Using Automated Voice Calls to Improve Adherence to Iron Supplements During Pregnancy: A Pilot Study

Niranjan Pai1, Pradnya Supe2, Shailesh Kore2, Y.S. Nandanwar2, Aparna Hegde3, Edward Cutrell1, William Thies1

1 Microsoft Research India 2 Lokmanya Tilak Municipal Medical College 3 ARMMAN

Contact: thies@microsoft.com

ABSTRACT
For years, researchers have explored the use of mobile phone reminders to improve adherence to medication. However, few studies have measured the direct medical benefit of those reminders, especially for low-literate populations in the developing world. This paper describes the use of automated voice calls to promote adherence to iron supplements among pregnant women in urban India. Unlike prior studies, we assess impact via a direct measurement of hemoglobin (Hb) levels in the blood. We enrolled 130 pregnant women from a low-income area of Mumbai, India and randomly assigned them to control and treatment groups. Both groups received a counseling session and a free supply of medication. The treatment group also received short audio messages, three times per week for a period of three months, encouraging them to take iron supplements. Results suggest that automated calls positively impacted Hb levels. However, because we could only recover 79 women for follow-up, and the effect size was small, our results lack statistical power (average change in Hb = 0.43 g/dL, 95% CI = -0.13 - 0.98 g/dL, p=0.13). We conclude that automated calls deserve further consideration for reducing maternal anemia, and we share our lessons learned for the benefit of future interventions.

Categories and Subject Descriptors
K.4 [Computers and Society]; H.5.2 [Information Interfaces and Presentation]: User Interfaces

General Terms
Human Factors, Measurement, Design

Keywords
mHealth, randomized controlled trial, interactive voice response, anemia, iron supplementation, pregnancy, India

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1. INTRODUCTION
The global spread of mobile phones has ignited broad aspirations regarding the potential role of technology in improving health in impoverished communities. However, mHealth interventions to date have often fallen short of these expectations. While international organizations have tracked hundreds of mHealth pilots [56, 57], very few have been taken to scale. This situation has led Uganda to declare a moratorium on new mHealth projects, until a coherent strategy can be formulated [58]. South Africa has also banned pilots of new electronic medical records systems [58]. Moving forward, governments and policymakers will look to the research community for rigorous, evidence-based recommendations on how to proceed with mHealth.

Unfortunately, the research literature up until now has little to offer in the way of rigorous evidence on mHealth interventions, a situation decried by many scholars [59, 60, 61]. The current status is nicely captured in a recent pair of comprehensive reviews by Free et al., who examine a total of 117 randomized controlled trials of mHealth projects [62, 63]. With the exception of two recent studies demonstrating impact of text-message reminders on treatment adherence in Kenya [64, 65], the reviews identify few high-quality trials undertaken outside of high-income countries. One of the barriers to quality is that the outcomes measured are only indirect indicators of health. The authors conclude that “high quality trials measuring clinical outcomes are needed”.

In this paper, we gather new evidence regarding the benefits of an mHealth intervention in a developing region. To the best of our knowledge, this paper is the first to measure the clinical impact of automated voice calls on medication adherence in a low-income setting. This fills an important gap in prior research on developing-country contexts, which either relies on text-messaging reminders that are inaccessible to low-literate populations [64, 65] or uses indirect measures of adherence that may be inaccurate [49, 50, 51]. While our study lacks the statistical power needed to draw independent conclusions, it suggests that further research is warranted in order to evaluate the intervention at a larger scale.

The specific focus of our work is to reduce anemia among low-income pregnant women in urban India. In India, 84% of pregnant women are anemic [66]. Anemia is tied to 40%
of maternal deaths as well as the health of the child [67]. As the most common cause of anemia is inadequate dietary iron, many government hospitals provide free iron supplements to pregnant women. If taken regularly, these supplements can greatly reduce the incidence of anemia at term [68]. However, for reasons spanning forgetfulness, side effects, and socio-cultural beliefs [69, 70], many women do not adhere to the prescribed medication. Prior work in the ICTD community has sought to improve adherence to iron supplements using mobile aids for rural health workers [71].

Our intervention is a set of short audio messages, delivered to women via automated phone calls for three months during pregnancy. The messages are personal: recorded in the voice of the doctor that women met in the hospital and delivered at times of women’s choosing. Message contents are personalized to the current week of pregnancy, conveying positive emotions, addressing salient beliefs, and encouraging women to adhere to the medication.

We measured the impact of the intervention via a small-scale randomized controlled trial. We randomly assigned 130 low-income, anemic women to a control group or a treatment group, which received automated voice calls. Both groups received an initial counseling session and a free supply of iron supplements. Adherence was measured by analyzing hemoglobin \(^1\) (Hb) levels in the blood before and after three months. Unfortunately, the statistical power of the study was compromised due to difficulty of retrieving women for follow-up. In part due to the large number of women who changed their phone number during the trial, only 79 women completed the follow-up.

Our results are as follows. At enrollment, women had an average Hb level of 9.6 g/dL (well below the WHO cutoff for anemia, which is 11 g/dL). In the treatment group, average Hb levels increased by 0.32 g/dL, but the increase is not statistically significant (t(38)=−1.74, p=0.09). In the control group, average Hb levels decreased by 0.10 g/dL. The difference of differences between treatment and control groups shows a positive trend (0.43 g/dL on average), but it is not statistically significant (t(77)=−1.52, p=0.13).

While our result lacks statistical significance, the trend suggests that automated voice calls are worthy of further consideration for combating anemia in low-income pregnant women. In addition to this result, this paper contributes a systematic review of related literature; a contextual survey of pregnant women in urban India; a design rationale for our audio messages, including access to the messages for reuse by others; and recommendations for improving participant follow-up. We hope that by disseminating the lessons learned in this exploratory study, we can help to guide future researchers in establishing rigorous evidence in support of mHealth interventions.

2. RELATED WORK
To situate our study relative to others, we conducted a systematic literature review. We searched PubMed, IEEE Xplore, and the ACM Digital Library for studies utilizing phones to improve medication adherence. On PubMed and IEEE Xplore, we included all studies that contained both an adherence keyword and a phone keyword in the title or abstract, with at least one of the keywords appearing in the title. For adherence keywords, we used “adherence”, “adhere”, “adhered”, “compliance”, “comply”, and “complied”. For phone keywords, we used “phone”, “phones”, “telephone”, “telephones”, “interactive voice”, “voice response”, “automated calls”, and “automated voice”. For the ACM Digital Library, we used a smaller set of keywords due to the absence of advanced boolean search capabilities. We searched for papers whose abstract contained either: “medication” and “adherence”; “medication” and “compliance”; “phone” and “adherence”; or “phone” and “compliance”. We subsequently examined all references in found review articles [1-30] (except for six that we could not find online [25-30]) as well as papers most closely related to ours [49-55], looking for additional references that utilized automated calls for medication adherence. We found only one such paper that was not revealed by our initial search [40].

This process resulted in 1,100 unique papers. First we narrowed the result set to the intended scope, which is the use of phones to improve medication adherence. Then we evaluated each paper for overlap with the two key elements of our study: (i) accessibility to low-literate populations in the developing world (i.e., using voice calls instead of text or expensive devices), and (ii) evaluating the impact on those populations using a direct biological measurement of adherence. The title and abstract were often sufficient to perform this assessment, though we consulted the full-text when needed.

The outcome of our review is illustrated in Figure 1. Starting with 1,100 papers, we iteratively filtered them as follows:

- 654 papers do not look at medication adherence. Often they look at other kinds of adherence, such as smoking cessation, weight loss, medical appointments, clinical protocols, sleep apnea, etc., while sometimes they deal with unrelated topics. We restrict our attention to medication adherence, which has its own dedicated literature; other kinds of adherence are out of scope.

- 30 papers are reviews of other studies on medication adherence [1-30]. We examined the full-text of each paper, except for some that we were unable to attain [25-30], to search for additional overlap with our paper. One paper provides a particularly useful review of automated calls in healthcare [2].

- 259 papers contain only a design proposal, needs assessment, opinion piece, or prototype system. Each paper in this category either: (i) lacks a user trial, (ii) lacks any role for technology, or (iii) is only a methodological contribution (no intervention).

- 26 papers offer technical interventions for medication adherence, but depend on devices or services other than phones. Examples include wearable sensors, mediated face-to-face counseling, etc.
1,100 papers matching search criteria

Not focused on medication adherence → 654 papers

Reviews of other studies → 30 papers [1-30]

Design prototypes and needs assessments → 259 papers

Focused on devices or services other than phones → 26 papers

Does not use automated voice calls

Live calls → 69 papers

SMS → 30 papers

Smart phones → 7 papers

Automated voice calls without biological measure of adherence

Rich-country context → 18 papers [31-48]

Developing world → 3 papers [49-51]

Automated voice calls with biological measure of adherence

Rich-country context → 4 papers [52-55]

Developing world → NO WORK PRIOR TO THIS PAPER

Figure 1: Overview of the literature review.

- **106 papers** use phones for medication adherence, but do not use automated voice calls. 69 papers use live calls, 30 papers use SMS, while 7 papers use smart phones. (Additional papers in these categories could be discovered with other keywords, e.g., “SMS” or “text messaging”. However, it was not our goal to index all papers on these topics. We sought only to discover papers that used automated voice calls.)

- **21 papers** used automated voice calls for medication adherence, but without any biological measure of adherence. Of these, 18 papers are set in a high-income context and have little overlap with our study [31-48]. Three papers (describing two interventions) are set in the developing world and are described in more detail below [49-51].

- **4 papers** use automated voice calls for medication adherence, and measure the outcome with a biological indicator [52-55]. However, all of these studies are set in a rich-country context. We discuss them in more detail below.

- **No prior work** encapsulates the core elements of our study: using automated voice calls to effect a biological measurement of medication adherence in a low-income context.

Two categories of related work are worthy of further detail. First are the two interventions that use automated voice calls in a low-income setting, but without a biological measure of adherence. A direct, biological measurement of adherence is important; researchers have shown that different results are obtained using indirect measurements such as self-reports [72] or pill counts [73]. One intervention utilizes mobile phone reminders for adherence to retroviral drugs in South India [50, 51]. All participants received both SMS and IVR medication reminders, once per week for six months. The proportion of participants with optimal adherence (assessed via pill counts) increased from 85% to 91% during the intervention period [50] (there was not any comparison to a control group). 87% of women expressed a preference for the voice reminders [51], which illustrates the importance of voice for this population. In another intervention, IVR and SMS were used to collect adherence data from 19 caregivers of HIV-infected children in Uganda [49]. However, weekly completion rates for adherence queries were low (0-33%), illustrating the challenges of effective training and incentives for health data collection.

A second category of work uses automated voice calls with biological measures of adherence in rich-country contexts. These studies used automated calls to improve adherence to hypertension drugs [52, 53], diabetes medications [54], and statin drugs [55]. Three of the studies reported significant improvements in the intervention group [52, 54, 55]. However, all of these studies took place in the United States and have limited generalizability to developing-country contexts. Among other differences, women in our study have lower levels of education, lesser technology literacy, and a weaker relationship with care providers.

There is also some closely related work that does not fit into the categorization above. The MOTECH project is a comprehensive mHealth intervention for maternal and newborn health, including audio messages for pregnant mothers [74]. However, the publications to date have not focused on medication adherence. Ramachandran investigates mobile tools for rural health workers to promote women’s adherence to iron supplements, but does not target the women directly with phone calls [71]. Chhittamuru offers a deep probe of the perceptions underlying non-adherence to iron supplements in rural India [70]. More broadly, Donner and Mecheal compile several mobile interventions for healthy behaviors in the developing world [75]. Sambasivan et al. describe a voice broadcasting system to help organizations reach out to disenfranchised populations in India [76]. All of these studies provide useful complements to our intervention and could serve as points of synergy in future programs.
3. BASELINE SURVEY
To better understand the opportunities for improving adherence to iron supplements among our target population, we conducted baseline interviews with 50 women. Interviews were conducted with pregnant women during their routine pre-natal visit. The site of the interviews was the same as that of our intervention: the gynecology and obstetrics department of the Lokmanya Tilak Municipal General Hospital (also known as Sion Hospital), a large government hospital located near the Dharavi slum in Mumbai. The interviews were brief, structured interactions in which we probed the women’s demographics, their awareness and prior experience (if any) with iron tablets, and their use of technology. Unlike our eventual trial, there were no inclusion criteria for these interviews; we engaged every woman who visited the clinic and consented to the interview. Interviews were conducted by a doctor who was fluent in the local languages. Responses were recorded using pencil and paper during the interview, and later transcribed to digital format.

The interviews confirmed that the hospital services a low-income population with limited education. On average, women were 25 years old and had completed 5 years of education. Almost all (82%) of women were housewives; the remaining were employed as cooks, maids, social workers, and similar informal jobs. Only 30% of women were visiting due to their first pregnancy; others were in the midst of their second (44%), third (22%), or fourth (4%) pregnancy. Of those who had been pregnant before, the majority had done all of their deliveries in a hospital (77%), while some had delivered only at home (14%) and others had delivered in both locations (9%). The majority (70%) of women made their first visit to the hospital during their fifth, sixth, or seventh month of pregnancy.

With respect to iron supplementation, almost all women (92%) had received them if they were eligible. However, out of women who received tablets, only 30% claimed to have finished the prescribed course of medication. In other words, 70% of women fell off the course of prescribed iron supplements, despite free availability of the tablets from the hospital. When asked about the biggest difficulty in taking the medication, the majority of women cited forgetfulness (54%), followed by general dislike of the pills (11%) and gastro-intestinal problems such as constipation (7%). One woman cited problems with giddiness, while another cited a different medical condition (leukorrhea). The remainder of women (24%) did not point to any specific challenge with taking the medication.

We also asked women to explain why iron supplements were prescribed. The majority of women (74%) were able to explain the intent of the pills in general terms (for example, “it is for the health of the baby”). This knowledge showed some correlation with the women’s likelihood of finishing prior courses of medication. Of those who could explain the purpose of the drugs, 33% claimed to have finished the last course of medication, compared to only 8% completion rate in those who could not explain the purpose of the tablets.

With respect to technology, almost all women (94%) had access to a cell phone. Of these, the majority (60%) were carrying a phone at the time of the interview and indicated that they personally answered calls which were made to that number. Other women indicated that their household had a phone, but it was most commonly answered by their husband (36%) or another family member (4%). However, despite the prevalence of mobile phones, there was limited use of text messaging. Only 38% of women indicated that they read text messages on their phone, and only 28% said that they sent text messages. Restricting attention to those who had 5 or fewer years of education (the majority of respondents), these figures go down to 15% and 12%, respectively.

4. DESIGN OF THE INTERVENTION
Informed by our background survey, we sought to design an intervention that encouraged women to adhere to prescribed iron supplements. Several outcomes from the survey had important implications for our design of the intervention. In this population, women had good access to iron supplements, but the majority were not finishing the course of medication. Poor adherence was often attributed to forgetfulness and a general dislike of the medication. Many women were unable to state the benefits of taking iron supplements, which was also correlated to poor adherence. While most women had access to cell phones, the majority did not utilize text messaging.

Taken together, these factors led us to develop a set of audio voice messages, delivered via mobile phone, that engaged women with positive messaging while also encouraging them to complete their medications. To guide the design of our voice messages, we reviewed prevailing theories of behavioral change, including the health belief model [77], social cognitive theory and self-efficacy [78], self-determination theory [79], the transtheoretical model [80], the theory of planned behavior [81], social influence [82], and the elaboration likelihood model [83]. However, following recent arguments by Heckler et al. [84], we came to believe that the practical design of the intervention should be driven by empirical data about the specific application context, using theoretical abstractions as a lens but not as a requirement in the design. In this vein, we were drawn to the framing of Ramachandran [85], who synthesized theories of behavioral change specifically in the context of iron supplementation among low-income women in India. To quote Ramachandran, health messages should:

- “Maximize involvement of and personal relevance to the listener to encourage more lasting attitude change. According to the elaboration likelihood model of persuasion, this happens through central processing of the message [83].”
- “Use positive effective appeals to arouse more positive feelings and acceptance toward the recommended action [86].”
- “Induce behavior change by addressing the underlying set of salient beliefs that cause a specific behavior[81].”
- “Appeal to the listener’s self-efficacy, or perceived ability to perform an action by recommending simple and achievable actions [78].”
Our messages were designed so as to satisfy all of these criteria. The author (and narrator) of the messages was a doctor who had practiced in low-income areas of India and thus had experience interacting with patients. Messages were further calibrated to match the profile of women encountered during the baseline survey. Each message is short (30 seconds long) and repeated twice per call. Calls are delivered three times per week. An example message is as follows:

Hello, this is Dr. Niranjan Pai. We met in Sion Hospital. In this period your child may be able to sense the sounds around you. For the normal growth and development of your child please take the prescribed pills regularly. I will call you again in a couple of days. Thank you.

The full audio content of our messages is available online at http://bit.ly/voicemessages. We recorded 48 messages in each language.

In the following sections, we explain how the messages satisfy each of the criteria listed previously.

**Personal Relevance to the Listener**
Our messages are personal in several novel ways compared to prior interventions. First, each message is recorded in the voice of the doctor that the women met at the time of enrollment. This doctor conducted the baseline interview and also counseled the women regarding the importance of iron supplements. This personal connection – renewed by the personal introduction at the beginning of each call – increases trust and reduces the chance that the listener dismisses the call [76].

To further familiarize listeners with the caller, we created an address book entry in each woman’s phone at the time of enrollment. We entered the phone number of our server (the origin of the automated calls) and saved the caller’s name as “Dr. Niranjan Pai, Sion Hospital”.

The content of the messages are also personalized. Every message that a woman receives is different and customized to her stage of pregnancy (as informed by data collected at enrollment). The language preference of women was solicited at the time of enrollment. All women chose either Hindi or Marathi; we prepared complete audio messages for both languages.

Finally, the timing of the messages was customized for each woman. Women chose three days per week, and a two-hour window in which they preferred to be contacted. Our server contacted them once near the beginning of this window; if the woman did not pick up the phone, the attempt was repeated up to three times, at 15-minute intervals. If a woman missed a message or wanted to hear the message again, she could always place a call to our server to hear the most recent message.

**Positive Affective Appeals**
Most messages begin with a positive and enthusiastic statement about the development of the unborn child. Depending on the stage of pregnancy, this message might focus on physiological development (“your child is starting to develop a nose”) or other aspects (“your child may be able to sense the sounds around you”). Our intention is to engage the listener in content that is exciting, entertaining, and positive, making them more likely to look forward to the calls and to listen to them in their entirety. These messages also foster positive emotions in the listener, enhancing their chances of accepting the message and embracing the recommended behavior. The messages are also spoken in a gentle, nurturing, yet enthusiastic tone that aims to amplify positive feelings in the women.

**Addresses Salient Beliefs**
Some messages address specific concerns that might prevent adherence to iron supplements. For example:

Hello, this is Dr. Niranjan Pai. We met in Sion Hospital. You may experience some constipation. This is expected. Have vegetables and a lot of water. Take the medication as prescribed. I will call you again in a couple of days. Thank you.

Hello, this is Dr. Niranjan Pai. We met in Sion Hospital. Your backache may increase. Don’t worry, take rest. Take the prescribed pills regularly as they are important for you and your child’s health. I will call you again in a couple of days. Thank you.

The latter half of the recordings always reinforces the message that adherence to iron supplements is important for the health of the mother and child. This message was conveyed in person by the doctor during counseling at the time of enrollment. Thus, the messages do not attempt to introduce the patient to brand new concepts: a task that is sufficiently difficult to perform face-to-face, let alone via an automated telephone call. Instead, the goal is to reinforce and remind the patient of concepts that they have already been exposed to – and hopefully, have already accepted – during personal counseling.

**Simple and Achievable Actions**
The message closes with the direction to take the prescribed iron supplements. Unlike in many rural areas [70, 71], women in our trial benefitted from a reliable supply of medication from an urban hospital. Thus, the task of taking medication is largely within their control. We avoid requesting women to undertake more drastic behavioral changes, which may be overwhelming or out-of-reach. Ingesting medication can be done relatively quickly, giving an immediate gratification for investing in one’s health and the health of the child.

5. EXPERIMENTAL METHODOLOGY
To evaluate the potential impact of our voice messages on adherence behaviors, we conducted a small-scale randomized controlled trial with 130 women. Participants were randomly assigned (1:1) to a control group, or to an intervention group that received voice messages for a period of 3 months. The impact of the intervention was assessed via measurements of Hb levels in the blood. This study was approved by the Institutional Review Board of Sion Hospital.
Enrollment Procedure
Enrollment was conducted over a period of two months (July and August) in the gynecology and obstetrics department of Sion Hospital. We intercepted women who were visiting the hospital for a routine pre-natal exam. Following their normal check-up, women met with the coordinator of our study: a doctor who established an independent counseling station for the duration of our enrollment.

For each woman, the doctor first collected demographic information and ascertained if she met with our enrollment criteria, which are detailed in the next section. If so, he explained the study (using the local language of her choice) and obtained informed consent by written means. (While we also offered the option of oral consent, it was not availed by any woman.) The doctor then conducted a brief counseling session for each woman, explaining healthy behaviors during pregnancy with a focus on adherence to iron supplements. In theory, similar counseling was available to all women who visited the hospital. However, in practice, the counseling offered by our doctor was more detailed than that which was previously available to others.

Following the counseling session, women were randomly assigned to an arm of the study. Randomization was performed using a table of random numbers that had been prepared in advance. Technicians who performed the laboratory analyses of Hb levels were blind to treatment allocation.

For the intervention group, additional steps were taken, including soliciting their preferred time of contact and programming the server’s number into their phone.

Our enrollment process did not include provision of iron supplements to women. Following the procedure that was already in place, we referred women to the hospital’s pharmacy to collect a free supply of iron-sulfate tablets. In retrospect, it would have been valuable to monitor this stage of the process, as access to medications is a key factor influencing ultimate adherence to iron supplements. However, by not interfering with this step, our intervention may be easier to replicate across existing hospitals and pharmacies.

Enrollment Criteria
Unlike our baseline survey, in our trial we restricted our focus to women who were most in need of our intervention. We enrolled all women who satisfied the following criteria:

1. In the second trimester of pregnancy (13th to 28th week).
2. Have anemia (by the WHO definition of at most 11 g/dL of Hb).
3. At most 10 years of education.
4. Do not read SMS messages.
5. Carrying their own phone, which they answer themselves.

Our baseline survey suggests that out of women who visit in their second trimester, roughly 28% satisfy the remaining criteria. While we did not keep track of the exact fraction of women who were eligible for enrollment, we assert that it is a significant population, defined by their anemia, low levels of education, and non-use of text messaging. While the requirement of phone ownership does disqualify some women, current trends suggest that the number of phone owners will only increase, making our intervention even more relevant as time goes on.

Our sample size was constrained by pragmatic factors: we enrolled as many women as we could within a two-month window during which our personnel were available for this study. Our sample of 130 women would have been sufficient to detect a 0.5 g/dL improvement in Hb levels, with 80% power and 0.05 level of significance, assuming a standard deviation of 1 g/dL at enrollment. However, unfortunately we were only able to retrieve 79 women for follow-up, which weakened our statistical power considerably.

For the sake of transparency, we also note that we enrolled three cohorts of participants who are not described in this report. First, we enrolled 126 women before discovering that the measurement of baseline Hb levels was too crude for the purposes of our study. The initial measurement (in place in the hospital) used a manual technique, the Sahli Helige method, which relied on a human judgement of color and offered precision of (at most) 0.5 g/dL. As soon as we recognized this problem, we replaced the technique with an auto-analyzer, accurate to 0.1 g/dL, and restarted the study.

The second cohort not described here is an experimental condition in which a live operator placed phone calls to women to encourage them to take iron supplements. We enrolled 50 women in this condition. While we were excited to evaluate this intervention, we needed to terminate the phone calls prematurely, as the operator left unexpectedly and we were unable to replace him. This experience highlights one of the advantages of an automated dialing system: it does not depend on human labor.

The third group of people who are not described in this report are twenty women who utilize text messaging. Our initial enrollment included these women as a precaution, in case there were insufficient numbers of women who satisfied all of our criteria above. However, as we were able to enroll 130 women satisfying all the criteria, we focus our evaluation where the intervention is most relevant: those who rely on voice communications due to their inability to use text messages.

Follow-up Procedure
We aimed to follow-up with each woman three months after enrollment. In practice, most follow-ups happened after 13 weeks. Because we needed to measure Hb levels in the blood, an in-person follow-up was required. In order to ease the burden of travel to the hospital, we reimbursed travel expenses for all women who reported for follow-up. However, we did not offer any other incentives.

We scheduled the follow-up by calling women in advance, about one week before their visit was due. Several women were unreachable, or did not report to the hospital despite repeated calls. The follow-up included a brief structured in-
Table 1: Demographics of participants who were retrieved for follow-up. Values represent averages, with standard deviations in parentheses. The last two columns show the t-value and p-value from a Student’s t-test comparing a given variable across the control and treatment groups; p-values greater than 0.25 are depicted as non-significant (n.s.).

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n=40)</th>
<th>Treatment Group (n=39)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>24 (3.5)</td>
<td>24.5 (3.8)</td>
<td>-0.58</td>
<td>n.s.</td>
</tr>
<tr>
<td>HH income (per month)</td>
<td>$120 ($50)</td>
<td>$110 ($50)</td>
<td>0.77</td>
<td>n.s.</td>
</tr>
<tr>
<td>Education (years)</td>
<td>7.3 (3.4)</td>
<td>8.3 (2.1)</td>
<td>-1.58</td>
<td>0.12</td>
</tr>
<tr>
<td>Prior pregnancies</td>
<td>0.8 (0.8)</td>
<td>0.6 (0.6)</td>
<td>0.91</td>
<td>n.s.</td>
</tr>
<tr>
<td>Stage of pregnancy at enrollment (weeks)</td>
<td>15.8 (2.4)</td>
<td>15.6 (2.4)</td>
<td>0.29</td>
<td>n.s.</td>
</tr>
<tr>
<td>Time between enrollment and follow-up (weeks)</td>
<td>13.2 (0.9)</td>
<td>13 (1.1)</td>
<td>0.80</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

The demographics of participants who were retrieved for follow-up. Values represent averages, with standard deviations in parentheses. The last two columns show the t-value and p-value from a Student’s t-test comparing a given variable across the control and treatment groups; p-values greater than 0.25 are depicted as non-significant (n.s.).

Implementation
We implemented the intervention using our own Interactive Voice Response server, using open-source telephony software (Asterisk) and off-the-shelf GSM modems (Topex Mobilink IP).

6. RESULTS
Of the 130 women enrolled in the trial, we successfully followed up with 79. Of those who did not follow-up, 32 were completely unreachable: either their phone number had gone out of service, or the person answering the phone did not know of a pregnant family member. Our hypothesis is that these women changed their phone number during the trial. This practice is all-too-common among low-income groups in India, who frequently switch carriers in response to special deals. Finally, there were 19 women that we were able to contact, but they did not show up for a follow-up visit despite our repeated requests.

The demographics of participants who completed follow-up are illustrated in Table 1. On average, participants were about 24 years old, had a household income of about $117 (Rs. 7000) per month3, had completed about 8 years of education, enrolled in the program after 16 weeks of pregnancy, and completed a follow-up visit after about 13 weeks. The control and treatment groups do not show any systematic difference in age, household income, prior pregnancies, stage of pregnancy, or time between enrollment and follow-up. The treatment group trends toward a slightly higher level of education (8.3 years versus 7.3 years, t(75)=-1.58, p=0.12).

The automated dialer ran successfully for the duration of the trial. For those who completed follow-up, it delivered 937 answered calls. This translates to 24 answered calls per woman (on average), which is about 62% of the 39 calls placed to each woman (not counting retries). Calls that were answered lasted 40 seconds on average, indicating that most people listened to the message in its entirety (and several people listened more than once).

The impact on Hb levels is illustrated in Table 2 and Figure 2. In both groups, the Hb level was about 9.5 g/dL at the time of enrollment, though there was high variation (stdev 1.0 g/dL). During the course of the trial, average Hb levels decreased slightly (by 0.10 g/dL) in the control group, but increased (by 0.32 g/dL) in the treatment group. Taking a difference of differences, the treatment group improved by 0.43 g/dL (95% CI = -0.13 - 0.98 g/dL) more than the control group. This trend is apparent in graphical form in Figure 2, where the treatment group displays a shift to the right (in the direction of increasing Hb) relative to the control group. However, this improvement is not statistically significant (t(77)=-1.52, p=0.13).

While we also conducted qualitative interviews during the follow-up visits, these interviews were very short and we are disinclined to trust the results due to the likelihood of participant response bias [87]. When asked if they completed the course of medication, only one out of 79 participants admitted to skipping any doses: a confirmation that direct measures of adherence are important for understanding the real benefits of interventions. Women offered positive feedback regarding the voice messages, describing them as informative, entertaining, and a service that they would recommend to friends. No adverse events (such as undue interruptions, annoyances, or breaches of privacy) were reported as a consequence of receiving the voice calls.

In this paper, we use an exchange rate of 1 USD = 60 INR.

Figure 2: Graphical illustration of trial results. Values are grouped into bins of 1.0 g/dL change in Hb.

Table 2: Results of the trial. Values are encoded in the same way as in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n=40)</th>
<th>Treatment Group (n=39)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Hb</td>
<td>9.69 (0.98)</td>
<td>9.53 (0.99)</td>
<td>0.72</td>
<td>n.s.</td>
</tr>
<tr>
<td>Final Hb</td>
<td>9.59 (1.06)</td>
<td>9.86 (1.06)</td>
<td>-1.12</td>
<td>n.s.</td>
</tr>
<tr>
<td>Change in Hb</td>
<td>-0.10 (1.32)</td>
<td>0.32 (1.16)</td>
<td>-1.52</td>
<td>0.13</td>
</tr>
</tbody>
</table>
7. DISCUSSION

Effect Size

Prior interventions have shown that it is possible to have a large effect on Hb levels using iron supplementation during pregnancy[88]. For example, Saha et al. enrolled anemic pregnant women in Chandigarh, India, and measured an increase of 2.9 g/dL (on average) over a period of 8 weeks by use of ferrous sulfate tablets [89]. This effect is about seven times larger than ours. However, Saha et al. restricted enrollment to patients with moderate anemia (less than 9 g/dL); on average, baseline Hb levels were 1.14 g/dL smaller than our treatment group. There is evidence that women with lower Hb levels derive greater benefits from iron supplementation [90], which may contribute to the difference in effect size.

While the difference between our treatment and control group (0.43 g/dL on average) may have clinical value, it is difficult to further quantify this benefit. Under the WHO’s definition of anemia (less than 11 g/dL), only 3 out of 39 people in our treatment group were “cured” of anemia, by increasing their Hb level across this threshold. It is conceivable that women in the treatment group could have benefited in ways that we did not measure; for example, among non-anemic women, it has been shown that iron supplementation can improve birth weights without further increasing Hb levels [91]. Among anemic women, however, the Hb level serves as an important proxy for other health outcomes, and therefore was the focus of our study. Overall, while the effect measured represents a step in the right direction, a greater effect will be needed in order to make a meaningful dent in anemia among this population.

Cost Analysis

The main cost of our intervention is that of mobile airtime. Women received about 24 voice messages, each lasting 40s on average; thus, the cost amounts to about 16 minutes of airtime. In India today, it is easy to find plans that cost $0.01 per minute (1 paise per second) for long-distance calls; with cooperation from a mobile carrier, this price can be cut by about a factor of two. Thus, our intervention currently costs about $0.16 per woman, while at scale it would cost approximately half that. We are not accounting for the costs of the server and development time, as they quickly become amortized. There is also expense involved in recording personal messages by the doctor who is in contact with the patient; at scale, we envision this could be done over an IVR system.

How does this cost compare to that of the overall treatment? Iron supplements (ferrous sulfate tablets) cost approximately $0.02 each, when purchased over the counter. If a woman adhered to daily medication for 13 weeks, the medication alone would cost roughly $1.82. In other words, our intervention is less than 10% of the cost of the medication. When accounting for additional costs of care, such as doctors and diagnostic tests, our intervention is even cheaper.

Do the benefits justify the costs? For an added 10% cost over the price of medication, our intervention offers (on average) a 0.43 g/dL increase in Hb levels. It is difficult to compare this cost/benefit ratio to other known interventions, due to the difficulty of quantifying the benefits of iron supplementation. However, given that medications are already being completely subsidized by care providers, it does not seem unreasonable to invest a fraction of that cost in improving the likelihood that the drugs will be taken.

Limitations and Future Work

There are two primary limitations of this work. The first limitation, and one that may be responsible for the small effect observed, is that we had limited information about – and limited control over – women’s access to medication. In retrospect, it would have been better for us to issue medications directly to women, or at least to verify that they received medications as intended, rather than relying on the existing distribution system in the hospital. Without more information, we are unable to say whether the barrier to improved Hb levels is that of adherence to medication, or unexpected difficulties in obtaining (or refilling) the medication.

The second limitation is that we did not connect with as many women as expected for follow-up appointments. If we had observed the same effect size and standard deviation, but had retrieved 100% of the women enrolled, our result would be significant at the 0.05 level.

One recommendation that we can make for future studies is to plan ahead for participants who change their phone numbers. In our sample, 25% of participants were unreachable at their original phone number within three months’ time. One way to guard against this problem could be to conduct occasional phone surveys, asking women if they have any intention of changing their phone number and reminding them to notify the hospital of any change. A reminder to this effect could also be written on the SIM card or phone battery using a magic marker, so that it is discovered exactly when the SIM card is about to be replaced. As a precaution, it would also be desirable to record alternate contact information at the time of enrollment – for example, the phone number of a spouse, family member, or even a friend – in order to contact women if their phone should become unreachable.

In the future, we hope to replicate this study while 1) enrolling more women, 2) retrieving a greater fraction for follow-up, and 3) tracking the supply of medications. Also, we hope to complete an arm of the study tracking women’s response to live phone calls from doctors. This condition would help us to understand how much gain in adherence is within reach of any telephonic intervention, even without automation.

8. CONCLUSIONS

This paper represents an exploratory study into the potential of mobile phones to combat maternal anemia among low-income pregnant women in urban India. In order to be accessible to low-literate populations, our intervention utilizes automated voice calls instead of text or smart phone solutions. Based on a systematic literature review, we believe that it is the first paper to attempt a biological measurement of medication adherence as impacted by automated voice calls in a low-income country. Unfortunately, due to unexpected challenges in retrieving women for follow-up visits, as well as a small effect size, our results lack statistical power. However, the trend observed suggests that automated voice calls may be beneficial – and are at least deserving of fur-
ther study— as a way to help women with limited education to adhere to iron supplements. We hope that the lessons learned from this pilot study will serve to inform the design and evaluation of future mHealth interventions.

9. ACKNOWLEDGMENTS

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10. REFERENCES


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