Study Title: Enhancing Health Care Access with Cellular Technology

NCT Number: NCT03180138

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Study design and participants
We prospectively enrolled children 24 months and younger and pregnant women from a rural community in the Mewat region located within the state of Haryana, India from July 11, 2016 to July 20, 2017. Recruitment and follow up were performed concurrently, though the recruitment target was met on February 11, 2017. The study was administered by Bal Umang Drishya Sanstha (BUDS), a New Delhi based non-profit organization with a focus on child health. This study was approved by the Research Ethics Committees of BUDS, New Delhi, India and the Johns Hopkins University, Baltimore, MD, USA. This trial is registered with ClinicalTrials.gov, number NCT03180138.

Study Procedures
An encrypted, cloud-based software platform developed by Royal Datamatics Pvt Ltd (RDPL), New Delhi, India was used for record keeping and delivery of automated mobile-phone reminders and compliance-linked incentives (Supplementary Figure 1). Any child 24 months or younger at the time of enrollment, with a mobile-phone in the household and the ability of their caregiver to provide written informed consent were considered eligible for this study. After obtaining written informed consent from the caregiver, basic demographic information, Global Positioning System (GPS)-location and caregiver's finger biometrics were collected. While the standard of care in this setting involves the use of written immunization records (cards and records at the local primary health center) and verbal notification of follow up visits, record keeping for all groups in this study, including the control group, was performed using the software platform. Eligible subjects were randomly assigned to one of three study groups: self-returns with software platform for record keeping (control), automated mobile-phone reminders alone, and automated reminders with compliance-linked incentives in the form of mobile-phone talk-time. At the time of enrollment, data on prior immunizations received by the child were obtained from government-issued immunization cards provided by the families. If cards were unavailable or lost, immunization records were verified using written records at the local primary health center. The government-run National Immunization program (Supplementary Table 1) provided and administered the immunizations. The date for the next scheduled immunization visit was provided at each follow up by the government staff and entered into the software platform by the field workers. Each follow up visit was also correlated with the scheduled return date (if recorded in the system) of the administered immunization. Since finger identification is unreliable in young children,[13, 14] the child's name along with their caregiver's fingerprint was used to ensure positive identification of individual children at every visit. The GPS coordinates (longitude and latitude) were also recorded at recruitment and at each follow up visit. All users (field staff and study team) were identified and logged onto the software platform using biometric identification. For the study groups receiving automated reminders, Short Message Service (SMS) in the local language (Hindi) were sent. At follow up visits, mobile-phone minutes equivalent to INR 30 (~USD 0·5) per completed immunization were provided in the compliance-linked incentives group. The amount of incentive was determined after input from the local investigators as well as the community workers. All data transfers and compliance-linked incentives transactions were automated and occurred in real-time.

Randomization and masking
Randomization was stratified by group (young children or pregnant) using a block randomization algorithm (block size of six), but in the current manuscript, only data for children is presented. All caregivers were informed of their child's group assignment and study field staff had access to group assignments for individual patients at the time of recruitment or follow up visits; however, all other study team members were blinded to the group assignments until the end of the study and after analysis of the blinded groups.

End Points
Immunization coverage was the primary outcome of the study and was calculated for each child as the proportion of the total number of immunizations received divided by the total number of immunizations required at the time of measurement (i.e. at enrollment, end of study, etc.). We also calculated the cost in mobile-phone messaging and compliance-linked incentives. Timeliness of immunizations was a secondary outcome measure and was defined as the proportion of immunizations administered before or within 14 days after the scheduled date recorded during the study.

Authentication and follow up: The field staff were locally recruited and trained prior to the study. A pilot run of the software platform was performed at the study site in May-June 2016 to assess web and mobile-phone connectivity and to ensure that all operations performed optimally in real-time. At the start of the study, each mobile-phone was authenticated by a two-step process using an automated Short Message Service (SMS) verification code sent to the caregiver's mobile-phone during enrollment. The authenticated mobile-phone would receive a welcome message which was verified by the field worker. For the group receiving compliance-linked incentives, an additional authenticated step was utilized to ensure that mobile-phone on different carriers could receive automated incentives. The field worker identified the carrier by inspecting the mobile-phone screen or the SIM card and entering this information into the software platform. This immediately triggered delivery of mobile-phone talk-time equivalent to Indian Rupee (INR) 20 (~USD 0·33) to the caregiver's mobile-phone, which was then manually verified by the field worker. INR 30 (~USD 0.50) per completed immunization was provided subsequently to this group. Pre-scripted instructions were verbally provided at recruitment and at each follow up visit as follows: caregivers of children assigned to the control group were informed to come back for immunization at the next scheduled date, caregivers of children assigned to automated mobile-phone reminders alone were informed to come back for immunization on the date indicated by the automated mobile-phone reminder and caregivers of children assigned to automated reminders with compliance-linked incentives were informed to come back for immunization on the date indicated by the automated mobile-phone reminder, and that they would receive a specified amount of mobile-phone talk-time at the follow up visit.

Biometric identification: Biometric information (right index finger print) for the caregiver was collected at enrollment and verified by scanning the same finger seven times. In rare cases where the right index finger was not reliable, the right thumb, left index finger or left thumb was used in that order. Additional caregivers could be added during follow up visits and mobile numbers for caregivers could also be updated, but these procedures required the same verification process as described earlier.

Automated reminders and compliance-linked incentives: For the study groups receiving automated reminders, SMS messages in the local language (Hindi) comprising the name of the child and the return date for the next scheduled immunization visit were sent. For the group receiving compliance-linked incentives an SMS message in Hindi stating that mobile-phone talk-time [in Indian Rupee (INR)] would be received on successful completion of the scheduled visit was sent simultaneously with the automated reminder. SMS messages were sent at 8:00 AM Indian Standard Time two days before and on the scheduled day of the immunization and messages were no longer than two sentences. For children who did not return on or before the scheduled date, two additional automated SMS reminders were sent the day after and seven days after the scheduled return date. At follow up visits, mobile-phone minutes equivalent to INR 30 (~USD 0·5) per completed immunization were provided in the compliance-linked incentives group. Immunizations received by a subject elsewhere during the study could also be added to the immunization records for both study groups and the control group, but compliance-linked incentives were only provided for immunizations registered by the software platform in the appropriate study group. Automated reminders were sent to all verified caregivers for a given child, but compliance-linked incentives were only provided to the primary caregiver's mobile-phone (identified during enrollment). All data transfers and compliance-linked incentives transactions were automated and occurred in real-time. We also calculated the cost in mobile-phone messaging and compliance-linked incentives. Since automated reminders were sent to multiple verified caregivers for each child, the costs for mobile-phone messaging (USD 0·0048 per message) was a cumulative of all messages send to all caregivers. However, compliance-linked incentives were only provided to the primary caregiver's mobile-phone and these costs were also included.

Statistical Analysis Plan

Sample size: Prior to the study, we anticipated that our best intervention would increase the baseline immunization coverage by least 20% compared to the control group. Assuming up to a 20% exclusion rate, we calculated that a sample of size 175 per group would yield us 90% power at 5% level of significance for this outcome.

Statistical analysis: Baseline data across the three study groups was summarized using either median and inter-quartile range (IQR) or frequencies and percentages. Multivariable Poisson regression analysis was used to estimate adjusted immunization rates in the two test study groups with the control group as reference. To compare immunization coverage at enrollment and at the end of the study, the incidence rate ratio was calculated accounting for median patient days in the study and the number of subjects for each intervention group. Unadjusted immunization coverage for each study group was calculated with Poisson exact 95% confidence intervals. Multivariable Poisson regression analysis was used to estimate adjusted immunization rates in the two test study groups with the control group as reference. Comparison between groups for timeliness of immunization was calculated using the Fisher-exact test. Data analysis was performed using Stata Version 14 (StataCorp LLC, College Station, TX USA) or GraphPad Prism Version 6·05 (La Jolla, CA 92037 USA).