ScaleMed: A Methodology for Iterative mHealth Clinical Trials

Peter Washington, Mayank Kumar, Anant Tibrewal and Ashutosh Sabharwal
Rice University
Houston, TX 77005
peterwashington@alumni.rice.edu, mk28@rice.edu, avt3@rice.edu, ashu@rice.edu

***Abstract*—mHealth, which involves using smartphones as a tool for healthcare monitoring and delivery, continues to gain traction worldwide. As a result, new pilot programs and clinical trials continue to be launched to establish clinical evidence. However, the continual need for software changes between iterations of the trial creates a lengthy time loop between clinical researchers requesting a change and software developers implementing the requested change. We propose a new methodology for performing clinical trials, called *ScaleMed*. The ScaleMed methodology involves decoupling low-level app functionality from high-level trial-related operational parameters, a common software development practice. By utilizing a centralized website that allows clinical researchers to rapidly update these trial parameters, iterative clinical trials have the potential to move at a much faster rate than in current practice. We demonstrate an example of the ScaleMed methodology applied to an ongoing mental health trial (codenamed *Lucy*). In addition, we conducted a separate trial on the usability of the ScaleMed-enabled Lucy platform and found a predominantly positive response from the potential clinical users. In our limited trials, we showed that the time to make changes to app parameters was cut from weeks to less than a minute.**

I. Introduction

One of the most critical steps in healthcare research is to establish clinical evidence. However, conducting at-scale trials is a complex and time-consuming process. Large-scale trials require recruiting diverse trial participants, ensuring safety and privacy for participants and their health data, and ensuring reliability of off-site studies. Recent advances in smartphone capabilities and their increasingly ubiquitous penetration create the potential for solving many of the challenges with conducting at-scale clinical trials [1], [2]. For example, trial participants can be recruited from anywhere in the world, their health data can be directly collected from their smartphones while being encrypted for safety and privacy, and app-based inbuilt checks can be set-up for data consistency and reliability.

However, the mHealth clinical study process is still complicated for clinical researchers as it now involves diverse contributors like app developers, web developers, clinical research staff and trial participants. Many clinical studies adopt a multi-stage iterative approach, where small pilots are conducted to refine the details of the trial before a larger scale study is launched. Thus, during the pilot stages, the clinical app often has to be tweaked many times, with changes to the user interface, trial text, types of data to be collected, data security settings, data storage location, and sequence of questions for the participants. Currently, most clinical teams rely on the active involvement of smartphone app developers for every tweak that is made. As a result, conducting iterative mHealth clinical trials is often a long process due to the delays involved in these development cycles. This, in turn, severely limits the ability for experimentation from the clinical researcher's perspective, largely to avoid additional delays from repeated app changes.

Furthermore, mHealth clinical trials are becoming especially prevelant in low-resource settings [3], [4]. Flexibility for organizational and functional change as well as robustness to low-resource contexts are essential for deploying an mHealth app in a low-resource setting [5]. Even in non-iterative clinical trials, researchers may learn of trial parameters that they wish to change mid-trial [6].

In this paper, we propose a clinical trial methodology called *ScaleMed*[1] that is designed to enable clinical researchers to rapidly customize their ongoing mHealth trials with little to no involvement from app developers beyond the initial development of the trial app. The methodology leverages current mobile and web software development techniques to decouple low-level app functionality from high-level trial-related parameters. The decoupling is performed as a part of the initial app design phase by carefully identifying trial parameters which might change during pilot stages and making them reconfigurable so that they can be easily changed by the clinical researchers.

The ScaleMed methodology spans the development of the core mHealth app that the clinical study participants install on their smartphones. This base app is designed such that all reconfigurable trial parameters reside in a separate configuration file. The configuration file is automatically updated and synchronized with the ScaleMed server so that any changes in trial parameters are seamlessly reflected in the app. Furthermore, the ScaleMed methodology consists of developing a website for clinical researchers to easily and intuitively update trial-related parameters during an ongoing study. A web portal can greatly simplify both application complexity and the overall clinical trial process [7]. Once the changes are submitted, all (or a subset of) the participant's apps are updated.

We also present a case study application of the ScaleMed methodology to an ongoing clinical study, codenamed *Lucy*, in collaboration with the Department of Psychology at Baylor

[1]The name ScaleMed is inspired by Scaling Medical mHealth trials.

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College of Medicine. The aim of the Lucy trial is to develop a better understanding of the relationship between the mood of patients diagnosed with depression and their mobile phone usage patterns. The Lucy study uses two apps that are installed on the patient's mobile phones — (i) a background logging app which records smartphone usage, and (ii) a survey app that periodically queries the patient regarding their mood at that time.

As the Lucy project is currently in its initial pilot stage, several changes and small tweaks are needed in both of these apps, such as in the exact wordings of the questions to be asked, the frequency of patient queries, and the types and frequency of mobile phone usage to be logged. We have adopted the ScaleMed methodology for the Lucy study in an attempt to reduce reliance on app developers and to give clinical researchers the independence to rapidly experiment with the protocol to be used in their trial. We evaluate the effectiveness of the Lucy implementation based on (i) ease of use for the clinical researchers, (ii) confidence of the clinical researchers while making changes using the web front-end, and (iii) acceptability of the methodology.

To determine the effectiveness of ScaleMed in terms of these three metrics, we conducted a trial with 25 participants. All participants were junior or senior pre-medical students at Rice University with no prior knowledge about ScaleMed or the Lucy study. We asked each of the trial participants to perform three generic tasks on Lucy's web interface, with a short training period but no assistance during the tasks. We observed that most of the participants found Lucy's web interface to be very easy to use. The time to update app behavior was less than a minute, compared to a pre-ScaleMed development cycle that would have taken weeks. In addition, most participants stated that they would be willing to use the ScaleMed methodology for their own clinical trials. The key lesson was that with adequate documentation and explanation of each functionality, nearly all participants will be comfortable with relying on the web-based app changes, *without* assistance from the app developers.

A. Related works

There are many native mHealth app development APIs such as open mHealth [8] and Ohmage [9]. Most of these focus on easing the development cycle by providing APIs to easily code common features present in mHealth apps, such as creating survey forms and questionnaires, recording sensor data, and dealing with clinical consent forms. There are also apps, such as Dimagi's CommCare, that allow developers to program mobile apps in only a few days [10].

By contrast, the focus of the ScaleMed methodology is to enable fast experimentation by clinical researchers *without* relying on app developers, and to reduce the time and cost involved in conducting at-scale clinical studies. In this way, the proposed ScaleMed methodology is analogous to website building platforms like Wix [11] and Squarespace [12], which simplify and speedup the website development process for the end-user.

II. The ScaleMed Methodology

ScaleMed is a methodology for performing mHealth clinical trials that allows clinical researchers to change an mHealth clinical app by using a simple and intuitive web interface without relying on app developers, directly propagating such changes onto the phones of clinical study participants with the single click of a button.

The aspects of the app that can be fine-tuned by trial and error are called **trial parameters**. Trial parameters can span many aspects of the app, such as the type of encryption applied to the user's input, the exact wording and ordering of text that appears on the app, the frequency of data collection, and simple UI-related decisions.

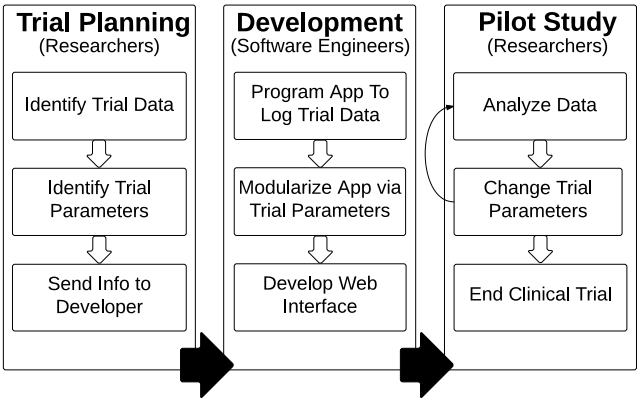

Fig. 1: The work cycle for clinical trials conducted using the ScaleMed methodology. There are three primary steps: trial planning, development and pilot study.

The ScaleMed methodology involves three stages: (i) the **clinical study planning stage** when the clinical researcher and app developer work together to identify the trial parameters which can change during the pilot phase of the study, (ii) the **app development stage** when the app developer builds the base app in a manner such that the app reads the values of all trial parameters from an external configuration file, and also builds a server side web-frontend which allows clinical researchers to make changes to the app's configuration files, and (iii) the **pilot study stage** when the clinical researcher can experiment with different settings for trial parameters and gather different sets of pilot data to quickly decide the best-suited parameter choices for larger-scale studies.

In a typical mHealth clinical study, the app used by clinical study participants on their mobile phones acts as a *client* that gathers patient-related data. The client app constantly communicates over the Internet with a secure computer in the cloud which acts as a *server* to store clinical study data persistently. This client-server architecture is only used for transferring clinical study data, and any app-related updates are done separately either by using the app-store mechanism (if the app is published) or by sending the app setup files directly to clinical study participants. Both of these methods

are complicated for clinical study participants considering that many of them are old-aged or suffer from some ailments.

In a ScaleMed-based clinical study, on the other hand, the clinical app's updates happen automatically over-the-air (OTA) and require minimal involvement from clinical study participants. The same client-server architecture in ScaleMed is used for transferring both the clinical study data as well as configuration files for app updates. The clinical researcher submits any request for trial parameter changes to the server using a web front-end, and a new configuration file is automatically generated on the server. These new configuration files are then propagated to the participant phones using either a PUSH or a PULL at a regular time interval. The client apps are automatically updated.

In the remainder of this section, we discuss specific steps that are to be followed at each stage of the ScaleMed software development methodology. We then detail how the ScaleMed methodology has been implemented for the ongoing Lucy clinical study, specifically focusing on the choices we made while following the ScaleMed methodology.

A. Clinical trial planning stage

The first step in the ScaleMed methodology involves thoughtful planning on the part of clinical researchers in order to identify trial parameters that might be changed over the course of the pilot study. These could include parameters that are not known during the planning stage but could be learned or fine-tuned by trial and error. Trial parameters should span all aspects of the app, from front-end decisions such as app text and ordering of questions to functionality-related decisions such as frequency of client-server communication.

B. Software development stage

Once all aspects of data collection and trial parameters have been decided by the clinical researchers, the software development stage can begin. From the beginning, all trial parameters are stored separately in a configuration file in a format such as XML (extensible markup language). The app is written in a manner such that all trial parameters are read from the configuration file. The configuration file is also read on app startup. Thus, the trial parameters can directly be changed by updating the configuration file.

The idea is to keep the parameter files in sync with the corresponding version on the server. This can be done either through regular querying for updates from the server (PULL architecture) or by letting the server notify each client about availability of new version using a PUSH notification.

The second aspect of the software development stage involves building a web frontend for clinical researchers to easily update the trial parameters. Each time a modification is made, an updated configuration file is generated. Apart from this, the web frontend provides an option to keep track of the version of the software running on a participant's mobile device. This helps clinical researchers to see when their submitted changes are propagated to each client device. It also helps identify possible Internet connectivity issues that some clinical study participants might face during the trial.

There are times when the clinical researchers may want to know which versions of the data correspond to a particular version of the app in order to conduct some comparative analysis on the collected data. This analysis can influence the changes that the clinical researchers make to the app in the following iterations. In order to facilitate this type of easy and unambiguous data analysis, the ScaleMed methodology requires the app developer to store the version of the app with all of the data on the server. The clinical researchers must always be able to access the data corresponding to particular version of the app.

There are also times when the clinical researchers may want to perform randomized trials using the apps. That is, they would want to assign one intervention (set of trial parameters) to one group of clinical study participants and another intervention to another group of clinical study participants. In order to facilitate this, the web interface for the clinical researchers needs to have an option to submit a change to all participants or to a group of participants. The clinical researchers must have the ability to designate each registered clinical study participant to a particular group.

C. Pilot Study stage

Once the initial version of the app is complete, the developers can step away and give the reseachers full control of the clinical trial. If the researchers perform a methodical isolation of all trial parameters, then there will not be any need for continuing developer intervention for the duration of the pilot study and beyond, allowing for a fast-paced and useful iterative clinical trial.

The clinical researchers can analyze data corresponding to different app versions to conduct a comparative analysis. By knowing which version of the app is associated with each data point, the clinical researchers can easily determine which version of the app is ideal for a large-scale clinical trial. This is very similar to the beta testing paradigm adopted by many software developers.

A significant advantage of the grouping of patients in the ScaleMed methodology is the ability to support the incremental deployment of trial changes made to the participants' apps. When the clinical researchers make any change to the apps, they can deploy to a few patients at a time rather than all patients at once. The grouping of patients also makes randomized trials much easier. The clinical researchers can deploy one version of a change to one group of patients and other version of a change to another group of patients. The clinical researchers can then compare the results from both groups of patients in order to determine which change, if any, was better.

III. ScaleMed Case Study: Lucy

In this section, we discuss the application of ScaleMed to an ongoing pilot trial, codenamed Lucy. Lucy involves two apps that both read from their own configuration files. The

first app, a logging app, records all the smartphone usage of the participant. The second app, a mood reminder app, asks mood-related questions on a daily basis. All forms of data are synchronized with the Lucy cloud and accessible only to the IRB-approved researchers.

When applying the ScaleMed methodology to the development of Lucy, it was determined that the most important trial parameters were the frequency of the data collection on both the mood reminder and logger apps, which data the logger app collects, and the wording of the questions that appeared in the mood reminder app.

During the App Development Phase, the team created a simple web interface allowing the clinical researchers to change the trial parameters. The web interface is hosted on the Amazon EC2 servers and implemented using the Python Flask framework.

The two mobile apps both read their trial parameters from a single database on the Lucy server. The mood app gets from the server the specific questions asked to the patient as well as the label text from the server via a periodic PULL request. The logger app obtains all of the types of data that should be logged via frequent PULL requests from the server.

During the Pilot Study Phase, the researchers at the Baylor College of Medicine initially recruited 3 patients to test the software and obtain pre-trial data, with more patients scheduled for future iterations of the pre-trial. Because the Lucy clinical trials are trying to determine patterns over a long period of time, we have yet to see the final results of the trial. The team plans to open-source the codebase for Lucy once the pre-trial stage has been completed, and all the major debugging has been performed.

IV. Usability Trial and Results

The primary aim of the experiments presented here were to measure the effectiveness of the ScaleMed development methodology via its implementation for the Lucy project. We selected three metrics to determine the effectiveness of the ScaleMed methodology: (i) ease of use for clinical researchers (ii) confidence of clinical researchers while making changes using the web frontend, and (iii) acceptability of the methodology.

A. Trial Design

To evaluate ScaleMed in terms of the above metrics, we conducted a trial with 25 participants.[2] All participants were Rice University pre-medical students who had no prior knowledge about ScaleMed or the Lucy trials. We described the basic idea of the ScaleMed methodology to each of the trial participants and then introduced them to the ongoing Lucy study. We then showed them the web interface that is used by the clinical researchers to change trial parameters. Next, we asked each of the trial participants to perform three generic tasks on Lucy's web interface without any assistance. The three tasks were to: (i) change the wording of the questions the patients would be asked by the mood reminder app, (ii) change the labels of the input that the patients could enter into the mood reminder app, and (iii) change the set of sensor data that is continuously recorded by the logging app.

To measure the ease of use, we recorded the time that it took the participants to correctly perform each of the required tasks without any guidance. We also asked participants to rate the difficulty of using Lucy's web interface from 1 to 10 after performing the tasks, where 1 corresponded to a very simple task and 10 corresponded to an extremely difficult task. To measure the confidence of the clinical researcher while making these changes, we directly asked the trial participants whether they were confident about the correctness of the committed changes, or whether they feared that wrong changes were committed to the apps. To measure the acceptability of the ScaleMed methodology, we asked trial participants whether they would like to make changes to the clinical trial parameter themselves, or instead rely on an app developer to make such changes on their behalf.

B. Results

The mean time for completing all 3 tasks was always less than 10 seconds. Furthermore, there was not a single participant who took more than 45 seconds to perform any particular task. According to the trial participants, the average difficulty rating was 1.4 on a scale of 1 to 10 where 1 meant the easiest. These results indicate that the participants found the web interface to be extremely intuitive to use and were able to quickly adapt to its user interface.

Out of the 25 participants, only 5 stated that they were worried that they were making the wrong changes when interacting with the web interface. According to discussions with these 5 participants, most of this worry was due to a confusing user interface design. For example, one of the participants did not understand the description of some of the trial parameters that could be logged. Therefore, the software engineer creating the web interface should ensure that the web interface is easy for the clinical researchers to use in order to prevent any confusion. Clear documentation is crucial.

As shown in Figure 2, most of the study participants (18 out of 25) stated that they would definitely prefer to have control over the trial parameters rather than having the software developer updating the app every time a small change needs to be made. By contrast, 5 participants stated that they would definitely prefer to have a software developer make changes to the app, as they believed that the software developer is the only one who is professionally qualified to make these technical changes. They do not feel qualified, as doctors, to make changes to the application. The final 2 participants stated that they would only be comfortable with having control over simple trial parameters. If the changes were too complicated, they would not want to be involved. In the case of Lucy, one participant specified that they would be comfortable with making changes to the text of the mood reminder app, but not necessarily with changing the device statistics that are involved in the logger app.

[2]The trial has been approved by Rice IRB: protocol number $733053 - 1$, dated 4/1/2015

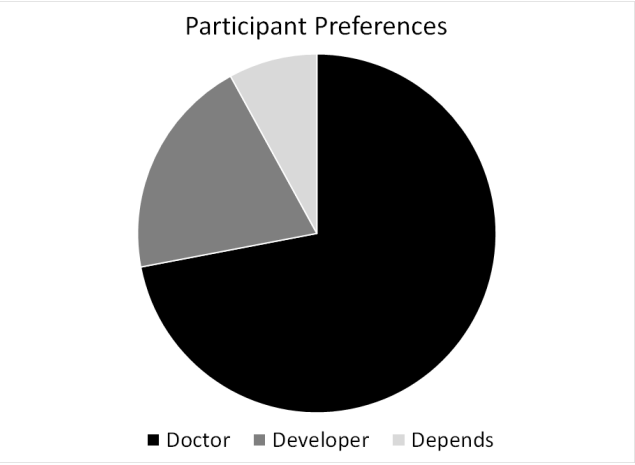

Fig. 2: Out of the 25 study participants, 18 stated that they would prefer to control the clinical trial parameters themselves, while only 5 stated that they would prefer a software engineer. 2 stated that the decision depends on the complexity of the trial parameters.

Based on these results, it is clear that ScaleMed clinical trial methodology provides significant benefits to mHealth clinical study projects, like Lucy, which are in their pilot stage and have important features that can easily be parameterized. App updates which generally would have taken days can now be performed within minutes without any reliance on app developers. Clinical research participants largely felt confident using the web frontend to make changes in trial-related parameters, and given a choice, most of them would prefer to make small changes in clinical study apps themselves, rather than relying on app developers. This clearly validates the utility of ScaleMed methodology for designing clinical apps.

V. Conclusion and Future Work

The ScaleMed methodology is a clinical trial methodology which brings the clinical researchers and clinical study participants to the center of the mHealth app design process. The steps highlighted in the ScaleMed methodology reflect the need for listening to different stakeholders and for developing clinical study apps which are both flexible and easy to use. Flexibility is crucial, as many study parameters change during the course of a trial. Ease of use is also important since the end-users come from diverse and varied backgrounds.

The last year has seen the release of new mHealth related APIs and frameworks by both Apple and Google. Apple has released an open source software framework called ResearchKit [13] which allows doctors and scientists to easily gather clinical data more frequently and accurately from participants using an iPhone. ResearchKit provides modules to quickly build survey questionnaires, incorporate consent forms within the app, and gather active and passive sensor data. Apple's ResearchKit builds on top of the HealthKit API it launched last year to allow health and fitness apps to share data in an open standard. Google has a similar API known as the Google Fit SDK [14]. These APIs simplify the life of app developers and help speedup mHealth app development. The ScaleMed methodology proposed in this paper empowers the clinical researchers to better design and manage their ongoing clinical study and simplifies the involvement of clinical study participants. Thus, combining the ScaleMed methodology with the new SDKs that are being released will help mHealth researchers to significantly cut down the cost and time required for conducting large-scale clinical studies.

Our future work is two-fold. First, we plan to adopt ScaleMed to all of our future clinical trials, and thus develop a bank of apps that explore a bigger space of mHealth apps. Among these apps are the Rice mobileSpiro [15] and CameraVitals [16] projects. Second, we plan to crystallize our collective experience from multiple clinical trials, utilizing the ScaleMed methodology, and will release an actionable guide for future mHealth clinical trial app development.

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References

[1] R. Littman-Quinn, C. Mibenge, C. Antwi, A. Chandra, and C. L. Kovarik, "Implementation of m-health applications in botswana: telemedicine and education on mobile devices in a low resource setting," *Journal of telemedicine and telecare*, vol. 19, no. 2, pp. 120–125, 2013.
[2] A. Bastawrous and M. J. Armstrong, "Mobile health use in low-and high-income countries: an overview of the peer-reviewed literature," *Journal of the royal society of medicine*, vol. 106, no. 4, pp. 130–142, 2013.
[3] W. H. Curioso and P. N. Mechael, "Enhancing ?m-health?with south-to-south collaborations," *Health Affairs*, vol. 29, no. 2, pp. 264–267, 2010.
[4] H. Thirumurthy and R. T. Lester, "M-health for health behaviour change in resource-limited settings: applications to hiv care and beyond," *Bulletin of the World Health Organization*, vol. 90, no. 5, pp. 390–392, 2012.
[5] T. A. Sanner, L. K. Roland, and K. Braa, "From pilot to scale: Towards an mhealth typology for low-resource contexts," *Health Policy and Technology*, vol. 1, no. 3, pp. 155–164, 2012.
[6] Z. A. Rajput, S. Mbugua, D. Amadi, V. Chepn?eno, J. J. Saleem, Y. Anokwa, C. Hartung, G. Borriello, B. W. Mamlin, S. K. Ndege *et al.*, "Evaluation of an android-based mhealth system for population surveillance in developing countries," *Journal of the American Medical Informatics Association*, vol. 19, no. 4, pp. 655–659, 2012.
[7] P. Yu, M. X. Wu, H. Yu, and G. Q. Xiao, "The challenges for the adoption of m-health," in *Service Operations and Logistics, and Informatics, 2006. SOLI'06. IEEE International Conference on*. IEEE, 2006, pp. 181–186.
[8] "Open mHealth," Tides Center, http://www.openmhealth.org/.
[9] "Ohmage," Ohmage, http://ohmage.org/.
[10] "Commcare HQ," Dimagi, https://www.commcarehq.org/home/.
[11] "Wix," Wix.com Inc, http://www.wix.com/.
[12] "Squarespace," Squarespace.com, http://www.squarespace.com/.
[13] "ResearchKit," Apple, https://developer.apple.com/researchkit/.
[14] "Google Fit SDK," Google, https://developers.google.com/fit/.
[15] "Project mobileSpiro," Scalable Health Initiative, http://sh.rice.edu.
[16] "Project CameraVitals," Scalable Health Initiative, http://sh.rice.edu.