussions: Community discussion 1 included 1210 adult participants (752 from IG villages and 458 from CG villages). Community discussion 2 involved 1140 participants (593 IG and 547 CG). Community discussion 3 involved 946 participants (604 IG and 342 CG).[Supplementary Table 1] (ii) Additional participants in the endline survey: 139 additional community members (96 (69%) IG; 43 (31%) CG) volunteered to take the endline survey.[Figure 1]

Toll-free number

IG and CG villages differed in use of the toll-free number, with more calls originating from IG villages (n=11) versus CG villages (n=3). Monthly call volume was lower than anticipated; there were 14 calls from the 12 villages over four months.

Immunisation day footfall

Inspection of monthly immunisation day footfall from April 2013 to May 2014 revealed no clear differences between IG and CG villages.[Supplementary Figure 1] Quality of administrative data was poor. One of six IG villages and one of six CG villages had no immunisation records. Four months of data were missing for the IG including two months during the intervention period. Two months of data were

missing for the CG, but none in the intervention period. Records were incomplete and often related to only one immunisation centre rather than to the entire village. The precise number of children eligible for vaccination in the catchment area was not known in any village.

Analysis of individual responses to baseline and end line surveys

Table 3 describes proportions of correct responses given by the 373 mothers who completed both baseline and endline surveys for selected indicators of knowledge and understanding about vaccination. Results were heterogeneous; regression analyses modelled the change from baseline to endline to clarify patterns of variation.[Table 4, Supplementary Table 2] General knowledge about vaccination improved in the IG (OR 2.38 [95% CI: 1.60 to 3.58], p-value <0.001) but not the CG (OR 1.29 [95% CI: 0.56 to 2.99], p-value 0.545). Ability to interpret the child's immunisation card did not improve in either study group. Knowledge of the vaccination calendar increased markedly in the IG but not the CG, for all doses except the birth dose.[Table 4] For these indicators, odds ratios for the intervention effect ranged from 7.55 to 18.25; adjustment for maternal education and wealth quintile resulted in larger IG effect sizes. [Table 4] Maternal education (ever having attended school) confounded the intervention effect in several analyses. Wealth quintile was not an important confounder in any analysis. [Table 4, Supplementary Table 2]

Table 3: Proportions of correct responses given by 373 participating mothers on selected indicators of knowledge and understanding about vaccination, by study group (*n* (%))

Indicator	Control (N=178)		Intervention (N=195)	
	Baseline *n*=178	End line *n*=178	Baseline *n*=195	End line *n*=195
General knowledge of vaccination[1]				
Vaccination protects against how many diseases?	102 (57)	113 (63)	90 (46)	131 (67)
Questions related to the immunisation card[2]				
What is the child's date of birth?	42 (23)	47 (27)	32 (16)	36 (18)
Why does the immunisation card have multiple boxes?	114 (64)	72 (40)	85 (43)	86 (44)
How many doses has the child received?	31 (17)	27 (15)	30 (15)	16 (8)
Which vaccine has the child received?	34 (19)	30 (17)	26 (13)	21 (11)
Questions related to the immunisation schedule[3, 4]				
Do you know the immunization schedule of your child? (yes)	20 (11)	111 (62)	21(11)	182 (93)
At birth	11 (6)	93 (52)	15 (8)	170 (87)
Dose at 1.5 months	4 (2)	31 (17)	7 (4)	148 (76)
Dose at 2.5 months	4(2)	22 (12)	5 (3)	156 (80)
Dose at 3.5 months	5 (3)	15 (8)	3 (2)	148(76)
Dose at 9 months	11 (6)	47 (26)	12 (6)	172 (88)

[1] Surveyors informed participants of the correct answer directly prior to asking the question. See [15]
[2] A sample filled vaccination card was used to elicit responses to these four questions. See [15]
[3] These are spontaneous responses to the question "Do you know the immunization schedule of your child?" If yes, please name all the doses." See [15]
[4] We recorded as correct all responses recommended in the Indian immunisation schedule; however, this table presents only doses for children less than 12 months.

Table 4. Univariate regression models describing knowledge of the vaccination schedule at end line versus baseline for 373 participating mothers, by dose and study group

Vaccine Dose[1]		Model 1[2]			Model 2[3]	
	OR	(95%CI)	p-value	OR	(95%CI)	p-value
Birth						
IG	5.23	(0.57 - 48.29)	0.145	5.52	(0.53 - 57.38)	0.152
CG	4.17	(1.51 - 11.57)	0.006	4.34	(1.62 - 11.61)	0.003
1.5 months						
IG	7.55	(3.25 - 17.29)	0.000	10.01	(3.51 - 28.58)	0.000
CG	1.45	(0.49 - 4.37)	0.500	1.35	(0.42 - 4.41)	0.614
2.5 months						
IG	14.11	(5.90 - 33.78)	0.000	18.56	(8.08 - 42.65)	0.000
CG	0.76	(0.27 - 2.11)	0.598	0.70	(0.21 - 2.29)	0.558
3.5 months						
IG	18.25	(7.43 - 44.83)	0.000	25.04	(8.79 - 71.3)	0.000
CG	0.43	(0.13 - 1.44)	0.170	0.38	(0.08 - 1.73)	0.209
9 months						
IG	11.30	(3.42 - 37.31)	0.000	15.37	(5.12 - 46.17)	0.000
CG	0.60	(0.34 - 1.05)	0.073	0.53	(0.27 - 1.03)	0.061

IG - intervention group; CG - control group

[1] These are spontaneous responses to the question "Do you know the immunization schedule of your child? If yes, please name all the doses."

[2] Models adjusted for village-level clustering.

[3] Models adjusted for village-level clustering, mother's education (mother attended school yes/ no), and wealth quintile.

Analysis of the 59 mothers lost to follow up revealed no significant differences with respect to the 373 mothers remaining in the study in terms of household characteristics, personal characteristics, or

baseline survey responses.[Supplementary Tables 3-5] The proportion of correct responses was generally higher among the 139 additional community participants who volunteered to take the end line survey, as compared to the 373 participating mothers. The child's father had the highest proportion of correct responses among all categories of participants.[Supplementary Tables 6-8; Supplementary Figure 2]

DISCUSSION

Key findings from the pilot study

We highlight six findings from the pilot study: (1) Pre-established criteria for feasibility of the planned main study related to recruitment, randomisation and retention were fully satisfied for clusters and individuals; (2) Intervention fidelity was excellent; (3) Community participation was high but weaker in the CG; (4) As hypothesised, use of a toll-free number was higher in the IG than in the CG. Notwithstanding, call volumes were low overall; (5) No clear conclusions could be drawn concerning trends in immunisation centre footfall; (6) Multiple analyses revealed a very strong effect of the immunisation intervention on individual participant learning, but results were variable across indicators.

Methodological lessons for the planned main study

Reflection on pilot findings and experiences suggests several lessons for the future study.

1. Study groups were unbalanced on characteristics likely to be related to study participation and child vaccination status, with IG participants systematically disadvantaged as compared to controls. (i) During the pilot, we adopted two strategies to enhance community partnership and ensure participation of households and individuals. First, we learned to cultivate support from influential members of the community and to seek their help in motivating others to join the study. Second, we diversified our field teams to include underrepresented groups. We view these strategies as essential to successful recruitment, randomisation, and retention. (ii)

Randomisation failed to achieve balance between study arms due to the small number of clusters involved in this pilot study. The future study should consider design options to improve balance and increase study power and precision, such as inclusion of a larger number of clusters, stratification,[25] and restricted randomisation using balancing criteria.[27] (iii) Substantively, pilot results show that the intervention was successful on many measures in a very disadvantaged population.

2. Although intervention fidelity was excellent, the value of a parallel control intervention was unclear. Through discussion with our study teams, we learned that that active presence of field staff in control villages lead to opportunities for contamination as villagers requested field team members to share information and advice on child health themes raised by the baseline survey. All content for the main study should likely be delivered through an intervention arm.
3. The first round of community discussions were delivered as one large gathering per village. In the control group, the first community discussion coincided with local religious festivals in two of the six control villages, while in one control village, people were reluctant to meet together due to caste and class divisions. The second and third community discussions were delivered in rounds of three to six smaller meetings per village, and groups were more homogeneous with respect to age, sex, and status. This strategy was more effective.
4. Use of a toll-free number was lower than anticipated. To our surprise, in endline discussions with the community we learned that the toll-free service was extremely valued. However, active presence of our field teams meant that questions were addressed preferentially to them. Toll-free and KTE intervention components should not be evaluated together.
5. Administrative data on immunisation was inadequate for scientific use. The Government of India is investing to improve vital statistics using biometric and digital technologies. Until this process

reaches maturity, the future main study should consider undertaking a census of participating villages at baseline to determine target population denominators.

6. Analysis of individual participant survey responses showed a compelling effect for some but not all components of the main vaccine intervention on proxy outcomes. (i) These results provide an evidence base to improve aspects of the main intervention prior to fielding the larger study. Different communications methods were used for the different components. (ii) Results also encourage us to consider the adequacy of our questionnaires. We used a previously developed survey with only marginal modifications.[15] Questions were only distantly related to the study interventions to ensure that both study groups had a reasonable chance to reply correctly. Questions related to the immunisation card may have been difficult to interpret. The main endpoint of the future study will be immunisation status rather than knowledge or health literacy, avoiding some of these difficulties. (iii) The intervention had an indirect effect. In our sample, community participants had higher scores than the mothers who were the target participants, with fathers having the highest scores on average. This likely reflects how gender biases shape ability to learn over the life course in this context. The community sample was not randomly selected.

Conclusions

This pilot study provided rich lessons to inform design of a future trial and to refine interventions. Criteria related to feasibility of the main study were satisfied. Based on our extensive knoweldge of the district,[15 28] we believe that evidence of feasibility can be generalised to other settings in Hardoi,

Uttar Pradesh. In addition, cluster-randomised trials of participatory learning interventions have been conducted in similar locations,[29 30] lending support to our assessment that the study is feasible.

This pilot study is part of a series of targeted research efforts encompassing formative and evaluative dimensions. Prior to the main trial, we will continue to refine our interventions to ensure that they are effective, responsive to policy context, scalable, and sustainable. In December 2014, the Government of India announced a new strategy for periodic intensification of routine immunisation in 201 high priority districts including Hardoi.[31] Week-long immunisation sessions will be offered four times per year to improve coverage levels. Our NGO partner, Pratham Education Foundation, has achieved considerable success in improving child education in India often through literacy campaigns.[32 33] Pratham has been able to sustain large cadres of community volunteers through non-financial rewards enabling low cost operation at national scale. With their guidance, we may simplify and streamline our interventions to be deliverable in campaign mode.

Lessons from this pilot study give us confidence that we can successfully design and conduct a cluster randomised trial to assess the effectiveness of KTE interventions to improve vaccination coverage among children less than 24 months of age in rural northern India.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no conflicts of interest in relation to this work.

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AUTHOR CONTRIBUTIONS

MJ had principal responsibility for conception and design of the study, interpretation of data, and drafting of the manuscript; DC contributed to data acquisition and revision of the manuscript for important intellectual content; GKK had principal responsibility for statistical analysis and revised the manuscript for important intellectual content; SD contributed to data acquisition and revision of the manuscript for important intellectual content; MPS contributed to conception and design of the study, analysis and interpretation of the data, and revision of the manuscript for important intellectual content; JKS contributed to conception and design of the study and revision of the manuscript for important intellectual content; SP contributed to conception and design of the study and revision of the manuscript for important intellectual content.

All authors approved the final version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA SHARING STATEMENT

Statistical code and data are available from the corresponding author.

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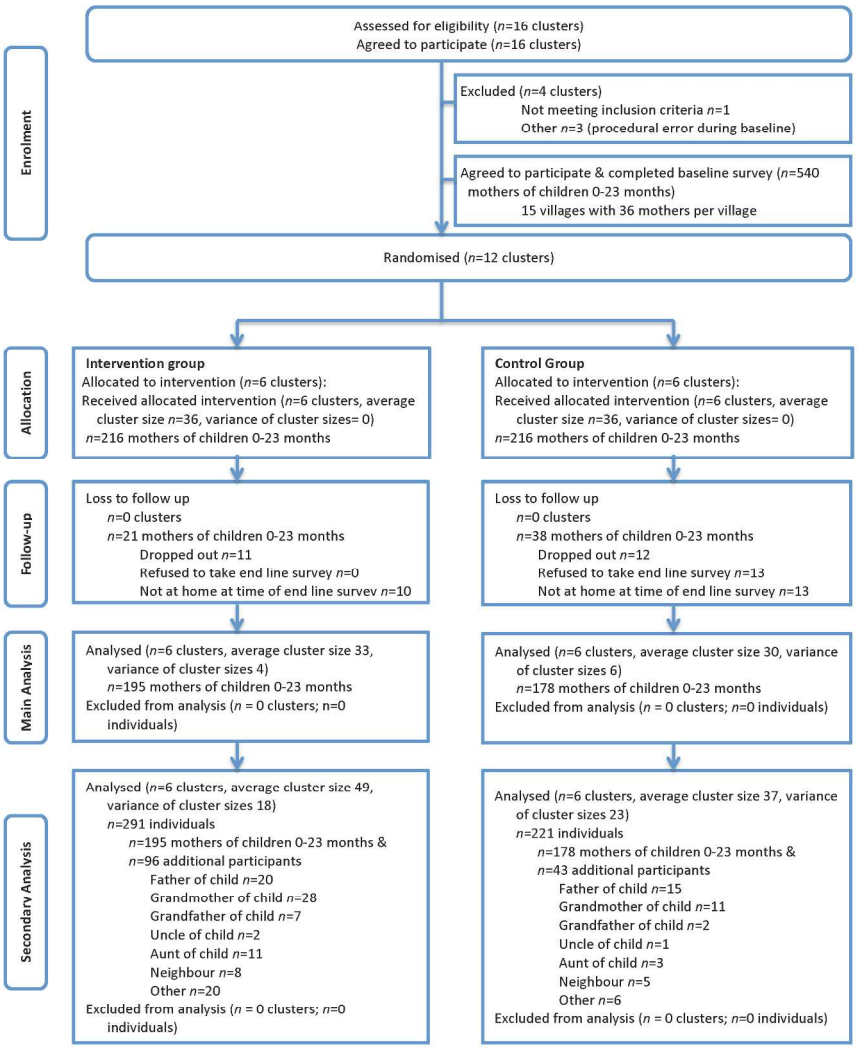
Figure 1. Flow diagram of progress of clusters and individuals through the study



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APPENDIX FOR THE STUDY: INTERVENTIONS TO INCREASE IMMUNISATION COVERAGE AMONG CHILDREN 12-23 MONTHS OF AGE IN INDIA THROUGH PARTICIPATORY LEARNING AND COMMUNITY MOBILISATION: PILOT STUDY FOR A CLUSTER RANDOMISED TRIAL (JOHRI ET AL., 2015)

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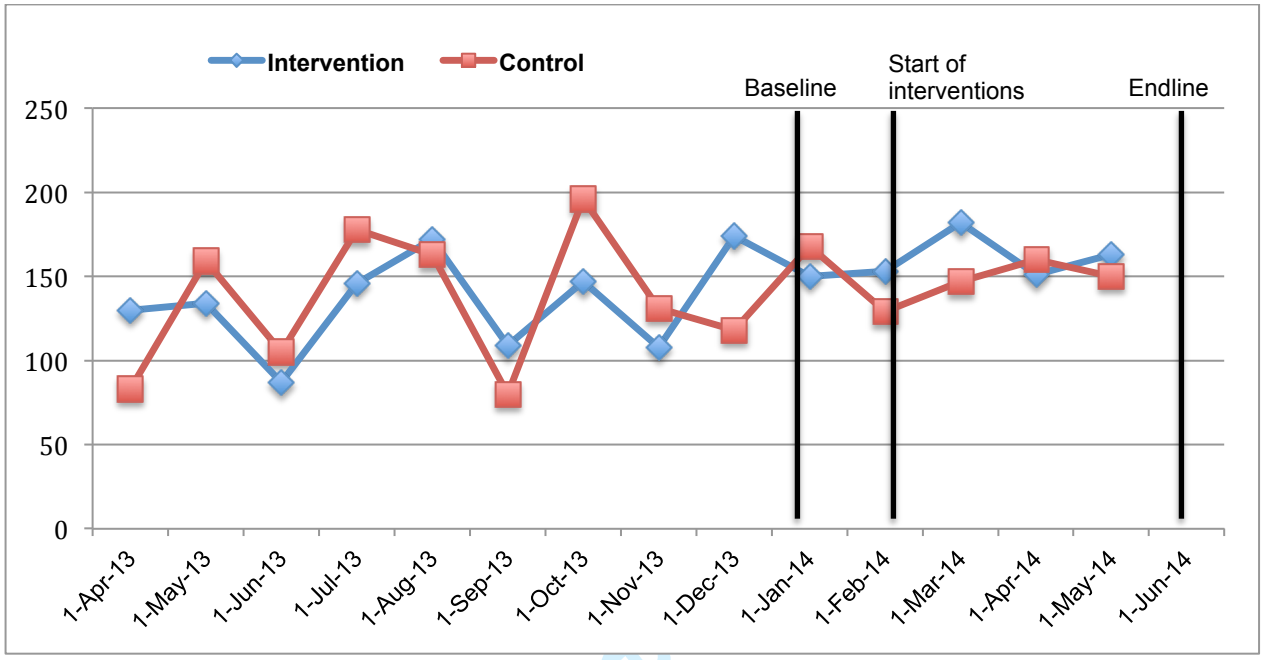
Supplementary Figure 1. Total number of children vaccinated in intervention and control villages, April 1st, 2013 to May 1st, 2014[1]



[1] A total of 12 villages participated in the pilot study, 6 villages in the intervention group and 6 in the control group

Supplementary Table 1: Full results of univariate regression models for selected indicators of immunisation intervention performance at end line versus baseline for 373 participating mothers, by dose and study group

General information about vaccination

Vaccination protects against how many diseases?	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	2.38	(1.60 - 3.58)	0.000	2.80	(1.72 - 4.56)	0.000
CG (end line vs. baseline)	1.29	(0.56 - 2.99)	0.545	1.36	(0.50 - 3.72)	0.543
Mother attended school				4.53	(3.01 - 6.81)	0.000
Quintile of wealth index						
Q1 (poorest)				Ref.		
Q2				1.03	(0.56 - 1.90)	0.924
Q3				0.95	(0.58 - 1.57)	0.853
Q4				1.53	(0.94 - 2.49)	0.085
Q5				2.14	(0.89 - 5.15)	0.091

Knowledge of the immunisation card

What is the child's date of birth? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	1.15	(0.95 - 1.40)	0.148	1.20	(0.94 - 1.53)	0.137
CG (end line vs. baseline)	1.16	(0.99 - 1.36)	0.075	1.21	(0.99 - 1.48)	0.061
Mother attended school				20.89	(8.35 - 52.28)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.71	(0.66 - 4.46)	0.272
Q3				1.54	(0.71 - 3.33)	0.27
Q4				2.14	(0.93 - 4.91)	0.073
Q5				3.58	(1.66 - 7.72)	0.001

Why does the immunisation card have multiple boxes? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value

IG (end line vs. baseline)	1.02	(0.54 - 1.92)	0.948	1.02	(0.52 - 2.03)	0.948
CG (end line vs. baseline)	0.38	(0.14 - 1.07)	0.066	0.34	(0.11 - 1.04)	0.059
Mother attended school				2.38	(1.89 - 3.01)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.67	(0.47 - 0.95)	0.024
Q3				0.87	(0.51 - 1.51)	0.632
Q4				1.07	(0.65 - 1.74)	0.799
Q5				1.78	(1.08 - 2.94)	0.024

How many doses has the child received? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	0.49	(0.26 - 0.94)	0.031	0.43	(0.21 - 0.88)	0.02
CG (end line vs. baseline)	0.85	(0.66 - 1.09)	0.193	0.82	(0.61 - 1.11)	0.206
Mother attended school				24.73	(8.90 - 68.73)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.19	(0.47 - 3.01)	0.716
Q3				1.52	(0.50 - 4.60)	0.457
Q4				1.28	(0.48 - 3.44)	0.618
Q5				3.11	(1.49 - 6.49)	0.002

Which vaccine has the child received? (Correct)	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	0.79	(0.47 - 1.30)	0.349	0.75	(0.41 - 1.38)	0.357
CG (end line vs. baseline)	0.86	(0.67 - 1.10)	0.229	0.84	(0.62 - 1.12)	0.233
Mother attended school				8.76	(3.97 - 19.36)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				1.43	(0.61 - 3.36)	0.416

Q3	1.62	(0.78 - 3.32)	0.193
Q4	1.36	(0.48 - 3.84)	0.558
Q5	4.00	(1.60 - 10.00)	0.003

Knowledge of the immunisation schedule (by dose)

	Model 1			Model 2		
Birth Dose	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	5.23	(0.57 - 48.29)	0.145	5.52	(0.53 - 57.38)	0.152
CG (end line vs. baseline)	4.17	(1.51 - 11.57)	0.006	4.34	(1.62 - 11.61)	0.003
Mother attended school				1.37	(0.79 - 2.36)	0.258
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.45	(0.19 - 1.10)	0.080
Q3				0.48	(0.18 - 1.25)	0.131
Q4				0.36	(0.12 - 1.03)	0.057
Q5				0.63	(0.16 - 2.59)	0.527

	Model 1			Model 2		
Dose at 1.5 months	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	7.55	(3.25 - 17.29)	0.000	10.01	(3.51 - 28.58)	0.000
CG (end line vs. baseline)	1.45	(0.49 - 4.37)	0.500	1.35	(0.42 - 4.41)	0.614
Mother attended school				2.74	(1.66 - 4.53)	0.000
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.69	(0.36 - 1.33)	0.270
Q3				0.59	(0.24 - 1.46)	0.257
Q4				0.53	(0.25 - 1.12)	0.096
Q5				0.83	(0.46 - 1.52)	0.553

	Model 1			Model 2		
Dose at 2.5 months	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	14.11	(5.90 - 33.78)	0.000	18.56	(8.08 - 42.65)	0.000
CG (end line vs. baseline)	0.76	(0.27 - 2.11)	0.598	0.70	(0.21 - 2.29)	0.558

Mother attended school				2.26	(1.12 - 4.53)	0.022
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.81	(0.47 - 1.39)	0.436
Q3				1.02	(0.47 - 2.22)	0.964
Q4				0.48	(0.22 - 1.07)	0.073
Q5				0.89	(0.44 - 1.82)	0.756

Dose at 3.5 months	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	18.25	(7.43 - 44.83)	0.000	25.04	(8.79 - 71.3)	0.000
CG (end line vs. baseline)	0.43	(0.13 - 1.44)	0.170	0.38	(0.08 - 1.73)	0.209
Mother attended school				2.17	(0.93 - 5.06)	0.074
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.69	(0.34 - 1.42)	0.316
Q3				0.75	(0.33 - 1.70)	0.491
Q4				0.42	(0.17 - 1.03)	0.058
Q5				1.01	(0.27 - 3.86)	0.983

Dose at 9 months	Model 1			Model 2		
	OR	(95%CI)	P_value	OR	(95%CI)	P_value
IG (end line vs. baseline)	11.30	(3.42 - 37.31)	0.000	15.37	(5.12 - 46.17)	0.000
CG (end line vs. baseline)	0.60	(0.34 - 1.05)	0.073	0.53	(0.27 - 1.03)	0.061
Mother attended school				2.41	(1.03 - 5.62)	0.041
Quintile of wealth index						
Q1 (poorest)	ref					
Q2				0.67	(0.22 - 2.08)	0.488
Q3				0.58	(0.17 - 2.01)	0.386
Q4				0.93	(0.33 - 2.60)	0.891
Q5				0.90	(0.22 - 3.63)	0.886

Model 1 adjusted for village-level clustering.
Model 2 adjusted for village-level clustering, mother's education (mother attended school yes/ no), and wealth quintile.

Analysis of loss to follow up (Supplementary Tables 2 – 4)

Supplementary Table 2: Household characteristics of 59 women lost to follow up (A) with 373 women who participated in the pilot study (B)

		Baseline survey only (A)		Baseline & Endline surveys (B)		
Caracteristics of household		n	mean(sd)	n	mean(sd)	T test (B-A)
Number of people living in the household (mean (sd))		59	6.2 (2.7)	373	6.9 (2.9)	0.1280
Number of rooms in the house (mean (sd))		59	1.9(1.4)	373	1.8 (1.5)	0.7595
Type of family		n	%	n	%	P-value
	Nuclear	29	49.2	187	50.1	0.889
	Joint	30	50.8	186	49.9	
Religion of head of household						
	Hindu	49	83.0	330	88.5	0.238
	Muslim	10	17.0	43	11.5	
Education level of father (years)						
	None(0)	11	18.6	99	26.5	0.573
	Some Primary (1 to 5)	13	22.0	81	21.7	
	Some upper primary (6 to 8)	2	3.4	8	2.1	
	Some secondary (9 to 12)	33	55.9	185	49.6	
Father's employment status						
	Daily wages	21	35.6	155	41.5	0.211
	Work on own land	15	25.4	111	29.8	
	Fixed Income	13	22.0	41	11.0	
	Self employed	8	13.6	50	13.4	
	Unemployed	2	3.4	16	4.3	
Type of Dwelling						
	Natural (kachcha)	10	17.0	80	21.5	0.594
	Intermediate (Semi pucca)	39	66.1	244	65.4	
	Solid (Pucca)	10	16.9	49	13.1	
Type of flooring						
	Sand/dung	50	84.7	328	87.9	0.762
	Cement/stone/brick	5	8.5	23	6.2	
	Other	4	6.8	22	5.9	
Wealth index of household						
	Poorest (quintile 1)	8	13.6	80	21.4	0.733
	Second	14	23.7	81	21.7	
	Middle	12	20.3	65	17.4	
	Fourth	13	22.0	75	20.1	
	Richest (quintile 5)	12	20.3	72	19.3	
Possess child's immunisation card?						
	No	38	64.4	409	54.8	0.154
	Yes	21	35.6	337	45.2	

Vaccine coverage (0 to 8 doses)					
None (0)	4	6.8	22	5.9	0.965
Partially vaccinated (1 to 7)	46	78.0	293	78.5	
Fully vaccinated (8)	9	15.2	58	15.5	

Supplementary Table 3: Characteristics of 59 women lost to follow up (A) and 373 women who participated in the pilot study (B)

	Baseline survey only (A)		Baseline & Endline (B)		
Participant Characteristics	n	Mean (sd)	n	Mean (sd)	p- value
Mother's age (mean (sd))	59	26.0 (3.6)	371	26.1(4.5)	0.8164
Education level of mother (years)	n	%	n	%	
None (0)	24	40.7	179	48.0	0.255
Some Primary (1 to 5)	3	5.1	39	10.5	
Some upper primary (6 to 8)	2	3.4	8	2.1	
Some secondary (9 to 12)	30	50.8	147	39.4	
Mother's employment status					
Daily wages	1	1.7	0	0.0	0.052
Work on own land	0	0.0	2	0.5	
Self employed	0	0.0	3	0.8	
Housewife	58	98.3	368	98.5	
Place of delivery of child					
Government hospital	36	61.0	205	55.0	0.895
Private hospital	2	3.4	18	4.8	
At home	21	35.6	148	39.7	
On the way to hospital	0	0.0	1	0.3	
Other	0	0.0	1	0.2	

Supplementary Table 4: Comparison of number of correct responses to selected questions for 59 women lost to follow up (A) and 373 women who participated in the pilot study (B)

Indicator	Baseline only (A)		Baseline & Endline (B)		
	n	%	n	%	p- value
Vaccination protects against how many diseases?	36	61.0	192	51.5	0.172
What kind of water to prepare ORS?	47	79.7	298	80.5	0.874
What is first step in preparing ORS?	49	83.0	293	79.2	0.493
What is the child's date of birth?	12	20.3	74	20.1	0.960
Why does the immunisation card have multiple boxes?	37	62.7	199	53.8	0.200
How many doses has the child received?	10	17.0	61	16.5	0.929
Which vaccine has the child received?	10	17.0	60	16.2	0.887

Analysis of additional community participants who joined the end line survey (Supplementary Tables 5-7; Figure 2)

Supplementary Table 5: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by study group (*n* (%))

	Main analysis: 373 mothers present at baseline and end line						Secondary Analysis: 139 participants					
	Control n=178		Intervention n=195		Total N=373		Control n=43		Intervention n=96		Total N=139	
	n	%	n	%	n	%	n	%	n	%	n	%
Vaccination protects against how many diseases?	113	63.5	131	67.2	244	65.4	32	74.4	79	82.3	111	79.9
What kind of water to prepare ORS?	164	92.1	163	84.0	327	87.9	40	95.2	85	89.5	125	91.2
What is first step in preparing ORS?	162	91.0	168	86.6	330	88.7	40	93.0	80	84.2	120	87.0
What is the child's date of birth?	47	26.4	36	18.6	83	22.3	17	39.5	37	38.9	54	39.1
Why does the immunisation card have multiple boxes?	72	40.5	86	44.3	158	42.5	24	55.8	52	54.2	76	54.7
How many doses has the child received?	27	15.2	16	8.3	43	11.6	10	23.3	18	18.8	28	20.1
Which vaccine has the child received?	30	16.9	21	10.8	51	13.7	13	30.3	29	30.2	42	30.2
Do you know the immunization schedule of your child?[1]	111	62.4	182	93.3	293	78.5	19	44.2	68	70.8	87	62.6

[1] As declared by the respondent (not necessarily correct)

Supplementary Table 6: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by study group[1]

	Community, N=139		Mothers, N=373		P- value
	n	%	n	%	(B-A)
Vaccination protects against how many diseases?	111	79.9	244	65.4	0.002
What kind of water to prepare ORS?	125	91.2	327	87.9	0.290
What is first step in preparing ORS?	120	87.0	330	88.7	0.585
What is the child's date of birth?	54	39.1	83	22.3	0.000
Why does the immunisation card have multiple boxes?	76	54.7	158	42.5	0.014
How many doses has the child received?	28	20.1	43	11.6	0.013
Which vaccine has the child received?	42	30.2	51	13.7	0.000
Do you know the immunization schedule of your child?[2]	87	62.6	293	78.5	0.000

[1] We used the χ^2 test to compare results between groups
[2] As declared by the respondent (not necessarily correct)

Supplementary Table 7: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by type of participant

	Total additional community participants (B), N=139		Father of child, N=35		Grand mother of child,N=39		Other , N=65		Mother of child (A), N=373	
	n	%	n	%	n	%	n	%	n	%
Vaccination protects against how many diseases?	111	79.9	30	85.7	26	66.7	55	84.6	244	65.4
What kind of water to prepare ORS?	125	91.2	29	85.3	37	94.9	59	92.2	327	87.9
What is first step in preparing ORS?	120	87.0	29	82.9	33	84.6	58	90.6	330	88.7
What is the child's date of birth?	54	39.1	22	64.7	5	12.8	27	41.5	83	22.3
Why does the immunisation card have multiple boxes?	76	54.7	23	65.7	15	38.5	38	58.5	158	42.5
How many doses has the child received?	28	20.1	11	31.4	5	12.8	12	18.5	43	11.6
Which vaccine has the child received?	42	30.2	17	48.6	5	12.8	20	30.8	51	13.7
Do you know the immunization schedule of your child?[1]	87	62.6	13	37.1	28	71.8	46	70.8	293	78.5

[1] As declared by the respondent (not necessarily correct)

Supplementary Figure 2: Comparison of correct responses to selected questions on the end line survey for 373 women who participated in the pilot study (A) and 139 additional community participants who volunteered to take the end line survey (B), by type of participant