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Final CE Submission

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Title: Feasibility and Desirability of a Smartphone-Based Behavioral Intervention for Adherence to 6-Mercaptopurine in Pediatric Acute Lymphoblastic Leukemia

Abstract:

Introduction: Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer and requires daily doses of 6-MP to achieve durable remission. Smartphone-based behavioral interventions are a novel way to provide reminders and information through a ubiquitous medium, and could be useful to parents of patients with pediatric ALL in remission.

Methods: We developed several questionnaires through an online tool (REDCap) and administered them to parents of patients with ALL in remission at the Lurie Children's Hospital outpatient ALL clinic. These questionnaires focused on four areas of interest: desired reminder features, desired application features, technology access, and technology comfort. Demographic information, including age, sex, race, and level of school completed, was also collected.

Results: 17 parents completed the surveys. Respondents were aged 25-46 years old and were mostly white women. All 17 respondents reported access to a smartphone. 16/17 were at least somewhat comfortable connecting to the Internet with their smartphone. All participants reported fast or very fast Internet at home, had home WiFi, and stated the home WiFi was fast

or very fast. Approximately half of respondents desired daily reminders to give 6-MP and monthly reminders to give steroids. Respondents were more interested (11/17) in clinic reminders. In terms of format, there was slightly more interest in text messages than app reminders in all three of the above scenarios. All participants desired a way to check their child's blood tests online and 16/17 were interested in getting information about 6-MP through the app. Finally, technology comfort varied amongst participants. Scores ranged 19-53 out of a possible 60 with a mean of 42. A small proportion (4/17) of participants received comparatively lower scores between 19 and 33.

Conclusion: Parents of patients with ALL in remission have high access to the technology necessary to implement smartphone-based interventions for medication adherence. In terms of format, text messages were preferred over application notifications. Respondents were most interested in checking their child's blood tests online as well as getting information about 6-MP through their smartphones. However, technology comfort may be a limitation to some parents, requiring education before uptake.

Background:

Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer[1,2]. 6-Mercaptopurine (6-MP) is a critical component of maintenance therapy for ALL; typically, treatment lasts two years or more[2]. Recent advances in therapy have resulted in a 4-year event-free survival (EFS) rate approaching more than 88%, even in high-risk patients[3]. However, adherence to 6MP remains suboptimal in some groups[4-8]. Lower adherence rates are associated with an increased risk of relapse[5,6,7].

One avenue to improving adherence to 6-MP is through utilizing smartphone technology. We now recognize that most patients and their caregivers have access to smartphones[9-11], though currently, applications for healthcare uses are limited. Smartphones can collect and deliver health information as well as facilitate communication with families on a large scale. In terms of public health relevance, we see that using smartphone applications as behavioral interventions to improve 6-MP adherence is a novel yet promising use of a ubiquitous technology[12]. If impactful, similar standalone applications can have wide-reaching public health effects for many chronic disease patients.

Aims and hypotheses:

For pediatric ALL patients and their primary caregivers, we plan to:

- **Aim 1:** Assess barriers to 6-MP adherence.

  Hypothesis 1: Forgetfulness and other barriers contribute to low 6-MP adherence.

- **Aim 2:** Examine access to smartphone technology and the Internet, and explore preferences for potential smartphone app features that might be useful to overcome barriers to 6-MP adherence.

  Hypothesis 2: Smartphones are easily accessible tools with broad access to the Internet. Patients and their caregivers will identify their preferred app features.

- **Aim 3:** Evaluate comfort in using different technological media.

  Hypothesis 3: Patients will vary in their comfort in utilizing certain technologies.

Methods:

<u>Participant enrollment:</u>

Eligible patients were identified by the ALL care team at Lurie Children's Hospital. Included patients were required to have a diagnosis of ALL in remission and be prescribed 6-MP therapy. The parent of the patient with ALL also had to be able to speak and read English or Spanish. We excluded parents with cognitive or physical impairments limiting their ability to complete study assessments. Patients were enrolled after their scheduled outpatient ALL appointments from November 2017 to March 2018 by researchers TH and LB. Written consents and assents were obtained. The study was approved by the Institutional Review Board of the Ann & Robert H. Lurie Children's Hospital of Chicago.

Feasibility and desirability questionnaires:

Our team developed a series of questionnaires to evaluate the feasibility and desirability of a smartphone-based intervention for patients with ALL in remission and their families. We most focused our analysis on four areas of interest: desired reminder features, desired application features, technology access, and technology comfort. Demographic information, including age, sex, race, and level of school completed, was also collected. A full questionnaire codebook is included in a separate attachment.

Data collection:

Study data were collected and managed using REDCap electronic data capture tools hosted at Northwestern University. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.[13]

After consents and assents was obtained, the questionnaires were administered by iPad through REDCap with online access. The researchers remained outside the room to answer questions and fix any technical issues that arose. After the study, family units received a parking voucher and a $25 Amazon gift card. A record of participants who had completed the study was compiled and maintained in a secure location on campus.

Statistical analysis:

As the sample size for this sub-study was small (17 parents of patients), no statistical analyses were completed. However, descriptive analysis of the data is noted below. For questions requiring answers via 5 point Likert scale, answers 1 and 2 were combined and answers 3-5 were combined for categorical analysis.

Results:

Participant characteristics:

17 parents of patients with ALL in remission were included in our analysis. Demographic information is included in table 1. Parents were aged 25 – 46 years old (mean: 37.6) and most questionnaires were completed by a female parent. Most participants identified as white and had completed at least an associate's degree. 100% of participants who began the study chose to and were able to complete it.

Interest in in app features and functionality:

Table 2 describes interest in app and text message reminders for ALL in remission. Approximately half of respondents desired daily reminders to give 6-MP and monthly reminders to give steroids. Respondents were more interested (11/17) in clinic reminders. In

terms of format, there was slightly more interest in text messages than app reminders in all three of the above scenarios.

Tables 3.1 and 3.2 describe interest in specific features of an application for ALL in remission. When asked to select any features that interested them, participants unanimously desired a way to check their child's blood tests online and all but one respondent was interested in getting information about 6-MP through the app. Participants were overall the least interested in encouraging messages when 6-MP was taken, but a majority of respondents still found it desirable (10/17). When asked to rank the 4 most desired features, the vast majority of #1 ranks went to reminding the parent to give 6-MP every day, followed by providing the results of their children's blood tests. Most lowly ranked/most often not ranked at all was providing information about ALL alone.

Technology access and comfort:

Tables 4.1 and 4.2 outline technology access trends in parents of patients with ALL in remission. All 17 respondents reported access to a smartphone, and the majority (13/17) owned Apple iPhones. 16/17 were at least somewhat comfortable connecting to the Internet with their smartphone. In terms of access to other electronic devices, 15/17 owned or had access to a laptop, 14/17 owned or had access to a desktop computer, 15/17 owned or had access to an Apple iPad, and 8/17 owned or had access to another type of tablet. With regards to cell phone plans, 16/17 participants had an unlimited texting plan and 11/17 had unlimited data plans. 12/17 reported sending between 10-100 messages a day and 10/17 used between 1 and 3 hours of Internet on their phones each day. All participants (17/17) reported fast or very fast Internet at home, had home WiFi, and stated the home WiFi was fast or very fast.

Figure 1 exhibits total technology comfort scores, with a possible range of 12-60. The minimum score seen was 19 and the maximum was 53 with an average of 42. 4/17 participants had a score below 34; 5/17 had a score between 34 and 47 and 8/17 participants had a score 48 or higher.

Personal learning:

Through completing this study, I learned several valuable tenets of research. For one, I was responsible for developing and submitting the IRB, a crucial part of conducting ethical research. Furthermore, I wrote the questionnaires and uploaded the surveys to REDCap, which allowed me to consider how to best elicit information from the participants and also strengthened my knowledge of the online software. Finally, I was responsible for outlining the data in a readable format through graphs and tables, which helped me consider the readability and understandability of the data we collected.

Discussion:

Overall, parents of patients with ALL in remission had high access to technology. Text messages were preferred over application notifications and respondents were most interested in checking their child's blood tests online as well as getting information about 6-MP through their smartphones. However, a subset of participants showed low comfort when it came to utilizing smartphones.

Respondents showed mixed interest in daily 6-MP and monthly steroid reminders, with higher desire for clinic reminders. One explanation may be the regularity of daily and monthly medications in contrast to clinic appointments, which may be more irregular. Several families verbally noted that they no longer had trouble remembering 6-MP, as it had become a daily

habit after several weeks of dosing. A systematic review of electronic interventions to provide alerts and reminders for patients found that of the 75% of studies evaluating appointment reminders showed a positive impact, with the rest showing no change.[17] In combination, these findings suggest that providing smartphone-based reminders may be useful for some patients, especially if provided earlier in the course of care.

In terms of desired features, respondents were extremely interested in getting results of their child's blood tests online as well as receiving 6-MP reminders, and were less interested in more general information about ALL as well as getting encouraging messages. Interestingly, Lurie Children's provides an online portal on which blood tests can be viewed, so it may be useful to include a separate, more accessible portal if parents do not feel they have adequate ways to find such information. In addition, it may be less useful to include communication features in the app, as these were not highly ranked among participants.

Participants overall had very high access to the technology required to utilize text messaging or app interventions. All participants had some kind of smartphone and reported access to fast WiFi at home. The vast majority also had unlimited text messaging and a smaller majority had unlimited data. Taking into account the slight preference for text messaging interventions earlier seen among respondents, some combination of text messaging and Internet-based links may be optimal for this population. Furthermore, more in-depth interventions on a laptop or desktop computer may also be of use, as respondents have high access to these technologies as well. A similar study conducted with residents of New York state found that the vast majority of participants owned a mobile phone, and most had smartphones. In addition, over 80% used the Internet at least sometimes.[18] These data mirror our study

findings that suggest that most adults would be capable of utilizing a smartphone-based behavioral intervention.

Finally, technology comfort varied amongst participants. Most participants fell into a larger group (13/17) with moderate/high technology comfort. A small subgroup (4/17 participants) showed low technology comfort (equal to or lower than 33 on a 60 point scale). These respondents may be worth targeting for further education before offering a technology-based intervention. A useful follow-up study might explore unique traits among this subgroup, including trends in age, technology access, and even desire for technology-based interventions.

Limitations of this study are most related to the observed population and nature of the data. We observed a small number of patients, limiting our ability to perform statistical analyses. Furthermore, we focused our study on parents of pediatric patients with ALL in remission. Such a population is naturally older and may be less tech savvy than younger patients who can utilize more complex technologies to manage their own care. Finally, the data we captured was qualitative in nature and focused on the opinions and self-reported capabilities and comforts of the respondents. This may make it difficult to compare results with those of other researchers, due to phrasing and the lack of a quantifiable component to many of the results.

The implications of our current research are that parents of patients with ALL in remission have specific desires regarding smartphone-based interventions. In addition, most have access to the technology and network infrastructure to participate in such programming. Important further research may involve the development and usability testing of an application intervention as well as comparison of these qualitative results with quantified adherence

through bioassay or electronic medical records data. In addition, larger sample sizes with more concise questioning would allow for a thorough statistical analysis.

Conclusion:

Parents of patients with ALL in remission have high access to the technology necessary to implement smartphone-based interventions for medication adherence. In terms of format, text messages were preferred over application notifications. Respondents were most interested in checking their child's blood tests online as well as getting information about 6-MP through their smartphones. However, technology comfort may be a limitation to some parents, requiring education before uptake.

Table 1: Demographics

Age (y)	Mean: 37.6 sdev: 7.0
% female	82.4
% white	64.7
Education completed	At least associate's degree: 64.7% Less than associate's degree: 35.3%

Table 2: Interest in app and text message reminders

	% somewhat, quite a bit, or very interested	Interested in text message reminders (n)	Interested in app notifications (n)
Daily 6-MP reminders	52.9	9	8
Monthly steroid reminders	47.1	11	10
Clinic reminders	64.7	14	12

Table 3.1: Interest in app features

Would you like the application to…	% answering yes
Remind you to give your child 6-MP every day?	82.4
Record when your child takes 6-MP every day?	88.2
Provide encouraging messages when your child takes 6-MP?	58.8
Send you a text message reminder when your child hasn't taken 6-MP?	88.2
Virtually connect you to other patients with ALL and their families?	76.5
Provide information about ALL?	88.2
Provide information about ALL medications (such as 6-MP and steroid medications) and how they work?	94.1
Show you the results of your child's blood tests?	100

Table 3.2: App feature rankings:

Would you like the application to…	1st ranks	2nd ranks	3rd ranks	4th ranks	Unranked
Remind you to give your child 6-MP every day?	9	0	1	1	6
Record when your child takes 6-MP every day?	0	4	1	3	9
Provide encouraging messages when your child takes 6-MP?	0	1	0	2	14
Send you a text message reminder when your child hasn't taken 6-MP?	1	4	4	3	5
Virtually connect you to other patients with ALL and their families?	1	1	2	1	12
Provide information about ALL?	0	0	0	1	16
Provide information about ALL medications (such as 6-MP and steroid medications) and how they work?	1	3	3	3	7
Show you the results of your child's blood tests?	5	2	4	1	5

Table 4.1: Access to physical media and text message/data plans

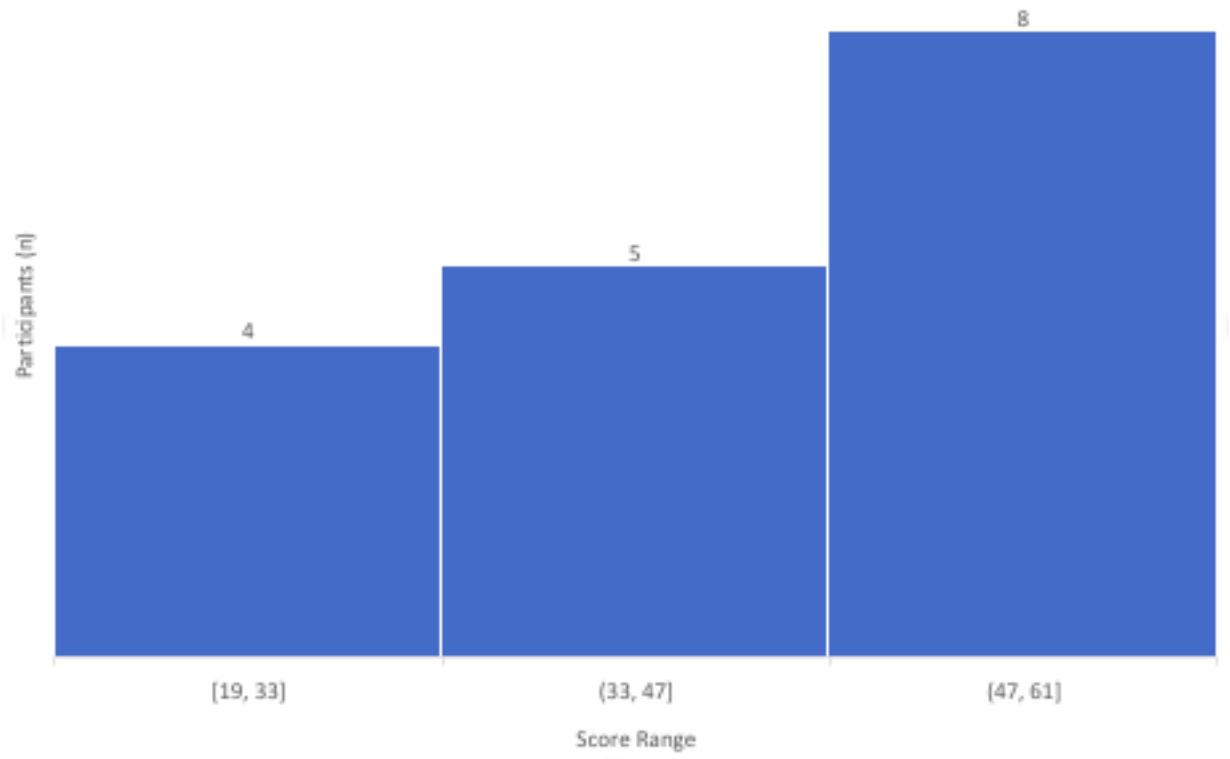
Do you…	% of respondents answering "yes"
...own a smartphone?	100
...own an Apple iPhone?	76.5
...own or have access to a laptop?	88.2
…own or have access to a desktop computer?	82.4
...own or have access to an Apple iPad?	88.2
...own or have access to another tablet?	47.1
…have an unlimited text messaging plan?	94.1
…have an unlimited data plan?	64.7

Table 4.2: Smartphone/Internet comfort, access to WiFi, and text message and Internet use.

How comfortable are you connecting to the Internet on your smartphone? (% answering "somewhat," "quite a bit," or "very" comfortable)	94.1
What is the quality of your phone's Internet connection at home? (% answering "fast" or "very fast")	100
Do you have Wi-Fi Internet at home? (% answering "yes")	100
What is the quality of the Wi-Fi internet at home? (% answering "fast" or "very fast.")	100
On average, how many text messages do you send and receive on your phone daily?	
% answering "fewer than 10"	23.5
% answering "10-100"	70.1
% answering "more than 100 messages"	5.9

On average, how many hours do you spend using the internet on your phone daily?	
% answering "less than 1 hour"	23.5
% answering "1-3 hours"	58.8
% answering "more than 3 hours"	17.6

Figure 1: Technology Comfort Questionnaire Total Scores



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