Integrative Review

Mobile applications for sickle cell disease management: an integrative review

Aplicativos móveis para o manejo da doença falciforme: revisão integrativa

Aplicaciones móviles para el tratamiento de la drepanocitosis: una revisión integrativa

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Keywords
Sickle cell disease; Educational technology; Cell phones; Mobile applications

Descritores
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Descriptores
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Abstract
Objective: This paper reports on a literature review of articles on mobile applications available for the management of sickle cell disease published in Brazil and abroad.
Methods: Searches were carried out in the Library of Medicine (Medline/via PubMed), Current Index to Nursing and Allied Health Literature (Cinahl), Web of Science and Scopus databases covering a period spanning September/2016 to March/2018. Levels of evidence of the selected articles were based on the categories of the Agency for Healthcare Research and Quality (AHRQ) for grading strength of evidence.
Results: A total of twelve articles were included in this review, two of them yielded by a query in Web of Science and the remaining ten in Pubmed.
Conclusion: The review showed the emergent nature of research on the development of mobile applications aimed at people with sickle cell disease. In the case of Brazil, no studies targeting sickle cell disease applications were found, despite the high incidence of this disorder in the country. This review points to the need for mobile applications to be developed as educational resources in supporting the self-care practices of people with sickle cell disease.

Resumo
Objetivo: Investigar, na literatura nacional e internacional, os aplicativos móveis existentes desenvolvidos para gerenciamento da doença falciforme.
Métodos: Estudo de revisão integrativa, conduzido nas bases de dados Medline/via PubMed, BVS, *Current Index to Nursing and Allied Health Literature* (Cinahl), *Web of Science* e *Scopus,* no período de setembro de 2016 a março de 2018. Os artigos selecionados foram analisados de acordo com a *Agency for Healthcare Research and Quality* (AHQR).
Resultados: Integraram esta revisão 12 artigos, sendo dois da *Web of Science* e o restante da *PubMed.*
Conclusão: Esta revisão mostrou a incipiência de estudos que contemplam o desenvolvimento de aplicativos móveis no contexto da doença falciforme. No Brasil não foram identificados estudos que utilizem aplicativos móveis direcionados à população com doença falciforme, apesar da alta incidência desta condição crônica. Este estudo aponta para a necessidade de desenvolvimento de aplicativos móveis como importante recurso educativo que possa apoiar a prática de autocuidado das pessoas com doença falciforme.

Resumen
Objetivo: Estudio informativo sobre revisión de la literatura de artículos acerca de aplicaciones móviles disponibles para tratamiento de la anemia drepanocítica publicados en Brasil y el extranjero.
Métodos: Búsquedas realizadas en bases: *Library of Medicine* (Medline/vía PubMed), *Current Index to Nursing and Allied Health Literature* (Cinahl), *Web of Science* y Scopus para el período desde septiembre de 2006 hasta marzo de 2018. Niveles de evidencia de artículos seleccionados basados en categorías de la *Agency for Healthcare Research and Quality* (AHRQ) para calificar la solidez de la evidencia.
Resultados: Doce artículos fueron incluidos en esta revisión, dos de ellos obtenidos por consulta en *Web of Science* y los diez restantes en Pubmed.
Conclusión: La revisión mostró la naturaleza emergente de la investigación sobre el desarrollo de aplicaciones móviles dirigidas a las personas con drepanocitosis. En el caso de Brasil, no se encontraron estudios sobre aplicaciones para la drepanocitosis, a pesar de la alta incidencia del trastorno en el país. Esta revisión señala la necesidad de desarrollar aplicaciones móviles como recursos educativos para apoyar las prácticas de autocuidado de las personas con drepanocitosis.

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Introduction

Sickle cell disease, a hereditary disorder of human hemoglobin, comprises a group of genetically determined diseases, widely disseminated in Brazil, with a higher prevalence in the black population.[1] Factors such as the chronic nature of the disease, the difficulties stemming from racial prejudice and complications that require the practice of daily care can pose problems of social adaptation for people with this chronic condition.[2,3]

Sickle cell disease management requires the daily follow-up of self-care practices, which include regular hydration, regular medications use, frequent visits to health services, follow-up of complications and resolution of problems related to emotional and psychosocial aspects.[3,4]

In recent years, *Mobile-Health* also known as *m-Health* has been introduced as a practice based on the use of information technologies and communication for healthcare purposes through mobile devices. *M. Health* is related to the provision of medical services and/or public health services through mobile devices that are directly connected to the user, such as mobile phones, sensors and other equipment. Also, *M. Health* encompasses conditions for evaluating health parameters, encouraging healthy habits, and supporting the self-management of people with a chronic condition. Thus, the barriers between the population and health services can be narrowed through the provision of preventive health information, especially in countries with multiple social problems, limited budget and recurrent staff shortages.[5]

Brazil is one such country. Although in the latest global survey on e-Health, conducted by the World Health Organization in 2011, Brazil reported that it was developing mobile health initiatives, little evidence has been provided on that.[5]

According to the American Society of Hematology, mobile applications should be adopted as an important information tool and educational support for people with sickle cell disease. Mobile applications allow people with sickle cell disease to acquire more knowledge about their health condition, monitor their symptoms and treatment, and become more autonomous in order to perform their self-care.[6-8]

Currently, emerging technologies, such as mobile applications with the feature of Animated Communicational Agents, also known as Avatars, are an important tool in healthcare. Mobile applications with Avatars have been modeled to perform one-on-one interventions and user-oriented guidelines that are now supported in the user's daily care needs. Thus, with increased interactivity, these applications have been assisting people with chronic conditions to adapt to healthy habits, improving their health-related behaviors.[9,10]

Within this context of rapid technological advances, the design of mobile applications aimed at people with sickle cell disease requires examining published evidence in order to assess the results and identify gaps in the literature.

This review is part of a project that targets the development of a mobile application with Avatar aimed at people with sickle cell disease. The following questions were posed to guide our review: "What studies on mobile applications for the management of sickle cell disease are there in the literature"? and "What guidelines and recommendations have been proposed for the development of these applications?"

The aim of this study was to review mobile applications developed for the management of sickle cell disease reported on in the literature and to examine published findings about their applicability based on scientific evidence reported in Brazil and abroad.

Methods

Review carried out during the period between September 2016 and March 2018. The following steps were followed: statement of hypothesis or guiding research question; database query and definition of criteria and extraction of information; evaluation of findings; interpretation of results and presentation of a synthesis review of literature.[11]

This review was carried out in the following databases: National Library of Medicine (Medline/via PubMed) and Virtual Health Library (VHL), Current Index to Nursing and Allied Health Literature (Cinahl), Web of Science and Scopus. The terms used in English and Portuguese were: Sickle

Cell Disease (doença falciforme), smartphones, cell phones (telefones celulares), mobile applications (aplicativos móveis), Educational technology (tecnologia educacional). For the query, the association between the Boolean operators OR and AND was used. Review articles and those that were not relevant to the study proposal were excluded and duplicate publications were considered only once. Inclusion criteria: online scientific articles, with no date limit.

Two researchers performed the first stages of the query independently. First, the researchers carefully read the title and the abstract of the articles. Second, they read the articles and assessed their relevance to the study proposal. The selected articles had their data recorded on a spreadsheet designed by the researchers as recommended in the literature.[11]

In order to achieve the classification of the level of evidence of the selected studies, the categories of the Agency for Healthcare Research and Quality (AHRQ) were used, which encompass six levels.[12]

- Level 1: evidence resulting from the meta-analysis of multiple controlled and randomized clinical trials;
- Level 2: evidence obtained in individual studies with experimental design;
- Level 3: evidence from quasi-experimental studies;
- Level 4: evidence from descriptive (non-experimental) studies or qualitative approach;
- Level 5: evidence from case or experience reports;
- Level 6: evidence based on expert opinions.

Quality of the output articles was assessed by two independent authors following the Strobe (Strengthening the Reporting of Observational Studies in Epidemiology). statement guidelines. One of the articles was excluded as it presented a qualitative approach. A score from 0 to 1 was used for each of the 22 items in the Strobe guidelines. A final score was obtained based on the mean of the scores given by the two assessors. Results were calculated as percentages which were used to classify the quality of the articles into three categories: A for studies meeting over 80% of the criteria established by STROBE; B for studies meeting 50% to 80% of those criteria; and C for studies meeting under 50% of the Strobe criteria.[13]

For the presentation of the selected articles a synoptic table was elaborated, containing the references, methodological and sample details, results and recommendations.

The methodology for selecting the articles is outlined in figure 1.

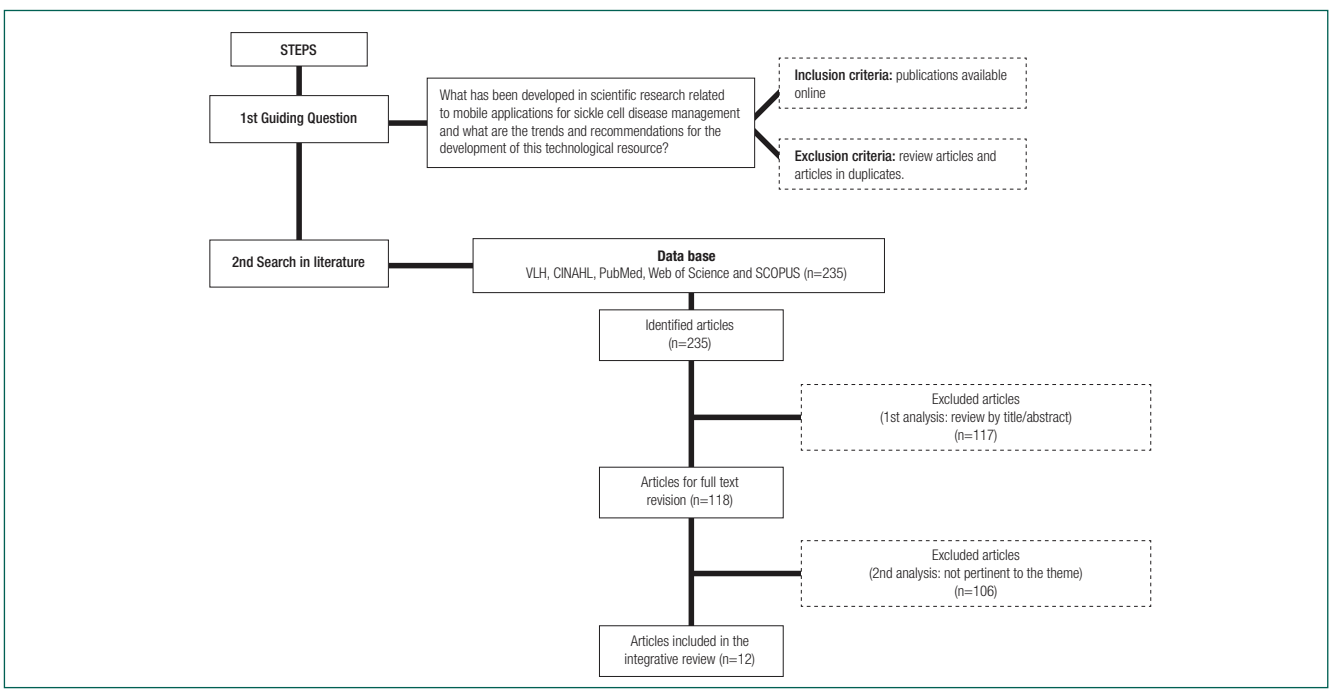

Figure 1. Stages of integrative review on mobile applications for sickle cell disease management

Results

The search in the established databases yielded 235 articles, initially selected on the basis of their title and abstract. A selection based on the inclusion and exclusion criteria and a detailed analysis of the publications further narrowed that count to 12 articles. Of these, two were found in the Web of Science database and the others in Pubmed.

A flowchart with steps in identifying eligible articles for this study is presented in figure 2.

An overview of the articles in this review is presented in the chart 1. According to the categories of the Agency for Healthcare Research and Quality (AHRQ), ten articles were classified as quasi-experimental studies (level of evidence: 3), one was classified as a randomized clinical trial (level of evidence: 1) and one was considered as a qualitative research (level of evidence: 4) The search criteria did not include any limitation on the date of publication. The first eligible article was published in 2009. All selected articles were published in the United States of America in the years 2009 (1), 2012 (1), 2014 (3), 2015 (3), 2016 (3), 2017 (1).

Quality of the studies analysed was classified as A category following the STROBE criteria, which supports the reliability of the present review.

The results of this review showed that the first mobile applications developed for the management of sickle-cell disease considered symptom recording, such as pain crisis episodes, the most important feature. Mobile applications that were later developed incorporated additional features, including personalized messages automatically sent to the user's cell phone. The most recent mobile applications feature multiple functions, including the recording of clinical data on sickle-cell disease, monitoring the patient's mood during the day, individual goals definition, and a visual calendar that allows the user to follow the frequency of symptoms and relate them to self-care behaviors. Principles of gamification such as motivational feedback and reward incentives are further added features in the most recent versions of the applications.

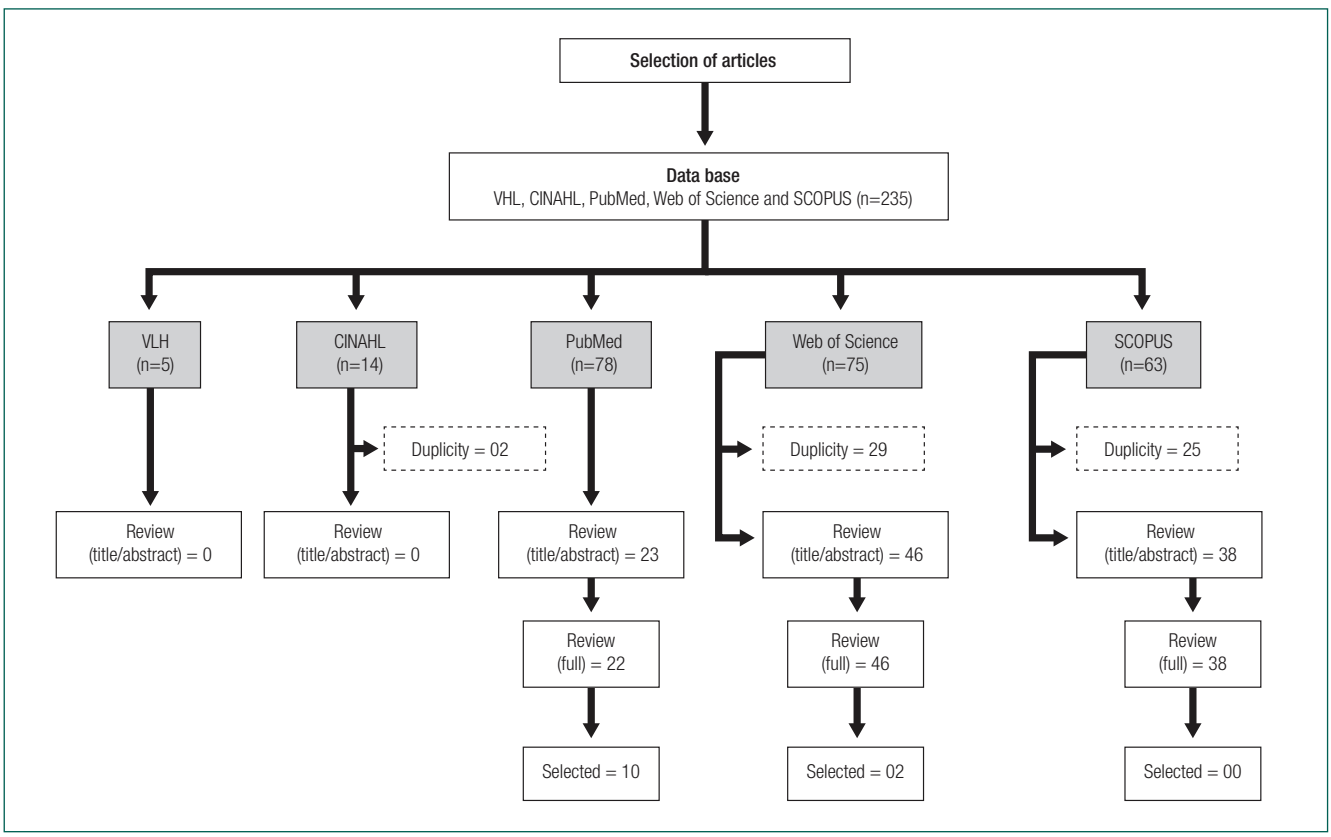

Figure 2. Flowchart of the integrative review on mobile applications for sickle cell disease management

Chart 1. Summary table of the mobile application review for sickle cell disease management

Author/year	Category (AHRQ)	Category STROBE	Sample and age group	Methodological details	Results	Recommendations
Leonard S et al[14] 2017	3	A (90,9%)	n=11 8 to 21 years	Intensive training program (ITP) mobile app was used by participants to produce daily self-recorded videos ("selfies") of medication administration and receive provider messages and feedback about adherence. Providers monitored "selfies" recorded and sent messages to patients every 7 to 10 days.	Participants exhibited a clinically relevant decrease in serum ferritin, which trended toward statistical significance. The mobile ITP was feasibly implemented in a clinical setting; in addition, high levels of compliance, disease knowledge retention, and acceptance encourage were observed.	Mobile technology intervention can be easily integrated to provide education to youth as well as map disease knowledge and compliance rates for pediatric patients receiving daily iron chelation therapy.
Crosby LE et al.[6] 2016	3	A (88,6%)	n= 70 16 to 24 years	Development study of the iManage application consisting of the steps: identification of barriers and development of App for smartphone, sessions of co-creation (participant and professionals) for validation of themes, characteristics and interface of App; Usability testing with the iManage prototype and institutional approval.	- The prototype presented satisfactory usability, contributed to improving the practice of self-care by attending to the needs and experiences of the participants, supporting communication between peers and professionals.	Apps can be used clinically to understand the frequency and intensity of symptoms and the effectiveness of self-care strategies. Future research should include a representative sample with a randomized clinical trial.
Badawy MS et al.[7] 2016	3	A (86,4%)	n= 107 12 to 22 years	Study encompassing three phases: 1st) development of a questionnaire (technological domains, accessibility, daily medications and barriers to adherence); 2nd) validation of the instrument by specialists; 3rd) App development for Smartphones	- Preference for Apps which prioritized health education actions to provide information on chronic condition, reminders for medication use and social interactions (friends and family).	Investtement needed in educational strategies drawing on digital technologies to improve communication between health professionals and patients.
Gupta N et al.[15] 2016	4	Not applicable	n= 22 4 to 17 years	Study of a qualitative approach consisting of cognitive interviews with the participants and evaluation of comprehension and usability of the electronic scale (Faces Pain Scale-Revised - FPS-R).	- Participants demonstrated familiarity with touchscreen devices (smartphones) and parents relied on this ability of their children. - Participants aged 4 to 6 years old did not have a clear understanding and ability to use the electronic scale for pain. - Children between 7 and 8 years old needed support from parents. - Participants over 9 years of age used the pain scale by themselves.	The scales developed for the electronic version should have simplified instructions, with terms that aid users comprehension, considering the biological, psychosocial and cultural characteristics of the target population.
Schatz J et al.[16] 2015	1	A (93,2%)	n=46 8 to 22 years	Randomized clinical trial. The control and intervention groups received training in coping skills.	- The intervention with smartphone support represented more active coping attempts. - Data from the electronic diary indicated that when participants adopted the skills developed from cognitive-behavioral therapy, there was reduction of pain on subsequent days.	Future research for Apps development should include usability assessment.
Jonassaint CR et al.[8] 2015	3	A (84,1%)	n=15 12 to 54 years	Participants used *Sickle cell disease Mobile Application to Record symptoms via Technology (SMART)* to record pain, symptoms, and control strategies and received automatic messages with guidelines on how to proceed in the face of disease intercurrences.	- The SMART app was evaluated as an effective tool to assess pain and other day-to-day symptoms, contributing to self-care and control behaviors.	Applications should incorporate functions promoting educational, games (gamification), feedback and interaction among users.
Bakshi N et al.[17] 2015	3	A (91%)	n=10 15 to 22 years	Study of adaptation of an "e-Ouch" pain diary of rheumatoid arthritis for sickle cell disease, encompassing the phases from the e-diary, content validation, cognitive interviews, elaboration of a preliminary conceptual model, e-diary development and evaluation.	- The multidimensional electronic e-diary for pain received a positive evaluation, because it integrated interesting layout and content for the users, who could access it through a laptop.	Socioeconomic status of the population should be considered in the development of an e-diary, with specific features that bring the reality of the target population as well as the availability of access to technologies and networks.
Estepp JH et al.[18] 2014	3	A (91%)	n=55 up to 19 years	A tool that sends electronic messages to the patient's cell phone to remind him/her to take his/her medication is introduced: "Scheduled Instant Messaging Over the Network" (SIMON1)	- The Simon1 App was considered a viable and effective tool to improve adherence to the treatment of daily hydroxyurea therapy, improving hematological parameters.	Future work should include extending this technology to other populations with different chronic conditions that require daily use of medication.

Continue...

Continuation.

Author/year	Category (AHRQ)	Category STROBE	Sample and age group	Methodological details	Results	Recommendations
Creary SE et al.[19] 2014	3	A (95,4%)	n= 14 1 to 22 years	Study on the development and evaluation of the Electronic version of "Eletronic directly observed therapy" (DOT) for hydroxyurea drug therapy. To evaluate the acceptance of the electronic version, participants were asked to record qualitative feedback of it.	- The electronic version for adherence to hydroxyurea (DOT) presented satisfactory characteristics related to the filling time of daily data and the efficiency of the reminders to make use of the drug, demonstrating good viability and improving adherence.	The electronic version of the DOT model was recommended because it presents a smaller cost, considering the population minorities.
Shah N et al.[20] 2014	3	A (81,8%)	n= 117 over 18 years	Study encompassing two phases: 1) included 100 participants who completed a survey on technology and use of mobile devices for self-management and communication with health professionals. 2) 17 participants tested the usability of the App.	- The application tested was useful to control pain, demonstrating to be beneficial and practical for self-care and support the communication of patients with professionals.	Mobile technology should be considered as an appropriate strategy to support the practice of self-care in an individualized way, with guided instructions for use of medication and control of signs and symptoms.
Jacob E et al.[21] 2102	3	A (95,4%)	n= 31 10 to 17 years	Study with two pilot tests: 1) ten participants used a smartphone and a record questions on paper. 2) 21 participants used an electronic diary (e-diary) in smartphone to record pain, symptoms, sleep information, thoughts and feelings experienced during the last 12 hours.	- e-diary improved reporting of symptoms by participants and communication with health professionals.	The Smartphone should be recommended for children and adolescents who present severe form of the disease, due to the fact that it is easy to use and because it involves the participants in the practices of self-care.
Mc Clellan CB et al.[22] 2009	3	A (95,4%)	n= 19 8 to 20 years	Study aimed at recruiting participants who used mobile application for daily pain scale control during a period of two months. Data were monitored by the researchers. Participants received training to develop behavioral skills to deal with their pain (such as breathing and relaxation).	- Comparison of practical skills rates for enrollment in the device provided important information about the use of electronic monitoring for behavioral interventions.	Electronic wireless technologies and data transfer are recommended to monitor sickle cell disease symptoms, and they are able to support communication between patients and health care professionals.

Discussion

The studies reviewed showed that digital technologies, especially smartphones, prove a suitable tool to support the self-care practices of people with chronic conditions.[23]

The reviewed articles suggest that mobile applications can be effective in self-management of sickle cell disease. Applications were found to be useful in managing pain monitoring and adhering to the use of medications, supporting users to develop strategies for coping with their illness, improving their communication with health professionals and their intra and interpersonal relationships.[6-8,14,16,18-22]

The most recent studies pointed out the need for applications targeting people with sickle cell disease to cater for the sociocultural and clinical demands of the users, their technology expertise, their frequency of access and internet use, type of device used and barriers encountered. Authors also indicate that health professionals who are experts in sickle cell disease should also participate in the development process of mobile applications, by validating the contents as well as evaluating their usability.[6,7] The reviewed studies recommended the use of smartphones to support the learning process of people with sickle cell disease, especially teenagers, who are particularly keen on using these devices.[6,22]

Usability assessment consists in measuring the quality of users' experience in performing specific mobile application tasks. Researchers argue that identifying all usability issues may not be viable, five evaluators being suitable enough to conduct a useful interactive evaluation cycle as long as patients are competent.[24] In the reviewed articles, the assessment of mobile applications usability was conducted through tests with specific instruments, as well as through guided interviews and focus groups, which involved users and professionals. Assessment reduced barriers in the use of the mobile applications. Reported results also showed that in order to facilitate the use of the mobile applications some adaptations are necessary.[6,8,15,20,21]

Mobile applications that include an electronic diary (e-diary) feature are designed to record users' activities, experiences, thoughts, and feelings along the day. However, the first mobile applications developed for sickle cell disease patients only offered an e-diary for recording pain episodes or monitoring users' use of medication.[21,22]

More recently developed mobile applications have multiple functions that allow the user to monitor the quality of sleeping, their feelings.[6,7] Mobile applications of a multidimensional nature allow the user to associate pain episodes (an important symptom of sickle cell disease) to daily activities, such as class attendance, sleep, and interactions with other people.[17]

Thus, the development of applications with multiple functions points out the need for validation of items and contents for the construction of a customized prototype that meets the users' interests and needs.

During the phase of developing a prototype of a mobile application, it is also necessary to identify the users' age range, besides the different types of access that can be offered through smartphones, tablets or desktop with different screen sizes and layouts.[19,23,25]

According to the Food and Drug Administration (FDA), users' cognitive ability should be considered when developing an application.[26] Hence, the applications to be developed for people with sickle cell disease are expected to be modelled upon the cognitive profile of prospective users. Among the reviewed articles, a study focused on the development of cognitive interviews with verbal techniques in order to gather data to inform the design of an application.[17] Other studies considered the need for prior user training to use self-care applications.[18]

Another study reported on the development of the application through joint sessions with utilizers and health care professionals. Those sessions will involve discussion about the use of the mobile application, characteristics and its interface. In other words, utilizers being exposed to the layout and commands of the mobile application using printed format. This strategy aimed at minimizing problems due to cognitive impairment which could eventually lead to failure to use the mobile application.[6]

Our review found that text messages sent by mobile applications helped to improve adherence to the use of medications, as well as social interactions (friends and family).[27] Finally, the results suggest that mobile application development must give the utilizers the possibility of its usability assessment. Besides, mobile application should bring games, feedback and interaction between utilizers and health care professionals.[8,20]

Conclusion

This article reviewed studies reporting on mobile applications aimed at people with sickle cell disease. The number of articles found points to the emergent role of mobile applications development, deemed very scarce in view of the high incidence of sickle cell disease worldwide. The lack of research on and development of mobile applications in Brazil is very alarming. No Brazilian studies with scientific evidence on mobile applications development aimed at people with sickle cell disease were found despite the high incidence of sickle cell disease in Brazil (1:1.000). As a result of this review it is suggested that future studies focus on the development of mobile applications that take into account the clinical, sociocultural and emotional aspects of their users, as well as interactive strategies that provide guided and individualized instructions, in order to effectively support the self-care practice of a population that is still a target of social discrimination. Findings of this review are expected to promote mobile application development as an integral part of educational interventions geared to the self-care practice by people with sickle cell disease.

As regards the focus of the mobile applications reported on in the articles reviewed, it has been observed that several studies use electronic diary (e-diary) to maintain the clinical data of the disease, which represent a less interactive form of communicating with application users. There is an emphasis on the development of prototypes

aimed at the clinical intercurrences of sickle-cell disease, applications with a multifunctional character, covering the psychosocial aspects that are part of the life of the individual with sickle cell disease, being very rare. The development of mobile applications in different areas has been incorporating interactivity features, such as conversational agents also known as Avatars, emulating human-human interaction. No such applications were reported on in the reviewed articles. The results of this review suggest that future studies should target the development of prototypes that make use of intelligent interfaces with avatars. Avatars can promote interactivity, supporting the improvement of skills and behaviors that need be adopted and maintained by sickle cell disease users in everyday healthcare practices.

Collaborations

Pereira SAS, Cecilio SG, Lima KCS, Pagano AS, Reis IA and Torres HC contributed to the project design and execution, manuscript writing, and approval of its final version.

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