Chapter 24

A Digital Tool to Improve Patient Recruitment and Retention in Clinical Trials in Rural Colombia—A Preliminary Investigation for Cutaneous Leishmaniasis Research at Programa de Estudio y Control de Enfermedades Tropicales (PECET)

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Abstract Programa de Estudio y Control de Enfermedades Tropicales (PECET) is a multidisciplinary tropical medicine research group based at the University of Antioquia, Colombia. PECET is currently conducting clinical trials in the treatment of Cutaneous Leishmaniasis (CL) in rural Colombia, using the OpenMRS database (an open source health record). Like many research groups in the developing world, PECET has encountered challenges recruiting and retaining study patients. This paper investigates the potential use of mobile digital tools to assist PECET with recruitment and retention of patients in clinical trials. We will explore how a ‘pre-screening’ digital tool and ‘patient messaging’ tool might generate value for patients, community health workers, and PECET staff to improve patient recruitment and retention and ultimately result in more efficient and effective clinical trials. This paper is a preliminary study, and the recommendations therein will provide the foundation for further investigation, development, and iteration of these digital tools in the future.

Keywords PECET · OpenMRS · Mobile · Digital · Tool · Cutaneous leishmaniasis · mHealth

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24.1 Introduction

Cutaneous Leishmaniosis (CL) is a parasitic skin infection caused by the *Leishmania* species of parasites and is spread by the female *phlebotomine* sandfly. Although there are several forms of Leishmaniosis, the three most common forms from least to most severe, include Cutaneous (CL), Mucocutaneous (MCL) and Visceral (VL) forms. CL affects primarily the skin around the site where the insect vector bites, whilst MCL affects the mucous membranes of the nose, mouth and throat. Both CL and MCL forms can cause severe and permanent scarring. VL is the most severe of these forms and results in deep infection, that can affect the liver, spleen, lymph nodes and bones. VL can be fatal if not promptly and adequately treated (PECET 2015; WHO 2010).

In Colombia, CL accounts for 90.3% of all cases of Leishmaniosis with MCL and CL accounting for just 0.4% and 0.3% of cases respectively. Although present across the country, the majority of these cases occur in rural and remote areas (WHO 2010).

Although many individuals may be silent carriers of the *Leishmania* parasite, typically only those displaying symptoms are diagnosed and treated. Diagnosis of CL usually occurs via microscopic examination of scrapings of the skin lesion. Treatment of CL is via antimonial therapy for 20 days (injection only) or miltefosine for 28–40 days (oral treatment) (WHO 2010). Given the rural and remote location of the majority of cases, geographic location can provide a significant barrier to timely diagnosis, appropriate follow-up, and effective treatment of Leishmaniosis.

Programa de Estudio y Control de Enfermedades Tropicales (PECET) is a multi-disciplinary tropical medicine research group based at the University of Antioquia, Colombia (PECET 2015). In developing clinical trials, PECET faces challenges regarding recruitment and retention of trial patients. This is a common problem for all clinical trials but is particularly relevant in the developing world where access to health services is often limited (Kadam et al., 2016). To address this issue, this paper will investigate the potential use of mobile digital tools to assist PECET with patient recruitment and retention in clinical trials. Although these tools could be broadly applicable to many clinical trials, to narrow the scope of the project, we will focus on clinical trials for Cutaneous Leishmaniosis (CL)—as requested by the PECET team.

PECET is currently conducting a clinical trial comparing treatment modalities for CL in rural Colombia. Then OpenMRS platform (an open source health record) is used to manage patient health data (OpenMRS 2016). Trial candidates are identified by local clinical health workers (CHW) in the community and referred to a certified laboratory for further screening. Upon further evaluation at the certified laboratory, the research team then determines whether patients are eligible to participate in the trial (see below under Methods 2.1). In the current study protocol, trial patients are then divided into two treatment groups, thus allowing for comparison between treatment outcomes for single-dose thermotherapy (group 1) and for conventional CL treatment (group 2). Patients are then followed up at approximately 1, 2, 4, 6, and 16-week intervals in the PECET outpatient clinic. The recruitment process and

the frequent follow-up required during the trial is a burden on patients and their families, especially those that travel long distances for laboratory tests and clinic appointments. As such, there are a number of junctures where trial patients may be lost, either during the recruitment process or subsequent follow-up. Recruitment and retention of patients is critical to maintaining the validity of clinical trials (Gul & Ali, 2010). In this case, losing patients later in the trial can be especially damaging as clinical evaluation in CL is critical to ascertain the effectiveness of the treatment (i.e. did a patient not attend because their symptoms improved with treatment, or for an alternative reason such as travel burden?).

24.2 Methods

Given the key challenges of trial patient recruitment and retention, the existing workflows implemented by PECET were mapped out and documented. These workflows were later used to identify areas that could be streamlined using mobile digital tools. This analysis resulted in suggested design specifications for two potential digital mobile tools (i.e. smartphone/tablet-based applications), one for healthcare professionals and another for trial patients.

24.2.1 Trial Patient Recruitment Process—Existing PECET Workflow

Upon mapping the trial patient recruitment process (Fig. 24.1), there is a “pre-screening” phase (Steps 1–5) that occurs prior to the “screening” phase (Step 7). Steps 6, 8, and 10 involve travelling to either a certified testing centre or to the PECET outpatient clinic for further treatment and follow-up. Given travel is often a major

Fig. 24.1 Existing PECET trial-patient recruitment workflow

Fig. 24.2 PECET workflow using proposed digital mobile “pre-screening” tool

barrier to both recruitment and retention, it follows that the use of a digital mobile application to address these steps could improve trial retention and compliance.

24.2.2 Development of Digital Mobile “Pre-screening” Tool for CHWs

To address the issue of recruitment, a digital mobile “pre-screening” tool for CHW could address Steps 1–5 (Fig. 24.1). The CHW would gather qualifying information needed for participation in the trial, which would be immediately communicated to PECET via the digital tool, utilising the OpenMRS platform (Fig. 24.2). The tool could also allow for CHWs to send photos of lesions (in the case of CL) to PECET. Upon reviewing the images PECET could then more accurately determine if patients should travel for further confirmatory laboratory testing. As such, this “pre-screening” tool would ensure clear, transparent communication between community health workers and PECET and potentially reduce unnecessary travel for participants who would otherwise be erroneously sent for further testing.

24.2.3 Suggested Design Specifications for Digital Mobile “Pre-screening” Tool for CHWs

The proposed system would incorporate the following features and capabilities (in ideal circumstances):

- The interface would provide an overview of administrative module including the patients’ name, date of birth, identification number, nearest clinic location, date of first contact with CHW, date of first diagnosis and the number of clinic visits attended (as well as the number of visits requested).

- To protect patient data, each clinic will only have access to the patient information for patients that are actively visiting or would be nearest to their clinic. New patients and new data will be highlighted.
- When a patient’s record is open, it will display all current and previous information including images of the CL lesions.
- An appointment reminder will be coded into the system to send patients a reminder 1 week and 1 day before their clinic visits. This reminder schedule has been chosen to avoid overlap of reminder messages.
- Patient records will remain highlighted until an action is taken post-reception by the clinic. The clinic must acknowledge data has been read before it becomes un-highlighted from the data queue.
- For new patient inquiries, a different highlight colour will be used, and the clinic will be able to communicate with the patient via the communication module and make any inquiries necessary to determine whether the patient is eligible for the trial or not. Patient data of those not eligible for the trial will be deleted.

Figures 24.3, 24.4 and 24.5 highlight the interaction between a CHW and PECET for a new patient referred. This data will be securely transmitted using the tool to the PECET admin via the OpenMRS platform.

The module shown in Fig. 24.5 will allow information and photos from the health worker to be displayed and accessed by PECET. Through this same module, PECET

Survey

Name: _____

Address: _____ City _____ Zip _____

Phone: _____

Age: _____ Gender: M _____ F _____

Race: White _____ Black _____ Hispanic _____ Asian _____ Other _____

Allergies to medications: _____

Known Health Conditions: _____

Medications currently taking: _____

How long have you had the lesions? _____

Have you any family history with leishmaniasis? Yes _____ No _____

Have you participated in clinical trial before? Yes _____ No _____

If so, provide details. _____

If selected for clinical trial, would you be able to come back for follow up visits? Yes _____ No _____

Fig. 24.3 Initial survey including demographic and qualifying information

ID Number	Name	DOB	Nearest Clinic	# Clinic Visits	# App Inputs	
1 A		1/22/68	Bogotá	1	2	
2 B		2/4/79	Medellin	2	3	
3 C		6/8/90	Cartagena	1	1	
4 D		11/2/64	Call	1	3	
5 E		4/2/68	Bogotá	2	3	
6 F		6/2/97	Bogotá	1	0	

ADMIN MODULE

Fig. 24.4 First screen viewed by PECET administration, displaying new patient F (ID# 6) referred from a CHW

ID Number	Name	DOB	Nearest Clinic	# Clinic Visits	# App Inputs
6 F		6/2/97	Bogotá	0	1
Previous Pictures	CHW Comments	Last Clinic Visit:	Next Appointment:	Communicate with CHW:	
<div>[Photos]</div> <div>1/2/18 - experienced pain in lesion region with swelling, wants to get treatment</div>				<div>Hello CHW, Thanks for your interest. I believe patient F is a good fit for our trial, please schedule an appointment. We will reimburse the cost of travel and accomodation in Bogotá.</div>	

Fig. 24.5 Displaying expansion of the patient record for patient F (ID# 6)

administration can communicate about the patient’s eligibility with the community health worker.

24.2.4 Messaging Tool for Patients—to Improve “Patient Retention”

Another key difficulty in conducting clinical trials in remote locations is establishing a line of communication with patients. Currently PECET uses phone calls or occasionally video-calls as their primary mode of communication, which can be difficult to coordinate. We propose that a digital messaging tool could address this problem in the form of a web-app or mobile application system, allowing patients to send/receive secure messages with CHWs. This system would also allow for questionnaires, reminders, and photos (e.g. images of skin lesions in CL) to be sent, potentially in lieu of needing to travel to the clinic for follow-up appointments. Figure 24.6 displays the potential workflow of such a tool.

Figure 24.7 displays a basic representation of the proposed tool scheme that would allow for patients, health workers, and PECET to interact during the clinical trial.

Key features of the ‘Patient Messaging Tool’ might include:

- Option to take or upload photos via device camera along with reminder stating to use a standard coin for reference [to be chosen by trial administrator].
- Module to verify patient information and/or login to patient account (i.e. verify name, DOB, and patient ID each time application is opened after the first encounter).

Fig. 24.6 Proposed workflow for ‘patient messaging tool’

Fig. 24.7 Left—Login verification interface (to include survey of pertinent questions), Centre—Camera interface to allow transfer of lesion images, Right—Messaging interface allowing interaction between the patient and the clinic

- User-friendly interface with patient input and approval for opening screen and all elements of the app.
- Information source explaining CL disease, significance of clinical findings, treatment, compliance, and nearest clinic locations to the patient.
- Module for patient to input new information for transmission to clinic.
- Module for patient to receive reminders (e.g. appointments, to send a photo of lesion, etc.) or other correspondence from the clinic.
- Data uploads to database for analysis.

24.3 Results

This project was a preliminary investigation conducted on behalf of PECET regarding how digital mobile tools may potentially benefit patient recruitment and retention for CL research in remote Colombia. Given these tools are yet to be developed, trialed, and implemented, the results of this project consist of the development of the concept, an outline of the app structure and elements, and the creation of preliminary content for the app.

With the proposed workflow and key features in development, a tool can be created and deployed in conjunction with the OpenMRS system with the intention of improving communication and potentially allowing for digital assessment to alleviate the need for in-person clinic appointments (which are often a source of trial “drop-out”). Ultimately, we anticipate that the successful implementation of such a tool has the potential to increase patient retention in clinical trials (in this case, trials for CL). In the longer term, benefits may be realised through a reduction in unnecessary tests and overall costs, an improvement in data-gathering, and more high-quality clinical trials being conducted to completion.

24.4 Discussion

Recruitment and subsequent retention of patients in clinical trials is a well-known and challenging problem (OpenMRS 2016). This problem can be particularly difficult in rural settings and in developing countries where access to healthcare services can be obstructed by a number of factors (e.g. geography, transportation, healthcare infrastructure, socioeconomic status, education level) and difficult, inconsistent channels of communication (RHIB 2017).

Recently published data suggests that the use of mobile digital tools may be able to address some of these issues and that the use of such tools in clinical trials is increasing globally. With smartphone penetrance increasing rapidly in developing countries, mobile digital tools will undoubtedly play a more prominent role in this setting in the future. Despite the potential benefits, there are a number of implementation challenges to using these tools including data privacy/security compliance

issues, technology literacy and infrastructure, as well as maintaining user engagement (Kakkar et al., 2018).

Following analysis of the PECET CL research protocol, mobile digital tools may be used to assist with pre-screening of patients prior to recruitment in clinical trials—and for communication with patients during clinical trials—to address the recruitment and retention challenges and reduce need for in-person follow up clinic visits. A key factor in PECET's context is that these tools will add value from the perspective of all stakeholders: patients, CHWs, and PECET healthcare workers involved in the trials.

The pre-screening tool will help more accurately identify suitable trial candidates and potentially reduce unnecessary costly travel for patients that would have later been deemed “unsuitable” for the trial. The direct benefits to PECET, CHWs, and patients are clear; however, there are also indirect reputational benefits for PECET including the likelihood that potential patients (and their family, friends, community members) may be more receptive to future clinical trials if they had previously had positive experiences with the organization.

In addition, a digital patient messaging tool would allow a direct line of communication between PECET, CHWs, and patients. Improved communication alone may potentially improve patient retention in the clinical trials; nevertheless, the ability to potentially have “follow-up” appointments replaced by review of digital images could alleviate the need for frequent and costly travel and could improve patient retention further still (Asiri et al., 2018; Adams et al., 2015; Ricardo-Barreto et al., 2018). Although there is a clear potential benefit to patients and healthcare workers, the implementation of this communication tool will be critical to its success. Furthermore, this tool could be coupled with a suitable incentive program for patient involvement in the trial (if the offer of trial treatment alone is not enough) (Groth 2010; Bernstein & Feldman, 2015).

The ‘pre-screening tool’ offers communication between CHWs and PECET staff in a controlled environment, and therefore technology and internet solutions can be suitably evaluated, quantified, modified, and managed. A 2018 study found that, in the Antioquia region 35.2% of people are considered to have the highest effective level of mobile device penetration (defined as having ‘access to mobile device with internet and used it to access social applications’) and 87.5% having access to any mobile device (including access to SMS messaging). This is compared to 60.5% of people with the highest level of penetrance and 96.9% having any access, in urban Bogotá, Colombia (the country's capital city) (PubMed 2015). Despite this disparity, international trends suggest the use of internet-enabled mobile devices (e.g. smartphones and tablets) and internet penetrance in rural areas like Antioquia, is likely to continue to increase into the future (Schwebel & Larimer, 2018). While access to smart phones and cellular or internet data may initially be a challenge to the implementation of the ‘patient messaging tool’, the functionality of this tool would have to be reviewed and iterated until a suitable offering was established to reach as many patients as possible. A potential solution might be to leverage the OpenMRS messaging module, using SMS-messaging initially and later adding more advanced functionality (OpenMRS 2010, ITU 2017). Currently this module is in development,

but it may be a good first step in establishing communication with patients via the OpenMRS database.

24.5 Conclusion

Following a review of the current patient recruitment and communication challenges faced by PECET in their clinical trials investigating CL treatment, we believe that digital mobile tools could be implemented to address these challenges. Leveraging technology and the OpenMRS system, these tools would provide value to patients, CHWs, and PECET and could result in more efficient and effective clinical trials in the future. We recommend that the next steps involve further investigation and development of these digital tools (as a minimum viable product) and that they be trialed in-the-field to gain invaluable user feedback.

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