Use of a pictorial medication labeling system to improve comprehension of drug information and adherence to drug regimen: A randomized trial among pregnant women in a rural maternal and child health clinic in Kutch, India

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Executive Summary

Objective: To test the effectiveness of a pictorial medication labeling system in improving comprehension of medical information and adherence to drug regimen among low-literate patients attending a maternal health clinic. A secondary objective was to examine comprehension among low-literate women of pictorial labels designed by a local village artist as compared to a non-local artist.

Methods: A randomized trial was conducted with 137 pregnant women visiting a local maternal and child health clinic in Kutch, India from December 2007 to June 2008. Two intervention groups using sets of pictorial labels (one locally-developed, one non-local) were compared to a control group using the "standard care" method (a system of numbers and dashes placed directly on the medication packaging) commonly used by Indian healthcare providers. Comprehension of medical information (for dosage and drug indication-defined as the problem for which the drug was prescribed) and adherence to drug regimen were measured using items from a structured questionnaire administered between two and seven days after the clinic visit.

Results: Comprehension of dosage did not vary among control and intervention groups. Women receiving pictorial labels were significantly more likely to understand the indications of their medications compared to women in the control group (Local labels: OR 4.9 (95% CI: 1.3-18.5); Non-local labels: OR 5.1 (95% CI: 1.4-19.1)). Overall, women receiving some formal education were significantly more likely to comprehend the indications of their medications (OR 15.1 (95% CI: 1.4-160)). Adherence to drug regimens was significantly higher among women in the intervention group with non-local labels as compared to those in the intervention group receiving local labels (p=0.01); however; even in the non-local label group, the percentage of women fully adhering to their drug regimen was less than one-third (30.9%). There was no significant difference in adherence between the control group and either intervention group. Overall, women who completely understood the dosage of their medications were more likely to adhere fully to their drug regimen as compared to women with partial or no comprehension of the dosage of their medications (OR 6.6 (95% CI: 1.3-34)).

Conclusions: The results from this study demonstrate that use of a pictorial labeling system in tandem with oral and written instructions can improve understanding of drug indication and adherence to drug regimen among low-literate populations. Although these data suggest locally-developed pictograms may be more easily understood than non-local pictograms, further research is needed to support these findings.

Background

Poor comprehension of, and adherence to, drug regimens remains a critical challenge for many people around the world. Researchers have identified a number of social and health determinants for low comprehension and non-adherence, and numerous interventions have been developed to address these obstacles to achieving good health. Among the most common are educational materials incorporating visual images (pictograms) to depict health information, but results on the effectiveness of pictograms in improving comprehension and adherence of medical information are mixed.[4,8,25]

Health literacy is a crucial factor to consider when discussing comprehension of drug information. Health literacy is "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."[15] Poor health literacy is highly correlated with low literacy (defined as a poor ability to read and understand written words), in both high and low resource settings.[3] A study conducted with pregnant women in Egypt found that low literacy was associated with poor drug comprehension.[22] Additional studies conducted in the United States have confirmed that low literacy leads to poor comprehension of written medical instructions, such as information displayed on prescription labels and packaging.[3,25]

Other factors have been shown to be associated with low comprehension of medical instructions. For example, studies have found that providers often give confusing or inadequate information during patient visits,[19] leading to misunderstanding of medical instructions.[14] Poor comprehension of health information is associated with non-adherence to drug regimens and other health instructions.[12,25] Adherence, defined by the World Health Organization as "the extent to which a person's behavior...corresponds with agreed recommendations from a health care provider,"[1] is critical to ensuring positive health outcomes. Non-adherence to drug regimens can account for high rates of hospitalization and healthcare costs, disability, and death.[12,14,19,24] In fact, one study reported a 6.5 times greater risk of death from medication error in an outpatient setting as compared to in a health facility, with the majority of outpatient medication error deaths attributed to patient error.[20]

One of the reasons cited by patients for non-adherence to drug regimens is dissatisfaction with treatment, including confusion about medication information.[19] In fact, the use of pictograms in drug labels and information pamphlets was found to greatly increase patient satisfaction.[4,12] Drug indication is emerging as an important component of medical information. Adherence has been shown to be lower in patients who do not know the reason why they are taking each medication as compared to those with knowledge of their drugs' indications.[12,19] In addition, increased drug regimen complexity and number of medications is associated with decreased knowledge of drug indications and places patients at a higher risk of non-adherence.[11]

Globally, it is common for health providers not to inform patients of the reasons they are given drugs. A Turkish study found that less than half of providers communicated drug indications to their patients.[2] Moreover, this information, if given at all, is likely to be orally communicated to the patient. Given that patients may forget up to 72 percent of all oral information provided at their visit,[8] development of written materials that effectively convey drug indications is important. Materials that increase counseling and patient-provider communication may help to reposition drug indication as a higher priority among health providers.

Using pictograms to depict health information is not a new idea. Yet, only a handful of pictorial interventions have attempted to visually depict drug indication. Several studies have shown that low-literate populations, in particular, are better able to recall medical information when it is provided in pictorial form. [7,12,13] However, most of the pictorial interventions examined in these studies targeted illiterate or low-literate populations in *high*-income countries. These results are not easily translatable to communities in low-resource settings. One study conducted in Cameroon found that use of pictorial aids increased understanding of medical information in a low-literate population.[18] Mansoor and Dowse also found that, in a rural South African community, patient health materials containing pictograms and text were more easily understood than materials containing only text.[17] While these results are promising, more research is needed.

The present study further investigates the effectiveness of using pictorial materials among low-literate women in the Pachcham region, a remote area in western India. In the short term, we hypothesized that our new pictorial materials, when compared to the standard care system, would improve understanding of medical instructions, such as dosage and drug indication, by enhancing comprehensibility of instruction materials and improving patient-provider communication and counseling, as well as adherence (Fig.1).

This study also investigates the differences in comprehension of pictorial materials designed by local and non-local artists. We hypothesized that those pictograms developed by the local artist would lead to higher levels of comprehension of drug information among women as compared to those pictograms developed by the non-local artist. Dowse and Ehlers found that pictograms created with significant input from local communities are better understood by members of those communities when compared to pictograms designed by non-locals.[5]

The target population selected for this study was pregnant women. Due to the study population's high fertility rate, women spend a significant proportion of their reproductive years in pregnancy. Because of the high prevalence of risk factors (such as illiteracy and anemia) and poor access to basic and emergency obstetric care, it is especially crucial that this population be given the proper tools to understand their medical information.

Methods

Project site and IRB approval

The study was conducted at the Kutch Mahila Vikas Sangathan (KMVS) "Mother's Care Clinic" located in Khavda, a small town in the Pachcham Region of Kutch District, Gujarat State, India. The clinic served all 55 villages of Pachcham, a remote, socially conservative, and generally economically poor area with an adult female literacy rate far below the nation's average of 53.5 percent.[26] Even with a population of over 40,000, Pachcham had no gynecologist or obstetrician at the time this study was conducted. The region has one of the highest maternal and infant mortality rates in the state,[27] and the majority of women suffer from malnutrition and anemia. Although there are several religious and caste sub-communities within Pachcham, the region is approximately 80 percent Muslim.

Informed patient consent was obtained. Almost all women recruited were unable to read the written consent form; therefore, the consent form was read aloud to the women, who were then asked if they fully understood the study details. Informed consent was then given by either patient signature or thumbprint. This study was approved by the IRB of Johns Hopkins Bloomberg School of Public Health.

Study population

Pregnant women visiting the outpatient department of the clinic between December 15, 2007 and May 31, 2008 were eligible for the randomized trial. Patients were excluded if they lived more than 25km from the clinic, were educated above the 10th standard (roughly equivalent to the 10th grade), or received no prescription medications at the visit. Women previously exposed to our intervention (through pre-testing or interaction with family members enrolled in the study) were also excluded.

Sample size and study design

Sample size was determined for a balanced one-way ANOVA for 3 groups, assuming a medium effect size (f) of 0.30 (Cohen), two-sided significance level of 0.05 and power of 0.80. The sample size for each group was estimated as 35 per group; however, anticipating a 5-10% loss to follow-up, the sample size target was set to 40 per group.

All women visiting the clinic for medical services and meeting the inclusion criteria were asked to participate. All patients signed in with the clinic registrar prior to examination. Once a patient was determined to be eligible, she was directed to a private room to speak with the clinic health counselor (head member of the interview team). Family members were encouraged to accompany the patient during the study explanation. At this time, the interviewer introduced the intervention, described the objectives of the study, and read aloud the consent form. If the patient declined to participate, she was invited to return to the sitting room to await examination by the clinic physician and traditional birth attendant (TBA).

Women who agreed to participate were assigned, in an unbiased, sequential, systematic fashion, to one of the following three groups: 1) Control ("standard care" in the clinic: receiving only written and verbal medical instructions), 2) Intervention 1 (receiving pictogram labels designed by a local artist, in addition to written and verbal medical instructions), and 3) Intervention 2 (receiving pictogram labels designed by a non-local urban artist, in addition to written and verbal medical instructions). Participants were assigned to a group based on a pre-ordained sequence of days of assignment per individual week over the course of 6 months.

Pictogram label intervention: design and development

Pictograms for drug indication were designed by four artists. A series of focus groups and individual interviews with local women and healthcare providers were conducted to select the two artists whose pictograms would be incorporated into the label interventions for this study. See Appendix 1 for a full description of the methods and Figure 3 for an example of the development of a pictogram.

Development of survey tool

A survey tool for home follow-up was designed with the guidance of several women's health experts and public health researchers. The interview schedule was pilot-tested with several local TBAs before the questions were finalized, and it contained 76 questions to collect detailed demographic information on maternal characteristics and household size and occupation, care-seeking practices and obstetric history, comprehension of pictograms used on the labels, comprehension of dosage (number of pills and number of times a day) and indication for each medication prescribed, perceived utility of the labels, and adherence to drug regimen. The finalized survey tool was then translated into Gujarati. Because the local language, Kutchi, has no written form, the surveyors administered the questions by on-the-spot translation from Gujarati to Kutchi.

Interview process and data collection

Basic demographic data and prescription information were recorded from the medical files of consenting patients at the time of the visit, after which they were examined by the TBA and doctor. Women in the intervention groups received a label with each medication for which a label had been developed. Some medications, such as anti-itching agents and antibiotics for fungal infection, did not have corresponding labels; for these medications, the standard care method of tickmarks (sequences of numbers and dashes) was provided to all women, regardless of group assignment. (See Fig. 5 for an example of the standard care method and pictorial label.) Women received from one to six medications. The upper limit of six medications was determined by the doctors' avowal that they would prescribe no more than six medications to a patient at any given visit. The clinic pharmacist selected the appropriate labels for each medicine given to study participants, attached the labels to the medications, and entered the correct dosage information in the space allotted on the labels. Either the attending TBA or the doctor explained to participants their medical information (for control group: using the tickmarks; for intervention groups: using the labels) for each medication at the time of prescription. After leaving the examination room, each patient was counseled (standard clinic care) by the health educator, at which time any of the patients' additional questions were answered. Women in the intervention groups received the same care as women in the control groups, with the exception of receiving labels.

An all-female interview team, consisting of one surveyor, one observer, and one local TBA/community health worker, followed-up each patient at her home two to seven days after her visit to the clinic. Efforts were made to conduct follow-ups while the participants' medication courses were still active (Courses ranged from 2-30 days, but all patients were followed-up within one week of their visit to the clinic.) While the survey was administered by the lead interviewer in Kutchi, the local language, the TBA/community health worker provided any necessary assistance in translation or explanation. Responses to medication comprehension questions were judged to be correct or incorrect by the interview team either at the time of interviewing or after consultation with the clinic physician. One of two observers was present at all follow-up interviews, and reliability testing was conducted with these two individuals prior to the start of follow-ups.

Adherence was determined by combining two indirect measures: pill count and self-report. Each individual medication was evaluated, and the patient was judged to be adherent to the specific medication regimen if pill count was correct *and* self-report of dosage was accurate. The observer member of the interview team was responsible for assessing adherence by pill count. Self-report of dosage was determined using two items in the survey tool: 1) How many times do you take this medication each day? and 2) How many pills do you take each time? Self-report of dosage was considered accurate only if both questions relating to dosage were answered correctly. Based on their responses, patients were then placed in one of three categories of adherence: high, medium, or low. Patients adhering to all medications prescribed received a rating of high. Patients adhering to at least one medication (but not all) received a rating of medium. Patients adhering to no medications received a rating of low.

Medication Regimen Complexity Index

Variation occurred not only in number of medications prescribed, but in types of medications prescribed as well. Because medications can range widely in the complexity of instructions and difficulty of administration, a method was used to adjust for this variation in drug regimen complexity by patient. As shown in Table 1, an index for quantifying the complexity of each participant's drug regimen was adapted from an index developed by George *et al,*[6] in which a number of drug regimen characteristics were assigned weighted values for each prescribed medication. These characteristics were organized into three categories: A) *dosage form*, B) *dosing frequency*, and C) *additional directions*. *Dosage form* refers to the form of the medication, such as tablet, topical cream, or vaginal pessary. *Dosing frequency* refers to the instructions given regarding when to take each dose of a medication. *Additional directions* refers to all special instructions provided with each medication, such as multiple pills at each dose, take with food, or take at a specified time. Weights were assigned to each characteristic, as determined by several rounds of medication complexity ranking exercises by expert medical professionals conducted and reported by George *et al*. The total scores for each category (A, B, and C, Table 1), calculated from the weights assigned for every medication prescribed to a single participant, were then summed to calculate a final regimen complexity score for each woman. In this study, scores ranged from 2 to 24, with 24 being the most complex regimen prescribed.

Statistical analysis

Chi-square analysis was used to test for significant differences in the distribution of demographic, obstetric, and fertility characteristics between the control and intervention groups. Multiple logistic regression was used to test for associations between each of three outcome variables (adherence, dosage comprehension, and drug indication comprehension) and several predictor variables by each study group. Because the outcome variables experienced a ceiling effect in which the majority of observations fell in the highest scoring category, they were dichotomized between "perfect score" and "less than perfect score" for the purposes of regression analysis. Associations between the outcome variables and study group were adjusted for potential confounding variables. Variables such as distance from home to clinic were considered continuous in one model and categorical in another depending on whether the assumption of linearity of association could be made with the outcome variable of interest.

Qualitative data analysis methods were used to organize the research team observers' field notes for each participant follow-up.

Results

Demographic and Obstetric/Fertility Characteristics

One hundred and fifty-four women were recruited to participate in the study (Fig. 2). Seventeen women (11%) declined to participate, citing such reasons as inability to seek permission from her husband (who was absent on day of clinic visit) and issues with transportation back to her home village. A total of 137 pregnant women were assigned to one of the three study groups. Twenty-five women were lost to follow-up, resulting in a study population of 112 women: 31 in the control group, 40 in Intervention group 1 (local labels), and 41 in Intervention group 2 (non-local labels). Demographic and obstetric/fertility characteristics of the participants are presented in Tables 1 and 2. The three groups did not statistically significantly differ in any measured demographic or obstetric/fertility characteristics, although there was a suggestion of a higher percentage of wage laborers in the control group as compared to the two intervention groups.

The age range of women in this study was 17 to 38 years (mean: 26.2, median: 25). About two-thirds of women were Muslim, and the remaining one-third was Hindu. The overwhelming majority of women had received no formal education (94%), and 61% of women belonged to families in which wage labor constituted the primary source of income. About 11%

of women lived in Khavda, the town in which the clinic operated. Of the remaining women, half lived between 15 and 30 kilometers from the clinic (median: 10km).

Over half the women (53%) reported four or more previous deliveries, and three-quarters of women had no history of abortion. Half of all study participants with at least one previous delivery reported conducting all deliveries at home. The large majority of participants were in the second or third trimester of their current pregnancy (91%).

The median number of medications prescribed at the visit to the clinic was 3 (range: 1-6). About 77% of women reported using tickmarks to remember their dosage, while only one-quarter used oral instructions given by a provider (some women reported using both methods).

The range of drug regimen complexity during the clinic visit was 2 to 24, with the higher score reflecting a more complex regimen. One-quarter of women had drug regimen complexity scores of four or less (median complexity score: 9) (Table 5), and distribution of complexity scores did not statistically significantly differ among study groups (Fig. 6).

The same characteristics comparing the study population to the 25 women lost to follow-up are presented in Tables 6 and 7. Women lost to follow-up had more living children ($p<0.001$), more expired children ($p=0.001$), more pregnancies ($p=0.004$), and larger family sizes ($p=0.001$) than women who completed the study. Although the reasons for these discrepancies are unknown, we speculate that it may have been, in part, due to their inability to devote the extra time required to participate in the study aspects of recruitment, counseling, and the home survey.

Interpretation of the Pictograms

Comprehension of time-of-day pictograms was high among women in both intervention groups, with no significant difference in comprehension of each pictogram between intervention groups (morning: p=1.000; afternoon; p=0.560; night: p=0.723) (Table 8). Because the same pictograms were used for both intervention groups, no difference in comprehension between the two groups was expected. The night pictogram was the most easily understood, with 89% of women correctly interpreting its meaning. Overall comprehension of the morning and afternoon pictograms was 78% and 75%, respectively.

There was no statistically significant difference in comprehension of the drug indication pictograms between Intervention 1 and 2, with 65% of women in Intervention 1 group correctly interpreting all their drug indication pictograms as compared to 46% of women in Intervention group 2 (p=0.091) (Table 8).

Twenty-two pictograms for drug indication (eleven indications, each represented by both artists) were used in the study: abdominal pain, heartburn, anemia, body ache, common cold, constipation, malaria, UTI, nausea/vomiting, body weakness/fatigue, and white discharge. The indications most commonly observed in women in the two intervention groups included body weakness/fatigue (62), anemia (60), heartburn (28), abdominal pain (21), and body ache (12). Comprehension of pictograms for a given indication was not statistically significantly different between intervention groups (local versus non-local), with the exception of the pictogram depicting heartburn (see Fig. 4, iii for local and non-local heartburn pictograms), in which the local pictogram was better understood than the non-local pictogram (100% versus 60%, p=0.010) (Table 9). Comprehension was relatively lower in both intervention groups for those pictograms depicting more sensitive areas of the body, such as constipation and UTI, when compared to other pictograms in the study.

Dosage Comprehension

There were no significant differences in comprehension of dosage among the three study groups (p=0.916) (Table 10). Although not statistically significant, there was a suggestion that women living further from the clinic had lower dosage comprehension (OR 0.94 (95% CI: 0.87-1.01)) (Table 12, Fig. 8). In addition, women aged 17-20 years had lower dosage comprehension than women older than 30 years (p=0.04) (Fig. 8).

Education was perfectly correlated with dosage comprehension, as all women receiving any education earned a perfect correctness score. Therefore, education was not included in the regression model using dosage score correctness as the outcome variable (data not shown).

Drug Indication Comprehension

Women in both intervention groups demonstrated significantly higher comprehension of drug indication as compared to women in the control group (Table 10) (Intervention 1: p=0.001, Intervention 2: p=0.006). There was no significant difference in indication comprehension between the two intervention groups (p=0.745).

As shown in Table 13, after adjusting for number of children and maternal education, women receiving pictorial labels were more likely to understand the indication of all their drugs when compared to women receiving standard care (control) (Intervention 1: OR 4.9 (95% CI: 1.3-18.5); Intervention 2: OR 5.1 (95% CI: 1.4-19.1).

There was over a 75% reduction in the number of women comprehending all drug indications among those women who reported having one to five living children as compared to women reporting no children. In addition, education was highly associated with comprehension of drug indication, with women receiving at least one year of formal education being significantly more likely to understand all their drug indications (OR 15.1 (95% CI: 1.4-160)) (Table 13).

Adherence to Drug Regimens

Adherence levels did not differ between the control and either intervention group (Table 11). However, women in Intervention group 2, receiving non-local pictograms, had statistically significantly higher adherence levels than women in Intervention group 1, receiving local pictograms (p=0.005). Even in the group demonstrating the highest adherence levels (Intervention 2), less than one-third (31%) of women fully adhered to their drug regimen.

Results from the logistic regression analyses of adherence and study group are presented in Table 14. After adjusting for distance of home from clinic, family size, and dosage comprehension, there remained no significant difference in adherence between either intervention group and the control group (Intervention 1: OR 0.4 (95% CI: 0.07-1.8), Intervention 2: OR 1.8 (95% CI: 0.49-6.8)). Although not statistically significant, there appeared to be an association between adherence and distance of home from clinic. Those women living outside of Khavda village, the site of the clinic, were less likely to fully adhere to their drug regimen when compared to women living in Khavda. Women with larger families were also at higher risk of non-adherence or partial adherence (OR 1.2 (95% CI: 1.03-1.4)). Low dosage comprehension was highly associated with poor adherence (OR 6.6 (95% CI: 1.3-33.8)). Having at least one year of education was perfectly correlated with full adherence; therefore, education was not included in the regression model using drug regimen adherence as the outcome variable (data not shown).

Total Number of Medications and Drug Regimen Complexity

Total number of medications prescribed and drug regimen complexity were included in the logistic regression models for all three outcome variables; however, neither predictor variable added to the model (data not shown). For this reason, the final models did not adjust for these two variables. Although not statistically significant, there was a suggestion of a positive correlation of both number of medications and regimen complexity with adherence (Fig. 8).

Patient Acceptability of the Labels

The large majority of women in the randomized trial as well as those interviewed during the process evaluation were satisfied with the labels as a system to help them understand their medical information. Over three-quarters of the randomized trial participants found taking their medicines to be easier with the pictorial label system as compared to the standard tickmark system. Of the women receiving labels during the randomized trial, most found both the time-of-day pictograms (for dosage) and the indication pictograms useful in helping them comprehend their drug information (92% and 89%, respectively), and the proportion of women citing the labels' utility did not differ between intervention groups. In addition, 88% of women in the randomized trial claimed it was important to them to know the indication of each drug they are prescribed, as many women found that the labels empowered them to care for their own health (88%) (data not shown).

Moreover, 78% of women in the intervention groups reported that they do not take help from anyone in administering their medications, compared to only 47% of women in the control group reporting the same (p=0.007) (Table 15). Although this survey question was intended to report on medicine-taking habits, based on the stark difference in responses between control and intervention groups and the ambiguity of the wording of this question in the instrument, it is believed the women responded specifically according to their behaviors following the study visit.

In addition, while some health providers expressed concern about giving women information regarding indication of their drugs, 85 percent of all participants felt it was important to know why they were taking each medication (data not shown).

Reasons for Non-adherence to Drug Regimen

Participants cited several reasons for non-adherence in addition to poor comprehension. Among the most commonly cited were unpleasant side effects and forgetfulness; however, many women also visited a second clinic within days of their visit to the study clinic due to dissatisfaction with medications. For this reason, some participants were instructed by the second provider to stop taking medications prescribed at the study clinic, while some were taking two different brands of the same medication (prescribed by each clinic). Poor medication storage also led to poor adherence, since some women had loose and unmarked medications mixed together or unexplained missing pills (data not shown).

Less common reasons for non-adherence included apathy and taste preferences. Some women reported they did not think it really mattered whether or not they took the medications correctly. Others found the color, shape, size, or taste of the medications to be either unappealing or appealing leading to under or over-consumption, respectively. One 30-year-old woman stated,

> "I liked the taste of this one [calcium/multivitamin pill] so I took it three times a day instead of once."

Discussion

Comprehension and Drug Regimen Adherence

This study aimed to determine the effectiveness of the use of pictorial medication labels in improving 1) dosage comprehension, 2) drug indication comprehension, and 3) drug regimen adherence. The results show that use of pictorial labels, in tandem with oral and written instructions, can improve understanding of drug indication and drug regimen adherence among extremely low-literate populations. These findings are important, since few studies examining the use of pictorial materials have focused on an almost exclusively illiterate population. Our intervention did not significantly improve dosage comprehension when compared to the standard care method; however, it is common for interventions involving behavior change (on the part of both the provider and patient) to take time to be accepted and utilized properly. For this reason, we encourage investigators of future studies to employ a longitudinal design in order to track progress of comprehension and adherence over time.

Several factors were shown to be associated with the three outcomes measured. Women with at least one child were less likely to understand their drug indication compared to women pregnant with their first child. Education was also significantly associated with high comprehension of both dosage and indication, although level of education did not appear to affect adherence. Larger family size led to increased adherence among study participants, a finding somewhat contradictory to the observed association between indication comprehension and number of children. (Family size, reported as the number of individuals eating meals cooked on a single stove, was highly correlated with number of living children.)

An interesting trend was observed in the association of drug regimen complexity and total number of medications with adherence. The proportion of women fully adhering to their drug regimens increased with the number of medications and increased drug regimen complexity. There are many possible explanations for these trends, although this study did not examine these issues in depth. It is possible that women with higher regimen complexity and/or number of medications generally experienced poor health, resulting in a more frequent exposure to prescriptions and medication instructions (leading to increased adherence). Another potential explanation is that as regimens became more complex and number of medications increased, women began to pay more attention to the correct dosage and indications, whereas women with fewer medications and simpler regimens had a more cavalier attitude toward the information.

These findings also confirm that while comprehension is a necessary component of adherence, it is insufficient to ensure proper administration of medications. Many factors unrelated to comprehension of dosage and drug indication appeared to negatively affect adherence, including forgetfulness, side effects, and poor medication storage resulting in lost or mixed up medications. In order to improve adherence among the women in this rural community, these issues must be addressed at the same time that interventions to improve comprehension are implemented. Nevertheless, these pictorial labels have been shown to be highly effective in improving comprehension of drug indication compared to the standard care method. Studies have suggested that increased comprehension of drug indication can lead to improved adherence;[11] therefore, these labels should be considered a potentially important element for addressing the challenge of poor adherence.

In addition to the potential for improving adherence, these pictorial labels have the capability to empower uneducated and otherwise marginalized subpopulations to become agents of their own healthcare. The overwhelming majority of women receiving pictorial labels reported that the labels eliminated their dependence on others for understanding and administering their own medications (88%) (data not shown). A 35-year-old illiterate woman who received the labels reported,

> "Without the labels I'd have to ask my mother-in-law, with them I haven't had to ask once."

In addition, by increasing self-confidence and willingness to discuss sensitive female health problems, this intervention could empower women to ask more questions about their medications and health condition while in the clinic. Not only will this positively affect the patient's health, but it could also result in improved provider-patient communication and counseling, which is notoriously poor in many rural areas of India.

A third reason that the use of pictograms is crucial for low-literate populations is patient safety. There are cases in which clear knowledge of a drug's indication could prevent dangerous medication errors, especially among patients receiving multiple medications. Therefore, use of indication pictograms, in particular, has the potential to facilitate safe patient practices, regardless of adherence. Pictorial depiction of indication could help reduce adverse drug events among low-literate patients, thereby reducing the demand for care altogether.

Patient Acceptability of the Pictograms and Pictorial Labels

Patient acceptability of the pictograms and labels was high. The overwhelming majority of women receiving the labels preferred them to the standard care method, most citing the presence of the drug indication pictogram as the main benefit. One study participant, receiving five medications at her visit, said,

> "It is important to me to know why I am taking each medicine...I go to the other doctors and they'll give me a handful of medicines or more and I have to simply trust God and take them all. These pictures help me understand."

While some women exhibited low self-esteem, reporting that uneducated women like themselves would never understand their medical information, family members remained supportive and enthusiastic about the pictorial labels. For example, one 30-year-old patient's husband found the labels useful for literate and illiterate patients alike:

> "This system is better than the tickmark system. For illiterate people, the pictures help [them] to understand and in this system you have the pictures and the tickmarks...the system is convenient for both literate and illiterate people because you have included the words and pictures."

Local v. Non-local Pictograms

Dowse and Ehlers found that pictograms created in collaboration with local communities were better understood than pictograms created by non-local artists. Although our results also suggest that locally-developed pictograms may lead to improved comprehension of both dosage and drug indication when compared to non-local pictograms, the differences were not statistically significant. In addition, when local and non-local pictograms for each symptom were compared, only the two depicting heartburn led to significantly different comprehension (local version better understood). These inconclusive findings demonstrate the need for further research to examine the benefits of using local pictograms. This issue will have significant implications for implementation and scale-up of any pictorial interventions, since customizing pictograms and pictorial messages to each target community could be more costly and time-consuming than employing standardized icons.

Practical Implications

Additional factors will have to be considered before this intervention could be scaled up to government health facilities and community outreach programs. For example, many providers in the study clinic reported that the label system was more time-intensive than the standard care system of tickmarks. The increased patient volume in a government facility could introduce challenges for the staff regarding time management and increased waiting times for patients. However, it is possible that, as the intervention becomes more routine, staff will become more time-efficient at utilizing the pictorial labels.

In addition to the challenge of time, we found public and private providers outside of the study clinic resistant to use any system other than the deep-rooted standard care method. However, as is the case with many interventions, successive and routine use could increase utility and acceptability of the label system among health providers and clinical staff.

Some challenges faced in implementation of the intervention were particularly difficult in our study community. Highly conservative social traditions have made open discussion of female reproductive health almost taboo. For this reason, many women delay treatment and even lie about their symptoms once in the health facility. Use of these indication pictograms could potentially make all members of the community more accustomed to thinking and talking about these issues. In addition, some Muslim participants and family members remarked that their religion forbids the storage of materials depicting human forms in the household. While, in most cases, health counselors from the clinic were able to convince these women of the need to make an exception for the pictorial labels, religious concerns should be considered when developing and implementing such interventions.

Finally, interventions like the pictorial labels used in this study can be designed in a cost-effective way. Printing and production of the labels during the study phase was about Rs.1 per label (about 2.5 U.S. cents), and larger scale productions would further reduce this cost.

Limitations

Due to degree of funding and human resources, we chose to measure adherence using indirect methods (pill count and self-report). In order to better understand the association between use of pictograms and adherence rates, further research is required that measures adherence using direct methods such as urine or blood tests and mechanical devices.

Another limitation of this study was the difficulty in establishing a causal relationship between comprehension of the pictograms depicting dosage and indication information on the labels and actual comprehension of dosage and indication information for each medication. Some women understood the pictograms very well, but were not able to make the connection that the information depicted on the labels related directly to the attached medication. Conversely, some women were able to recall accurately the dosage and indication of their medications, but were unable to interpret the corresponding pictograms on their labels. In addition, there were a number of women in this study for which comprehension did not lead to adherence; therefore, it is important to note that, while comprehension is a necessary factor in facilitating adherence, it is by no means a sufficient one.

No literacy test was administered to women participating in this study, in part, because no such test existed for this region and language. Instead, women were asked if they could read the words displayed on the labels, and this was used as an informal measure of literacy.

Generalizability of the results of this study is somewhat limited. This study was conducted in a rural area in India among only pregnant women, although this intervention is appropriate and intended for all low-literate subpopulations.

Another weakness of this study was the size of the research team required to successfully conduct all the follow-ups within the necessary time window. The lead interviewer was also the clinic health educator; therefore, on days the clinic manager required her to remain on-site for delivery discharge counseling, alternate interviewers were used. Although the lead interviewer was able to conduct the majority of the follow-up interviews in the villages, the team relied on one of two other KMVS field workers to conduct 13 of the 112 interviews. In preparation, these two alternate interviewers accompanied the lead interviewer into the field to observe several interviews before conducting any themselves; however, there may have been inconsistencies in the styles of each interviewer. In addition, because the survey was written in Gujarati and then translated, into Kutchi by the interviewer at the time of interviewing, the wording of questions may have been slightly different from one interviewer to another.

As frequently occurs in survey studies conducted in rural, low-resource settings, it was often difficult to find a private space in which to interview the participant alone. In fact, the few times the team requested a more intimate setting, suspicions were aroused in the husband and mother-in-law that the content and purpose of the meeting was inappropriate, thereby making the participant uncomfortable and distracted. For this reason, we did not request to conduct the interviews in a private space, and at some interviews there were as many as 40 individuals present. For about 5% of the study population, when the participant was asked a comprehension question, another individual present at the interview would respond first, forcing the team to disqualify the women's subsequent response. Also, lack of privacy during interviews could have resulted in biased answers by the women due to shyness or cultural expectations of reticence. Many women were clearly unaccustomed to being asked for their opinion on a subject; therefore, some may have provided responses they thought the team wanted to hear instead of true personal opinions. To protect against this possibility, all interviewers were trained extensively in ways to avoid leading questions and encourage the women to provide accurate, honest responses.

Future Direction:

Following the completion of this study, the labeling system was implemented on a trial basis in the clinic. A qualitative process evaluation was conducted from January 8-15, 2009, 6 months post-implementation. During this evaluation, a total of 43 individuals (35 patients and 8 health providers on staff at the clinic) were interviewed regarding the feasibility and functionality of the label system. The quantitative results of this evaluation were not available at the time of submission, and will be the topic of a future manuscript.

This study focused only on pregnant women, 98 percent of whom were illiterate; however, the concept of the intervention was developed with a more diverse population in mind. Therefore, additional studies must be conducted to test the effectiveness of these labels in improving comprehension of medical information in a more representative group of participants with a range of reading abilities. Further research is also needed to determine if the pictorial labels improve rates of adherence among low-literate populations. In addition, longitudinal studies examining comprehension rates over several months would be a valuable way to evaluate the effectiveness of the labels by examining the comprehension of medical information by patients after multiple visits to a health facility and, thereby, multiple exposures to the labels.

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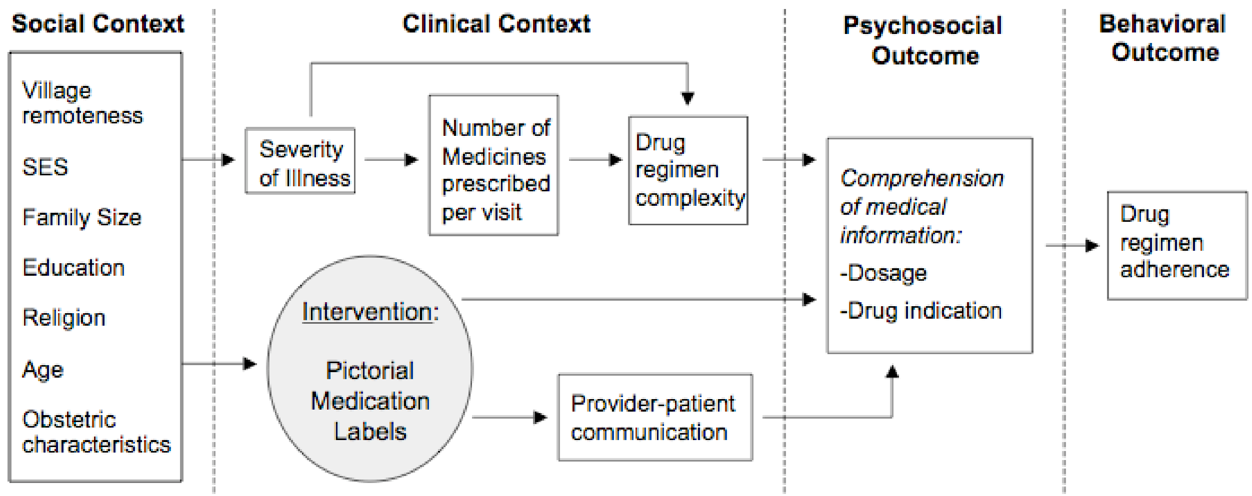


Figure 1. Logic Model for the use of pictorial medication labels as an intervention in the maternal and child health clinic in Khavda village, Kutch district, India.

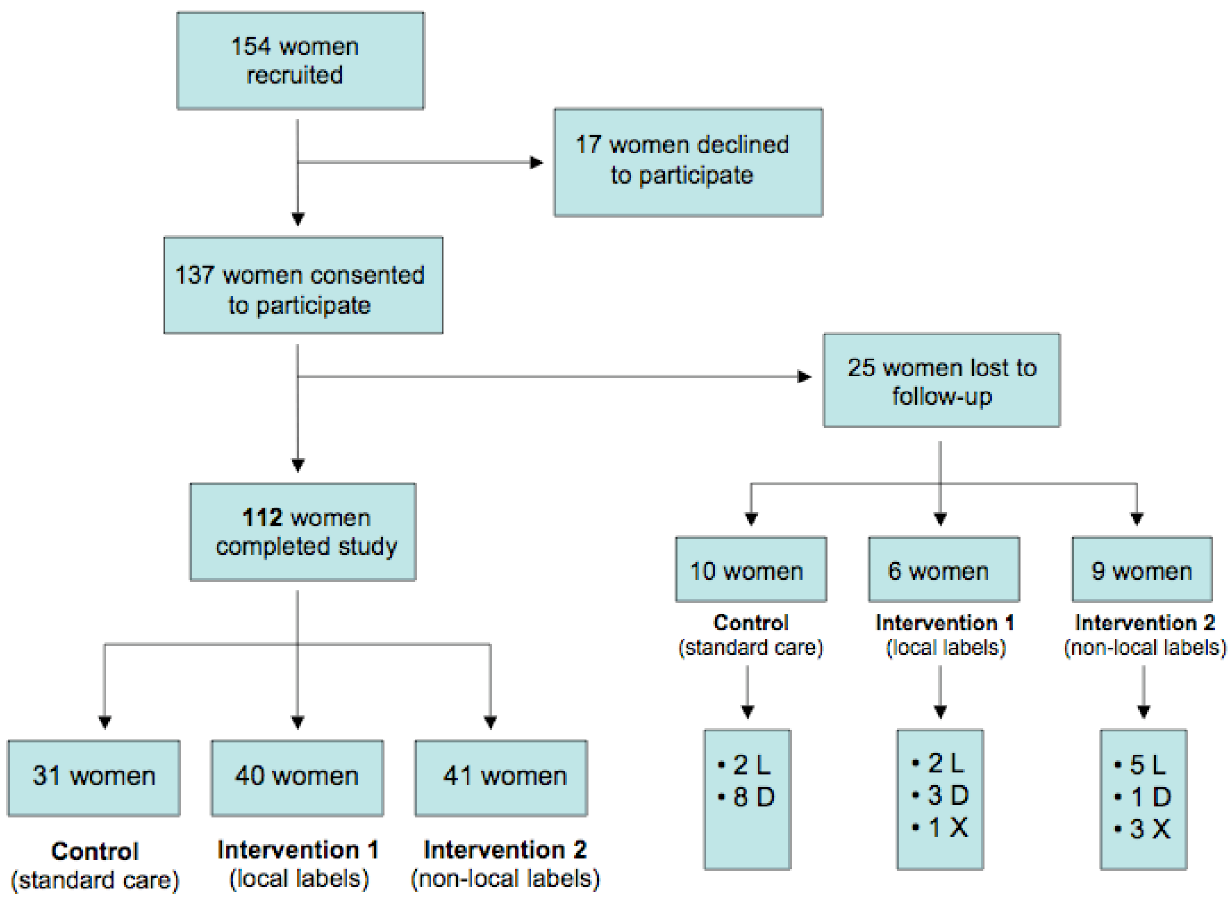


Figure 2. Consort diagram illustrating study sample sizes and participant flow. Twenty-five women were lost to follow-up, for reasons of logistical challenges (L), delivery prior to follow-up (D), and declining follow-up (X).

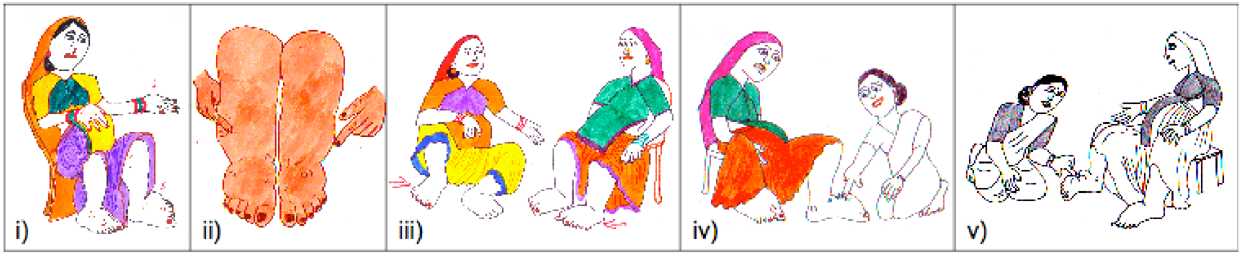


Figure 3. Evolution of local artist's pictograms for indication of swelling/edema during development phase. i) In this pictogram, arrows focusing on swollen hands and feet were not recognized, and the red outline on the woman's skirt was interpreted by many women to be blood. ii) The second pictogram aimed at drawing full attention to the health problem; however, many women in the pretest rounds had trouble contextualizing the "floating" legs. iii) The third pictogram used larger arrows, and two women with swelling shown at various angles; however, some women were confused by the presence of two women and thought they were simply chatting. iv) and v) These pictograms were better understood, since they used a government nurse to draw attention to the troubled body part, instead of arrows, with which women had no visual experience. The black and white pictogram was used in the randomized trial.

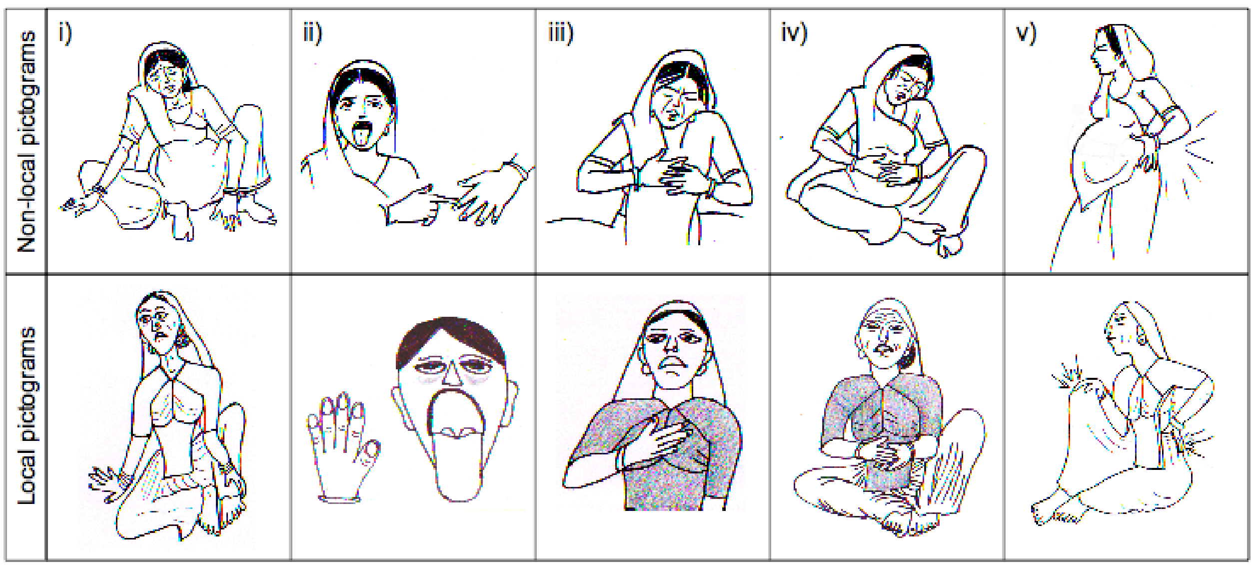
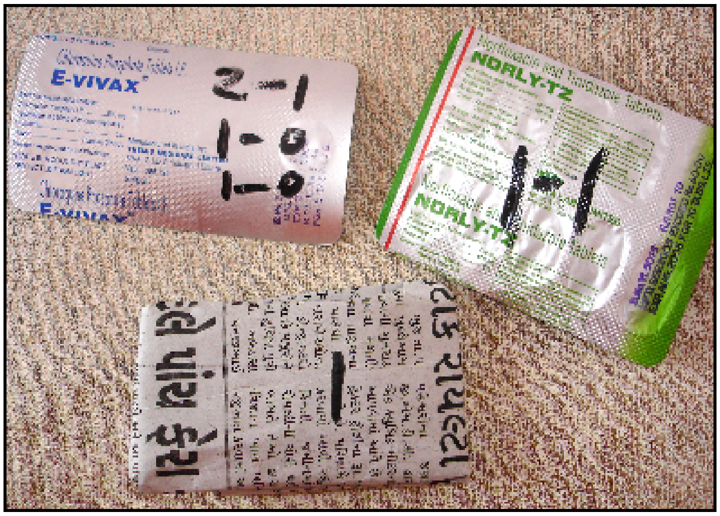


Figure 4. Non-local and local versions of the five most commonly used indication pictograms during the study. From the left: i) body weakness/fatigue, ii) anemia, iii) heartburn, iv) abdominal pain, and v) body ache. All indication pictograms appeared on labels with short text descriptions as shown in Figure 5.

a.



b.

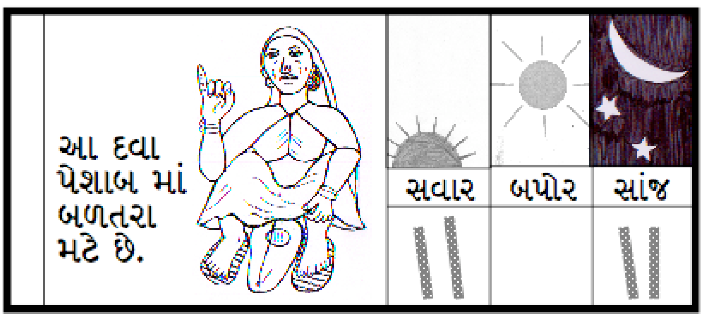


Figure 5. Comparison of two communication methods used in study. a) Standard care method used in the control group. Numerals represent number of pills and order of numerals represents time of day (e.g. "2-1" indicates 2 pills in the morning, and 1 pill at night). (N.B. Top left medication is for malaria. Dosage varies by day, with each row of instructions representing a single day.) b) Pictorial Label. (actual size) Text to the left of indication pictogram states: "This medication is for burning during urination." (for UTI) Text under each time of day pictogram states (from left): "morning," "afternoon," and "night." Space below each time of day pictogram is intended for dosage instructions (e.g. instructions given here indicate 2 units in the morning and 2 units at night).

Table 1. Distribution of demographic characteristics by study group

Variable	Participants, n (%) Control n=31	Intervention 1 n=40	Intervention 2 n=41	p-value	Total* n=112
Age (years)					
<=30	28 (90.3)	38 (95)	34 (82.9)		100 (89.3)
>30	3 (9.7)	2 (5)	7 (17.1)		12 (10.7)
				0.209	
Religion					
Hindu	11 (35.5)	10 (25)	14 (34.2)		35 (31.3)
Muslim	20 (64.5)	30 (75)	27 (65.9)		77 (68.8)
				0.564	
Education (standard completed)					
None	29 (93.6)	36 (90)	40 (97.6)		105 (93.8)
1-4th	1 (3.2)	1 (2.5)	1 (2.4)		3 (2.7)
5-7th	1 (3.2)	3 (7.5)	0 (0)		4 (3.6)
8-10th	0 (0)	0 (0)	0 (0)		0 (0)
				0.497	
Family size					
2	1 (3.2)	3 (7.5)	6 (14.6)		10 (8.9)
3-5	13 (41.9)	22 (55)	11 (26.8)		46 (41.1)
6-8	10 (32.3)	9 (22.5)	13 (31.7)		32 (28.6)
9+	7 (22.6)	6 (15)	11 (26.8)		24 (21.4)
				0.186	
Household occupation					
Wage labor	23 (74.2)	19 (47.5)	26 (63.4)		68 (60.7)
Other	8 (25.8)	21 (52.5)	15 (36.6)		44 (39.3)
				0.067	
Distance of home village from clinic (km)					
0	4 (12.9)	5 (12.5)	4 (9.8)		13 (11.6)
1-14	13 (41.9)	22 (55)	16 (39)		51 (45.5)
15+	14 (45.2)	13 (32.5)	21 (51.2)		48 (42.9)
				0.532	

* column percentages total to 100

Table 2. Distribution of obstetric and fertility characteristics by study group

Variable	Participants, n (%) Control n=31	Intervention 1 n=40	Intervention 2 n=41	p-value	Total* n=112
Gestation of current pregnancy (months)					
1-3	5 (16.1)	2 (5)	3 (7.3)		10 (8.9)
4-6	10 (32.3)	18 (45)	17 (41.5)		45 (40.2)
7-9	16 (51.6)	20 (50)	21 (51.2)		57 (50.9)
				0.501	

Gravida					
1-3	12 (38.7)	22 (55)	17 (41.5)		51 (45.5)
4-6	13 (41.9)	13 (32.5)	12 (29.3)		38 (33.9)
7+	6 (19.4)	5 (12.5)	12 (29.3)		23 (20.5)
				0.295	
No. of living children					
0	8 (25.8)	10 (25)	14 (34.2)		32 (28.6)
1-2	9 (29)	16 (40)	7 (17.1)		32 (28.6)
3-5	11 (35.5)	10 (25)	14 (34.2)		35 (31.3)
6+	3 (9.7)	4 (10)	6 (14.6)		13 (11.6)
				0.453	
No. of expired children					
0	21 (67.7)	28 (70)	27 (65.9)		76 (67.9)
1	8 (25.8)	11 (27.5)	9 (22)		28 (25)
2	1 (3.2)	1 (2.5)	5 (12.2)		7 (6.3)
3	0 (0)	0 (0)	0 (0)		0 (0)
4	1 (3.2)	0 (0)	0 (0)		1 (0.9)
				0.360	
No. of abortions					
0	22 (71)	33 (82.5)	30 (73.2)		85 (75.9)
1	4 (12.9)	4 (10)	8 (19.5)		16 (14.3)
2	4 (12.9)	2 (5)	1 (2.4)		7 (6.3)
3	1 (3.2)	1 (2.5)	2 (4.9)		4 (3.6)
				0.507	
Percentage of deliveries conducted at home (%)					
0 (none)	12.5	27.3	6.7		16.1
1-50	20.8	6.1	13.3		12.6
51-99	25	21.2	13.3		19.5
100	41.7	45.5	66.7		51.7
				0.131	

* column percentages total to 100

Table 3. Total number of medications prescribed to each woman by study group

		Participants, n (%)				
		Control n=31	**Intervention 1 n=40**	**Intervention 2 n=41**	**p-value**	**Total* n=112**
Total medicines prescribed at visit	1	1 (3.2)	2 (5)	4 (9.8)		7 (6.3)
	2	6 (19.4)	10 (25)	14 (34.2)		30 (26.8)
	3	10 (32.3)	13 (32.5)	10 (24.4)		33 (29.5)
	4	9 (29)	12 (30)	5 (12.2)		26 (23.2)
	5	3 (9.7)	2 (5)	6 (14.6)		11 (9.8)
	6	2 (6.5)	1 (2.5)	2 (4.9)		5 (4.5)
					0.496	

* column percentages total to 100

	Weighting	No. of Medications	Weighting x No. of Medications
Dosage Form			
Oral			
Tablet	1		
Syrup	2		
Powder	2		
Topical			
Cream	2		
Other			
Vaginal Pessary	3		
		TOTAL A =	
Dosing Frequency			
1X daily	1		
1X daily, as needed	0.5		
2X daily	2		
2X daily, as needed	1		
3X daily	3		
3X daily, as needed	1.5		
4X daily	4		
		TOTAL B =	
Additional Directions			
Dissolve powder	1		
Multiple units at each dose	1		
Variable dose (e.g. 3-4 spoonfuls)	1		
Specific times (e.g. 8a.m. or 6hrs following first dose)	1		
Take with food	1		
Alternating dose (e.g. 1 pill in the morning, 2 pills at night)	2		
		TOTAL C =	
		Regimen Complexity Score (A+B+C) =	

Table 4. Drug Regimen Complexity Index Scoring Sheet. Weightings were assigned in each category to each medication prescribed. Weightings for each of the three main categories were summed (A, B, and C) to generate a total score. Scores ranged in this study from 2 to 24.

Table 5. Drug Regimen Complexity Index Score by study group.

	Participants, n (%)				
	Control n=31	**Intervention 1 n=40**	**Intervention 2 n=41**	**p-value**	**Total* n=112**
Drug regimen complexity** (percentile)					
25^{th}	5 (16.1)	12 (30)	11 (26.8)		28 (25)
50^{th}	11 (35.5)	8 (20)	13 (31.7)		32 (28.6)
75^{th}	9 (29.0)	12 (30)	8 (19.5)		29 (25.9)
100^{th}	6 (19.4)	8 (20)	9 (22)		23 (20.5)
				0.648	

* column percentages total to 100
** drug regimen complexity index scores ranged from 2 to 24, with 24 being the most complex regimen prescribed.

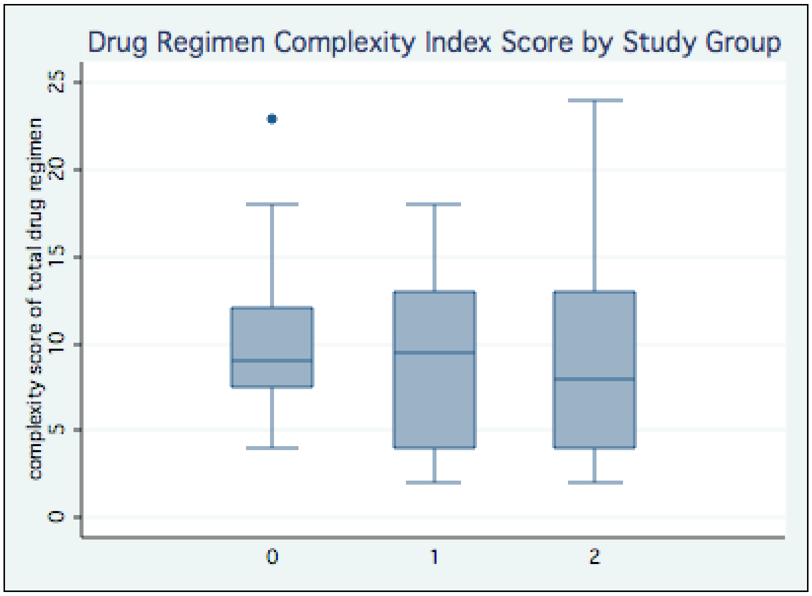


Figure 6. Box plot showing distribution of drug regimen complexity scores by study group (0=Control; 1=Intervention 1; 2=Intervention 2).

Table 6. Distribution of demographic characteristics in participants completing the study and those lost to follow-up

	Participants, n (%)			
	Completed study n=112	**Lost to follow-up n=25**	**p-value**	**Total* n=137**
Age (years)				
<=30	100 (89.3)	22 (88)		122 (89.1)
>30	12 (10.7)	3 (12)		15 (10.9)
			0.852	
Religion				
Hindu	35 (31.3)	6 (28.6)		41 (30.8)
Muslim	77 (68.8)	15 (71.4)		92 (69.2)
			0.807	
Education (standard completed)				
None	105 (93.8)	17 (100)		122 (94.6)
1-4th	3 (2.7)	0 (0)		3 (2.3)
5-7th	4 (3.6)	0 (0)		4 (3.1)
8-10th	0 (0)	0 (0)		0 (0)
			0.570	
Family size				
2	10 (8.9)	0 (0)		10 (7.3)
3-5	46 (41.1)	3 (12)		49 (35.8)
6-8	32 (28.6)	8 (32)		40 (29.2)
9+	24 (21.4)	14 (56)		38 (27.7)
			0.001	

Household occupation				
Wage labor	68 (60.7)	10 (40)		78 (56.9)
Other	44 (39.3)	15 (60)		59 (43.1)
			0.059	
Distance of home village from clinic (km)				
0	13 (11.6)	3 (12)		16 (11.7)
1-14	51 (45.5)	17 (68)		68 (49.6)
15+	48 (42.9)	5 (20)		53 (38.7)
			0.089	

* column percentages total to 100

Table 7. Distribution of obstetric, fertility, and other medicine-related characteristics in participants completing the study and those lost to follow-up

	Participants, n (%)			
	Completed study n=112	**Lost to follow-up n=25**	**p-value**	**Total* n=137**
Gestation of current pregnancy (months)				
1-3	10 (8.9)	3 (12)		13 (9.5)
4-6	45 (40.2)	4 (16)		49 (35.8)
7-9	57 (50.9)	18 (72)		75 (54.7)
			0.074	
Gravida				
1-3	51 (45.5)	5 (20)		56 (40.9)
4-6	38 (33.9)	7 (28)		45 (32.9)
7+	23 (20.5)	13 (52)		36 (26.3)
			0.**004**	
No. of living children				
0	32 (28.6)	2 (8)		34 (24.8)
1-2	32 (28.6)	2 (8)		34 (24.8)
3-5	35 (31.3)	6 (24)		41 (29.9)
6+	13 (11.6)	15 (60)		28 (20.4)
			0.000	
No. of expired children				
0	76 (67.9)	12 (70.6)		88 (68.2)
1	28 (25)	2 (11.8)		30 (23.3)
2	7 (6.3)	0 (0)		7 (5.4)
3	0 (0)	2 (11.8)		2 (1.6)
4	1 (0.9)	1 (5.9)		2 (1.6)
			0.001	

No. of abortions				
0	85 (75.9)	15 (88.2)		100 (77.5)
1	16 (14.3)	1 (5.9)		17 (13.2)
2	7 (6.3)	0 (0)		7 (5.4)
3	4 (3.6)	1 (5.9)		5 (3.9)
			0.504	
Percentage of deliveries conducted at home (%)				
0 (none)	16.1	14.3		15.8
1-50	12.6	14.3		12.9
51-99	19.5	28.6		20.8
100	51.7	42.9		50.5
			0.871	
Total medicines prescribed at visit				
1	7 (6.3)	5 (20)		12 (8.8)
2	30 (26.8)	10 (40)		40 (29.2)
3	33 (29.5)	5 (20)		38 (27.7)
4	26 (23.2)	3 (12)		29 (21.2)
5	11 (9.8)	1 (4)		12 (8.8)
6	5 (4.5)	1 (4)		6 (4.4)
			0.140	
Help taking meds?				
Yes	34 (30.6)	7 (46.7)		41 (32.5)
No	77 (69.4)	8 (53.3)		85 (67.5)
			0.213	
Share meds?				
Yes	28 (25)	5 (31.3)		33 (25.8)
No	84 (75)	11 (68.7)		95 (74.2)
			0.593	

* column percentages total to 100

Table 8. Comprehension of pictograms by Intervention group

	Participants with high comprehension* of pictograms, n (%)		
	Intervention 1	**Intervention 2**	**p-value**
Time of Day pictograms (n=80)			
Morning	31 (77.5)	31 (77.5)	1.000
Afternoon	28 (71.8)	31 (77.5)	0.560
Night	35 (87.5)	36 (90)	0.723
Drug Indication pictograms (n=81)	26 (65)	19 (46.3)	0.091

* "High comprehension" for time of day pictograms was defined as correctly interpreting the meaning of the given image (morning, afternoon, or night). (Time-of-day pictograms shown in Fig.5.) "High comprehension" for drug indication pictograms was defined as correctly interpreting *every* drug indication pictogram received.

Table 9. Comprehension of drug indication pictogram by type (symptom) and intervention group

	Participants with high comprehension of pictograms, n (%)		
	Intervention 1	**Intervention 2**	**p-value**
Drug Indication Pictogram*			
Weakness** (n=62)	24 (72.7)	22 (75.9)	0.778
Anemia (n=60)	22 (75.9)	26 (83.9)	0.438
Heartburn (n=28)	13(100)	9 (60)	**0.010**
Abdominal Pain*** (n=21)	14 (100)	7 (100)	1.000
Body ache (n=12)	6 (100)	5 (83.3)	0.296
Malaria (n=6)	1 (100)	1 (20)	0.121
UTI**** (n=6)	1 (50)	3 (75)	0.540
Constipation (n=5)	1 (50)	1 (33.3)	0.709
Vomiting (n=4)	2 (100)	2 (100)	1.000
White Discharge (n=4)	2 (100)	1 (50)	0.248
Cold (n=4)	NA	3 (75)	--

* Pictograms also were developed for vaginal bleeding, swelling/edema, dizziness/headache, and blood pressure; however, no medications requiring these labels were prescribed to women in the intervention groups.
** Twelve participants received two medications indicated for weakness. Of these twelve, nine produced concordant responses (e.g. both correct or both incorrect) for the weakness pictogram (comprehension tested once for each of the two medications), and were therefore included as a single correct response. The remaining three women produced discordant responses; therefore, they were dropped from the tabulation.
*** Two women received two medications indicated for abdominal pain. Both gave concordant responses for each of the two medications; therefore, both women were included in the tabulation as single observations.
**** One woman received two medications for Urinary Tract Infection (UTI). She provided discordant responses for the UTI pictogram (tested twice); therefore, her responses were dropped for this tabulation.

Table 10. Dosage and Indication Correctness Scores by Group

	Dosage Correctness Score			Indication Correctness Score		
	Mean	St. Dev.	p-value*	Mean	St. Dev.	p-value*
Control (n=31)	2.83	0.34		0.39	0.37	
Intervention 1 (n=40)	2.82	0.33	>0.05	0.71	0.33	**0.001**
Intervention 2 (n=41)	2.76	0.46	>0.05	0.65	0.36	**0.006**

* control as reference group

Table 11. Adherence to Drug Regimen by Study Group

	Control (n=30) n (%)	Intervention 1 (n=39) n (%)	Intervention 2 (n=39) n (%)
Full adherence	7 (23.3)	3 (7.7)	12 (30.8)
Partial adherence	11 (36.7)	11 (28.2)	15 (38.5))
Non-adherence	12 (40.0)	25 (64.1)*	12 (30.8)

* Adherence was significantly lower in the Intervention 1 group compared to the Intervention 2 group (p=0.005).

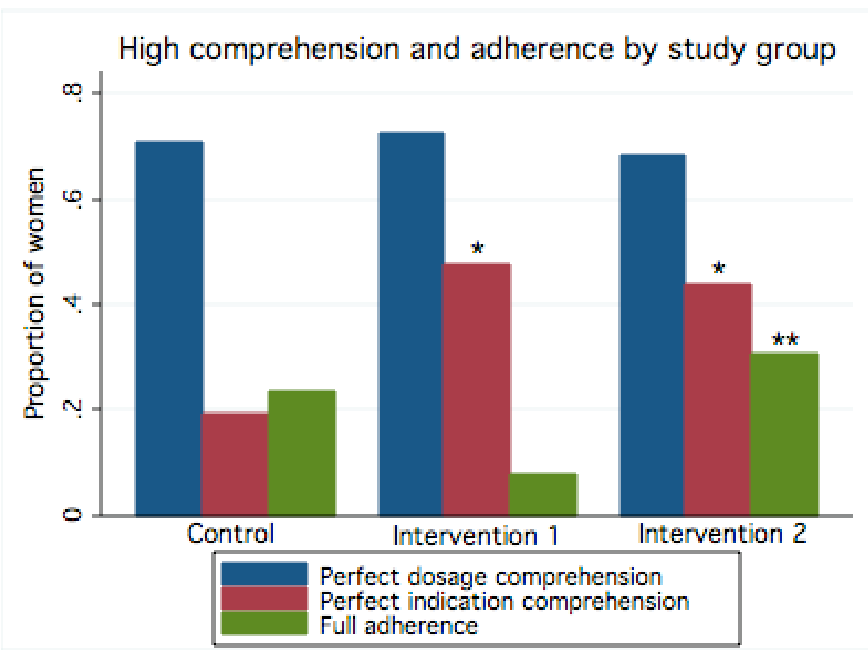


Figure 7. Dosage comprehension, indication comprehension, and drug regimen adherence by study group.
* A higher percent of women in both the Intervention 1 and 2 groups received a perfect score for drug indication comprehension as compared to the control group (p=0.014, 0.029 respectively).
** Percent of women with full adherence in Intervention 2 group was higher than Intervention 1 group (p=0.01).

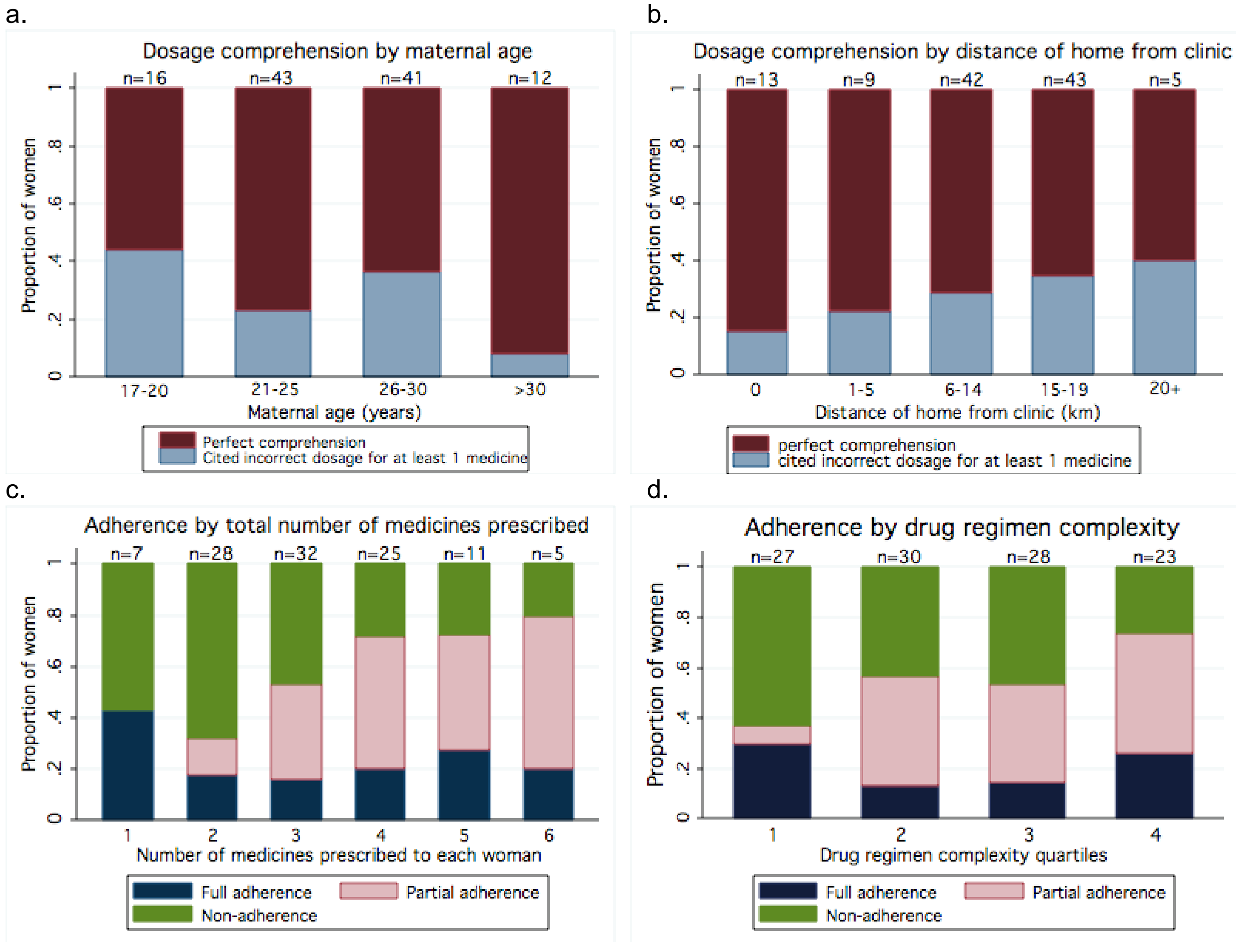


Figure 8. Percentage of women with perfect dosage comprehension and full adherence by demographic and drug regimen factors. a) A smaller percentage of women aged 17-20 years old had perfect comprehension than women above 30 years (p=0.04**).** b) A statistically insignificant trend was observed in decreasing percentage of women with perfect dosage comprehension with increasing distance of their home from the clinic. c) Percentage of women fully adhering to their drug regimen decreased with increasing number of medicines, although the trend was statistically insignificant. d) Percentage of women fully adhering to their regimen decreased as regimen complexity increased, although the trend was not statistically significant.

Table 12. Multiple logistic regression results for variables associated with high comprehension of dosage

	Unadjusted		Adjusted	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Study group (n=105)				
Control	1.0		1.0	
Intervention 1	1.2	(0.40-3.4)	1.1	(0.38-3.3)
Intervention 2	1.2	(0.42-3.5)	1.3	(0.44-3.9)
Distance from clinic (km)	0.94	(0.87-1.01)	0.94	(0.87-1.01)

* Adjusted for distance from home to clinic.
** 95% Confidence Intervals in bold represent p-values<0.05.

Table 13. Multiple logistic regression results for variables associated with high comprehension of drug indication

	Unadjusted		Adjusted*	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Study group (n=105)				
Control	1.0		1.0	
Intervention 1	4.1	**(1.3-13.2)**	4.9	**(1.3-18.5)**
Intervention 2	3.9	**(1.2-12.5)**	5.1	**(1.4-19.1)**
No. of children				
None	1.0		1.0	
1-2	0.22	**(0.07-0.7)**	0.22	**(0.07-0.72)**
3-5	0.25	**(0.09-0.73)**	0.23	**(0.07-0.74)**
6+	0.44	(0.11-1.7)	0.43	(0.1-1.8)
Education				
None	1.0		1.0	
At least 1 year	10.8	**(1.3-93)**	15.1	**(1.4-160)**

* Adjusted for number of children and maternal education.
** 95% Confidence Intervals in bold represent p-values<0.05.

Table 14. Multiple logistic regression results for variables associated with adherence to drug regimen

	Unadjusted		Adjusted	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Study group (n=102)				
Control	1.0		1.0	
Intervention 1	0.3	(0.07-1.3)	0.4	(0.07-1.8)
Intervention 2	1.5	(0.47-4.7)	1.8	(0.49-6.8)
Distance from clinic (km)				
0	1.0		1.0	
1-14	0.19	**(0.05-0.81)**	0.22	(0.04-1.08)
15+	0.5	(0.13-1.9)	0.48	(0.11-2.2)
Family Size	1.2	**(1.05-1.4)**	1.2	**(1.03-1.4)**
Dosage comprehension	4.9	**(1.07-22.7)**	6.6	**(1.3-33.8)**

* Adjusted for distance of home from clinic, family size, and dosage comprehension.
** 95% Confidence Intervals in bold represent p-values<0.05.

Table 15. Assistance in administration of medications by study group

	Participants, n (%)				
	Control n=31	**Intervention 1 n=40**	**Intervention 2 n=41**	**p-value**	**Total* n=112**
Do you need help taking your medicines?					
Yes	16 (53.3)	9 (22.5)	9 (22)		34 (30.6)
No	14 (46.7)	31 (77.5)	32 (78.1)		77 (69.4)
				0.007	

* column percentages total to 100

Appendix 1

Pictogram label intervention: design and development

Four artists were recruited to develop pictograms for the labels: 1) a female graphic designer working for *Galli Galli Sim Sim* (Indian *Sesame Street*) in New Delhi; 2) a male freelance artist living in Bhuj city, the nearest urban area to the study site; 3) a male professional, full-time artist living in Ahmedabad, the capital city of Gujarat, who had significant experience working with women's health NGOs on illustrations for health education publications; and 4) a female artist local to Kutch District, with experience producing illustrations for KMVS' weekly community newsletter. The pictograms depicted information on time of day ("morning," "afternoon," and "night"), and common illnesses and symptoms observed in pregnant women in the region (such as "vomiting," "vaginal bleeding," and "swelling"). Sixteen illnesses or symptoms were selected for depiction after careful consultation with three private and two public physicians working in the area, as well as several local TBAs.

Pre-testing was conducted to evaluate the individual pictograms produced by each artist. The final products each contained four pictograms on a single label (e.g. morning, afternoon, night, and one symptom pictogram). However, in order to ensure that appropriate attention was paid to each pictogram, pictograms were shown separately to the pretest participants. Pictograms were also slightly enlarged for the purposes of pre-testing. Sample layouts of the labels (e.g. one-sided vs. two-sided) were also shown to local women to determine the most comprehensible and efficient design. All label samples had dimensions of 3.5”x1.75.”

Three focus groups were conducted to inform changes for each image tested. The first focus group consisted of seven health professionals (6 females and 1 male), and assessed comprehensibility and clinical accuracy of the pictograms. Six participants were health coordinators and trainers for KMVS, and one participant was a government Attendant Nurse Midwife posted in the study region. Participants’ age range was 26 to 50 years.

The second focus group assessed comprehensibility of each of the four artists’ pictograms and appropriateness of the label design. The group included 27 local women ranging from 18 to 60 years of age. Fourteen women were village TBAs (who had received at least one formal training in obstetric and reproductive health care), and 13 participants were local women with no health education background. Twenty-five women were functionally illiterate, with no formal education. No women participating in this pre-testing focus group discussion were pregnant.

The third focus group, consisting of 15 local women, assessed comprehensibility and appropriateness of the label/pictogram size. All 15 participants had not received any formal education and had no health background. None of these women reported being pregnant.

In-depth interviews were also conducted with one government physician posted in the study region, one health trainer with KMVS, two local TBAs, and the clinic health educator. These interviews were unstructured, although all individuals were asked about label design and functionality. These professionals were also consulted on clinical accuracy of the sixteen indication pictograms.

Color pictograms were used in the initial focus groups, but for economic reasons related to potential scale-up, all pictograms were converted to black and white, and these new grayscale pictograms were used in the final focus group discussion and in-depth interviews. Simple written translations of each pictogram in Gujarati were also included on each label.

International Standard Organization's (ISO-3864) guideline of 65% comprehension for graphic symbols was used to determine whether pictograms were adequate for use in the study. Following the pre-testing, it was determined that the Ahmedabadi and local female artists' pictograms were correctly interpreted by the highest percentages of focus group participants; therefore, only these two artists' pictograms were used in the study. After finalizing the pictograms and label design on Corel Draw, files were given to a printing and production company in Bhuj city to be processed into labels. Labels used in the study were 3.5"x 1.4" and single-sided.