Int J Cardiovasc Pract. **Original Article**

Jan 2017, Volume 2, Issue 1 (10-16)

Evaluation of a Clinical Decision Support System for Dyslipidemia Treatment (HTE-DLPR) by QoE Questionnaire

Alberto Zamora [1, 2], Carme Carrion [2, 3], Marta Aymerich [2, 3], Xavier Castells [2], Lidia Blanco [2], Anabel Martin-Urda [2], Guillen Paluzie [1], Dolors Capella [2], Roberto Elosua [5], In Representation of Valida Group.

[1] Department of Internal Medicine, Hospital of Blanes, Blanes, Girona, Spain
[2] Group of TransLab Research, Department of Medical Sciences, University of Girona, Catalonia, Spain
[3] Open University of Catalonia, Barcelona, Spain
[4] Department of Internal Medicine, Integrated Health Services of Lower Emporda Hospital Palamos, Girona, Spain
[5] Group of Cardiovascular Epidemiology and Genetics, Hospital Del Mar Medical Research Institute, Barcelona, Spain

** Corresponding author: Alberto Zamora, Department of Internal Medicine, Hospital of Blanes, Blanes, Girona, Spain. Tel: +34 677852228, E-mail: azamorac.zamora@gmail.com*

DOI: 10.21859/ijcp-020105

Submited: 11.28.2016

Accepted: 06.01.2017

Keywords:

Decision Support Systems, Clinical

Program Evaluation

Dyslipidemias

Surveys and Questionnaires

Abstract

Introduction: Clinical decision support systems (CDSS) are computer systems designed to assist clinicians with patient-related decision making, such as diagnosis and treatment. CDSS have shown to improve both patient outcomes and cost of care.
Methods: A multi-center observational prospective study was conducted. Ten physicians agreed to participate. Seventy-seven patients with high or very high cardiovascular risk were included. After using CDSS for dyslipidemia (HTE-DLPR) for a 3 months period, participants were asked to evaluate their experience with HTE-DLPR using a quality of experience questionnaire (QoE) tool for mHealth applications.
Results: Total score on the QoE was 3.89 out of 5. The highest scores were received for precision, ease of use and content quality. The lowest scores were given to security, appearance and performance. Physicians were in strong agreement with the 1st HTE-DLPR recommendation in 86.1% and the system's use was described as comfortable in 85% of cases. Users positively evaluated the development of a new version of HTE-DLPR in the future receiving a total score of 4.25 out of 5.
Conclusions: A CDSS for dyslipidemia (HTE-DLP) has been positively evaluated by physicians using QoE questionnaire.

INTRODUCTION

Despite high serum cholesterol levels have been linked to major cardiovascular disease less than 20% of patients with very high cardiovascular risk have optimal lipid control [1]. The Reality Group showed that in Spain only 12.9% of patients attained the LDL-C goal on their initial lipid-lowering drugs and an additional 13.4% achieved the goal after a change of treatment [2]. On the other hand, 30% times, statins are prescribed with other drugs with potential interactions and 9% times, the prescribed treatments are non-recommended [3]. In a US-based internet survey among current and former statin users, 25% and 60% of the responders reported statin related side effects [4]. E-healths tools can be a good and safe instrument to increase significantly the number of high risk patients on goal of LDL-C [5].

Considering the latest study by Institute for Healthcare Informatics (IMS), more than 165.000 apps of health and medicine are offered including all the stores from different platforms. It is important to note that more than 50% of the available apps received less than 500 downloads and only five of them comprise 15% of all those in the health category. The IMS attributed this situation to different causes, which include: poor quality in many of them, the lack of guidance on the usefulness of the app and a low level of support from health professionals [6]. Furthermore, a meta-analysis con-

cluded that only around 60% of these new technological processes actually succeed in improving clinical practice [7]. On the other hand, this is an area of increasing concern for healthcare authorities, given that these heath applications are not always rigorously evaluated [8]. Users and Physicians should know the quality of the mHealth applications that they are using or prescribing. mHealth should be rigorously evaluated to ensure that they provide evidence-based effectiveness, safety and efficacy. These evaluation studies should be robust, standardized and their results should be reported in line with verified standards [9]. Certification schemes for mHealth applications should be developed to serve as reliable indicators for healthcare professionals and citizens [5]. Direct participation of users in the health technology assessment process allows them to be part of the decision-making process [10]. Some tools used to evaluate mHealth applications from users view such as the quality of experience questionnaire (QoE) [11] or the Mobile App Rating Scale (MARS) [12] have been suggested.

Patient data management systems (PDMS) integrated with a clinical decision support system (CDSS) can improve outcomes in chronicles diseases as hypercholesterolemia [13]. HTE-DLPR is the first CDSS and PDMS system developed to monitor dyslipidemia treatment in Spain and the first to be validated in clinical practice in Europe [14]. HTE-DLPR performs a sequence of clinical decisions as expert lipidologyst including all statins and ezetimibe and creates specific recommendations for each patient using efficiency, safety and cost criteria. A multi-center observational prospective study has revealed that the number of patients at very high cardiovascular risk, reaching the treatment goal defined by the European Guidelines for the Management of Dyslipidemia 2011 [15] (LDL-C < 70 mg/dL.), increases 4.4 times when expert clinicians in the lipidology field use HTE-DLPR [14]. So, This study demonstrated that in the "real-clinic-world" expert physicians in the cardiovascular field can improve cholesterol management by using a specific CDSS. The cost of reducing 1 mg/dL of LDL-C was less in the intervention group than in control group (0.89 EUR/day vs 1.10 EUR/day [14]. Physicians expressed good agreement with the 1st HTE-DLP recommendation in 86.1% of cases and use was described as ease in 85% of cases. It rating yet that using HTE-DLPR throughout Spain in 2020 may potentially lead to a decrease in fatal and nonfatal coronary events in patients between the 35 to 74 years by 5.4% and 7.4% in men, between 1.8% and 2.0% in women. This corresponds to a decrease in healthcare costs derived from coronary disease between 4.7% and 6.4% [16]. It showed too that using a specific CDSS can represent a cost-effective intervention. Before disseminating HTE-DLPR in clinical practice it is important to know clinicians' opinion about its usability.

The main goal of this study is to evaluate the quality of HTE-DLPR using a QoE tool for mHealth applications.

METHODS

Participants

Ten physicians (3 cardiologist, 4 lipidologist and 3 family doctors with an average age of 42 years) from three different hospitals and two primary healthcare centers in Catalonia (Spain) were invited to participate in a validation study of HTE-DLPR in a real clinic environment. It was performed a cluster-randomized trial comparing standard prescriptions with HTE-DLPR assistance. Included patients were randomly distributed into the intervention or control group by a computer program. HTE-DLPR assistance was blocked automatically if a patient was assigned to the control group. Each clinician was invited to include a maximum of 8 patients in the study to avoid bias of learning by repeated use of HTE-DLPR. Selection criteria for participants were to have clinical experienced in the management of patients with high vascular risk and to be highly motivated to use new technologies. It included 77 patients having established cardiovascular disease or a 10-year risk of developing cardiovascular disease based on a low SCORE risk >5%. After using HTE-DLPR for a 3-month period, clinicians were asked to assess anonymously its usability using QoE tool for mHealth applications. Also, physicians were also consulted regarding their degree of acceptance of the HTE-DLPR's first recommendation and their opinion about its ease-of-use. The study protocol was approved by a local ethics committee. All patients were asked about their voluntary entry into the study after signing the informed consent.

HTE-DLP Running

HTE-DLPR is a CDSS that mimics the clinical decision making to be performed when an expert lipidologist prescribing lipid-lowering treatment. HTE-DLPR was written in Java using Open Source tools (Open JDK, Netbeans, iText, POI). At this prototype stage it runs as a standalone desktop application. Its function is to provide a recommendation the best lipid-lowering therapy with criteria of effectiveness, safety and cost-effectiveness for a particular patient based on a lipid goals and taking into account clinical situation. The recommendation is a list of treatments that are effective (in the sense to achieve the objective) and compatible with the patient (not contraindicated). Moreover, this list is sorted by a number of criteria of safety, cost and efficiency so that the treatments considered "best" are presented before those considered "less good". The program works from a case that the user is defined by the following parameters: LDL-C initial, risk profile (with corresponding LDL-C target), sex, HDL-C (optionally), situations relevant and concomitant treatments of patient. Firstly, HTE-DLPR applies selection criteria to discard statins which are contraindicated if renal or liver dysfunction or severe drug interactions exist. Secondly, treatments are selected with the necessary power to reduce LDL-C. LDL-C/HDL-C is a secondary target applicable only when user-specified. Following this, HTE-DLPR applies order criteria to compare all selected treatment options in pairs. Drug interactions and market prices are parameterized, prioritizing first safer lipid-lowering therapy and then cheaper products. When HTE-DLPR detects a difference, the comparison process ends and the program orders all selected treatments from best to worst. Clinicians can choose any recommendations of treatment made by HTE-DLPR, regardless of place of order in the ranking assigned for the program. All of these processes are done with a single click on-screen in less than one second. HTE-DLPR allows on-line updating. Patients data are anonymized. Updates of HTE-DLPR were sent by e-mail to the platform administrator. It is based on

European Guidelines for the Management of Dyslipidemia 2011 [15] and its scientific content has been verified by two experts' lipidologist using peer-review method. Equally, two independent computer engineers have tested the software and hardware and certified that HTE-DLPR met the rules on confidentiality and data protection of patients.

QoE Questionnaire

QoE is a feasible tool for measuring the usability of technological applications from user perspective. It´s a tool developed from the Department of Signal Theory and Communications, and Telematics Engineering, University of Valladolid, Spain, to assess the Quality of Experience of mobile mHealth applications in order to improve the quality of the existing apps and the ones to be released. This tool has been positively evaluated using a sample of health applications. QoE consists in 18 questions with a Likert scale of five possible response options. Thus, all questions may be scored from 1 to 5 with the following meanings: 1: Strongly disagree; 2: Disagree; 3: Neither agree nor disagree; 4: Agree, and 5: Strongly agree. The following application fields are measured [17] (Table 1):

a) Accuracy (question 1): quantifies the accuracy of the application's calculations

b) Ease of use (questions 2-4): determines the difficulty of managing the application by the user

c) Content quality (questions 5-10): asses user perception of the quality of the application content

d) Ease of Learning (question 11) : rates specifies the ease of learning how to use the application

e) Availability (question 12): appraises guarantee of access to the information at any time

f) Security (questions 13-14): titrates data security level provided by the application

g) Appearance (questions 15-16): evaluate the product's external interface

h) Performance (questions 17-18): measure up errors, unexpected performance halts, application response time

Table 1: Specific Assessment of HTE-DLP by the QoE Questionnaire for mHealth Applications [a, b]

Questions	Results
Precision	4.5 ± 0.52
Do you think the calculations made by this application are correct?	4.5 ± 0.5
Ease of Use	4.16 ± 0.38
Do you think that the traditional method used thus far is more difficult or does not exist?	4.16 ± 0.38
Did you find what you needed?	4.33 ± 0.65
Is this application useful for monitoring the disease?	4 ± 0.73
Content Quality	4.08 ± 0.36
Does it provide the functions that you expected?	4.66 ± 0.49
Do you think the data is reliable?	4.42 ± 0.51
Does the application receive regular updates?	4.25 ± 0.75
Is it possible to send information on your status to your doctor?	4.08 ± 0.66
Is your quality of life better thanks to the use of this application?	4 ± 0.73
Can you identify with the health problems in this application?	3.91 ± 1.08
Learning	3.91 ± 0.51
Do you think that the time for learning to use the application is appropriate?	3.83 ± 0.83
Availability	3.91 ± 1.16
Are you guaranteed access to the application and its data at any time?	3.91 ± 1.16
Security	3.75 ± 1.05
Do you think that this application has adequate security methods to protect the data that is introduced?	3.75 ± 1.05
Do you think that the data obtained with this application is sufficiently protected?	3.75 ± 1.05
Appearance	3,41 ± 0.92
Do you find the appearance of this application to be adequate?	3.83 ± 0.83
Wouldn´t you change or add anything to this application	3 ± 1.20
Performance	3.41 ± 0.92
Do you think its performance couldn´t be more optimized?	3.6 ± 1.15
Haven`t you encountered any errors or problems when using the application?	2.5 ± 1.24

[a] Results are presented as Mean ± Standard Deviation.

[b] Maximum score is 5.

Each category is given a separate scoring based on a preparatory qualitative evaluation of the aforementioned aspects. Furthermore, QoE it is complemented by four questions regarding user views on the future possibilities of mHealth applications. Total completion time for the 22 questions was in 1-2 minutes. A total score is obtained by averaging each individual item. A total score < 3 was considered a negative assessment; a score between 3 and 3.5 was considered acceptable, a score between 3.5 and 4 was considered a good evaluation and score above 4 was considered an excellent evaluation.

Physicians were also consulted regarding their degree of acceptance of the HTE-DLPR's first recommendation and their opinion about its ease-of-use with the question "How would you rate the ease-of-use of HTA-DLPR".

Data were analyzed using IBM-SPSS Statistics v.21.0.0 descriptive statistics were used for comparison of the groups. Inter-group differences for continuous variables were evaluated using the t-test and Manne Whitney test. A univariate analysis with categorical variables was performed using the chi-square test and Fisher's exact test. All statistical tests were two-sided and a value of <0.05 was considered significant. The study was designed to have 95% power to detect at least a 40% difference between the intervention and the control group [14]. Results are expressed in mean and standard deviation (SD).

RESULTS

Overall, the total score on the QoE was 3.89 (0.48) on a maximum score of 5 (Table 1). All categories received scores that were above 3. The highest scores obtained were: precision, ease of use and content quality, all of them above 4.0. On the other hand, the lowest ratings were given to security, appearance and performance. Individually, the only question that scored a lower score than 3 (2.5 SD 1.24) was "Did you encounter any errors or problems when using the application? (Performance). An agreement of 86, 1% of the first HTE-DLPR recommendation was achieved among clinicians and it was defined as being comfortable by 85% of the participants. Users positively evaluated the potential development of a new version of HTE-DLPR in the future, especially in the app format, giving it a total score of 4.25 (SD 0.46) (Table 2).

Regarding clinical results, greater proportion of high cardiovascular risk patients reached the LDL-C < 70 mg/mL [55.0% vs 12.5%, p 0.003; OR: 3.26 IC (1.16-9.15)]. 75% of patients achieved LDL-C goal < 100 mg/dL in HTE-DLPR users vs 45% in control group (OR 1.70 IC 1.002-2.9). Mean decreased LDL-C was greater in intervention vs control group (LDL-C 63.3 SD 51 and LDL-C 33.8 SD 47 respectively). "High potency statins" and combined therapy were used more frequently in the intervention group than the control group (P = 0.001).

DISCUSSION

A specific CDSS (HTE-DLPR) not only improve the management of dyslipidemia in high and very high cardiovascular risk patients and but also has been positively assessed by expert clinicians in hypolipemiant drug prescription.

As far as we know, this is the first study in which a CDSS for prescribing lipid-lowering therapy has been analyzed with a standardized tool for mHealth applications. We believe that global positive evaluation of HTE-DLPR is due to the significant participation of vascular risk experts in the design of its hardware and software [14]. Therefore, clinicians have ensured that HTE-DLPR is faithful to top scientific evidence and the recommendations of the European Society of Arteriosclerosis [15]. A recent survey showed that only in 67% of medical APPs expert involvement and in 87% of cases adherence to medical evidence was found [18]. It is important to develop peer-review systems of medical Apps or CDSS assessing expert medical involvement and adherence of content to current guidelines as Health Apps Library, developed by the National Health Service in the United Kingdom [19]. Furthermore, the scores obtained by HTE-DLPR in the security area of QoE reflect the extreme importance that users give to safety of storing clinical data, in order to ensure patient confidentiality [20]. It may be the case that HTE-DLPR administrator update requirement resulted in a decreased user confidence regarding its security. However, updates were carried anonymously maintaining patient´s data privacy and HTE-DLPR does not store data that can identify a particular patient but these acts were not reflected in the instructions for users of HTE-DLPR. On the other hand, the fact that the first prototype of HTE-DLPR is a standalone desktop application which requires prior installation to use and that it lacks automatic data capture have been major factors in the lower assessment of appearance and performance. Both factors are critical factors that can act as limiting barriers in its dissemination in clinical practice [21].

Using QoE tool for mHealth applications may provide major assessment advantages in terms of providing the necessary feedback to users on the detection of potential areas of improvement, the ability to quantitatively assess a mHealth application and to thereby compare it with other similar applications or future versions [17]. Based on user feedback,

Table 2: QoE Measure for Future HTE-DLP Applications [a, b]

	Score
Would you use the app if developed?	4.4 ± 0.66
Would this future application help in treating diseases?	4.33 ± 0.49
Do you think that in the future it may be useful to society?	4.2 ± 0.62
Do you think it would improve the user's quality of life?	4 ± 0.85
Final Score	4.25 ± 0.46

[a] Results are presented as Mean ± Standard Deviation.

[b] Maximum score is 5.

researchers are working on a second version of HTE-DLPR before extending its use to clinical practice that will incorporate web oriented-design with automatic data collection from electronic records and databases, latest generation warning systems, informative videos explaining its use and additional data protection specification. Another novelty is the ability to interact with the patient: recording if there is any problem or undesirable effect with medication to avoid it in future prescriptions, detecting if not withdraw the medication prescribed of the pharmacy and facilitating communication with patient´s associations or platforms. A mobile medical application version of HTE-DLPR with specific module for Familial Hypercholesterolemia is anticipated.

However, user scales assessments must be supplemented by an analysis of the quality of the medical information prior to the introduction mHealth in daily clinical practice. The essential criteria governing the quality benchmarking of online medical/health-related information resources would be: a) provide authorship information, including detailed information about authors' affiliations and credentials and about any medical professional involvement in content preparation b) list all references or sources of content c) fully disclose of any sponsorship or other commercial funding arrangements, and any potential conflicts of interest, d) ensure a balanced, non-biased coverage of facts and information currency (up-to-datedness) [22]. All these items are included in the presentation page of HTE-DLPR. These factors should be routinely considered by mHealth developers and publishers. Examples of medical and health apps independent certification of scientific quality are Happtique Health App Certification [23] and validation process of "Distinctive App-Healthy" carried out by the Agency for Health Quality of Andalusia, Spain [24]. Developers of HTE-DLPR researchers will process its certification as "healthy APP/CDSS" by relevant Public Health Agencies or Scientific Societies as a mark of quality.

Future research is necessary in order to evaluate the mHealth prior its dissemination in clinical practice [22]. It is important to find a balance between the necessary development of mHealth, which should be characterized as being disruptive, innovative and quick and the imperative need to validate that their content is based on the best clinical evidence and that their use is safe and useful in the clinical setting as new drugs or medical device is required, classically highly regulated and a slow adopter [22]. Independent, public and dynamic evaluation processes based on different validated tools including feedback from users and patients are necessary [24]. A multi-disciplinary assessment process is required to ensure interoperability and confidentiality of clinical data, to determine the superiority of the intervention with respect to daily clinical practice [25], to ensure patient safety [26], to analyze implementation cost, impact on healthcare costs and innovation value [27] and to evaluate patient´s quality of life. We suggest a progressive process of verification of scientific content and technical standards (phase I), validation in a simulated environment [28] or/and real clinical daily (phase II), evaluation from users and patients (phase III), certification and on-going monitoring with periodic re-certification of mHealth applications before and after their introduction in daily clinical practices (phase IV) [29] (Table 3). Ideally, prior to release and use in clinical practice a mHealth should be required mandatorily to overcome at least Phase I, and Phase II if its use can have health risks from users. This first assessment should be discriminating, with pass or fail assessment. Phases III - IV could be an optional quality assessment, only mandatory in the case of the medical device. Phases III and IV also serve to compare with each other different mHealth. Currently, most of the mHealth applications used or prescribed in daily clinical practices have only received technical verification (phase I-A) or clinical validation based on a small group of patients (phase IIA) [30]. Following this proposed scheme, HTE-DLPR would pass the stage III-B.

Table 3: Proposed Steps for the Clinical Implementation of Health Technologies

Definition	Description	Executant
Verification	Verification of technological and clinical concepts Definition: A- Correct operation of hardware and software, standards of interoperability and safety in data handling B- Content is consistent with scientific evidence	Informatics Data protection agency Universities Expert health-worker Scientific societies
Validation	Clinical validation A- Clinical studies on small group of patients led by clinical experts in simulated or real clinical environments B- Clinical studies in a large group of patients conducted by healthcare worker expert and non-expert in real clinical practice Definition: Measuring the effectiveness (A), safety (B) and efficiency (B) compared to standard practices using a randomized study in a real clinical practice.	Health workers Scientific Societies
Evaluation	Evaluation of E-Health A. Evaluation by public and "standard platform" with different tools B. Analysis of implementation cost and impact on healthcare costs. Definition: A-Evaluation by different quantitative and qualitative tools including user feedback B-Report of cost-effectiveness of implementation	Users and patients Healthcare workers Scientific societies
Certification	E-Health Certification Definition: A-Certification by an independent accredited agency or societies that it meets technical and scientific standards. B-Monitoring and surveillance with periodic certifications post-implementation in clinical practice	Government agencies of quality Drug agency Health authorities Scientific Societies

This study has several limitations. First, as pilot study contains limited data of patients and participants and it has a short follow-up period. Furthermore, study participants were the same physicians that participated in the clinical validation study and this may have led to the overvaluation of certain aspects. On the other hand, participants that they are expert clinicians in management of dyslipidemia, feeling that they are being compared with the HTE-DLPR, may in fact underestimate its assessment. Another limitation of this study, it was not measured patient opinion. In future, it would be important to assess the effects on lipid control after incorporating the improvements proposed by users. Strengths must also be highlighted. It is notable the positive correlation between subjective assessment by users and the high score by QoE.

CONFLICTS OF INTEREST

This study concludes that HTE-DLPR has proved to be a satisfactory CDSS to management of dyslipidemia in high risk patients and also get a satisfactory assessment by clinicians using QoE tool for mHealths. Users have detected some points to be incorporated in the continuous and necessary process of quality improvement. QoE questionnaire can be a useful quantitative tool to comparing similar mHealths and can help to incorporate feed-back from users in the process of improving quality in future versions.

FUNDING

Authors declared there is no funding or support.

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