

Strategies for the follow-up of patients with chronic diseases and polypharmacy: development and implementation of a new health care approach based on mobile technology (DIPP-mHeart Study).

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Abstract

Background:

Multimorbidity is related to a high increase in costs for the health system and a poorer quality of life for patients. It is the professional's responsibility to establish new care models oriented to improve health outcomes in high complexity patients. We have developed a comprehensive care program for these patients based on carrying out sustainable highly effective interventions for the health system through technology.

The use of new technologies to improve health results is an unstoppable trend. The implementation in practice of new forms of healthcare based on telemedicine leads to a need for professionals to specialize in an often unfamiliar area.

Objective:

The main aim of the study is to design and **Develop**, **Integrate** and implement an mHealth tool to support monitoring of the chronic **Patient with Polypharmacy (DIPP-mHeart Study)**.

The secondary aim of our study is to make the development of these new technologies easier for other research groups through describing the limitations encountered by our team during the development of the project and the corresponding solutions implemented to overcome those limitations.

Methods:

The study was carried out in four stages: design, development, integration and implementation, followed by ensuring the quality, security and legal requirements of the mHeart® prototype. The design and development of the tool was based on a review of the bibliography and several surveys done to the main stakeholders (patients, health professionals, Health Authorities and experts in mHealth). All these findings allow us to focus mHeart functionalities on the user's expectations and the polymedicated patient's real needs as well as to discover realistic solutions to overcoming the main limitations of implementing the new tool within the health environment. The tool was adapted to the solid organ transplant population, a perfect example of the chronic patient of high complexity.

Results:

133 chronic patients, 26 stakeholders, as well as health authorities, patients' associations and scientific societies were interviewed. Based on the information gathered, the design of the new tool was focused on improving the management of polytherapy and the flow of communication between professionals, patients and care levels. After carrying out diverse tests, the final mHeart® platform prototype was obtained (website and mobile application). Its functionalities allow for the sustainable intervention of a multidisciplinary team in real time and in a patient's habitual context, thus empowering the patient through clinician feedback. The main limitations encountered were the integration of the tool with our health system's information technology system, ensuring quality and safety, as well as considering other legal aspects which the clinical team were not familiar with.

Conclusions:

The DIPP-mHeart project resulted in a new holistic eHealth tool that will be extremely useful for the follow-up of chronic patients with polypharmacy. Not only was this platform to be designed and developed, but its safety and quality, its implementation in our environment, and its continued use in the long term were also to be ensured. Sharing the key aspects involved in overcoming the major difficulties encountered could be highly interesting for the scientific community and widely applicable in our setting.

Keywords: Polypharmacy; Medication Therapy Management; Patient Empowerment; Chronic Disease; Interdisciplinary Health Team; Comprehensive Health Care; Organ Transplantation; Cell Phone; Telemedicine; Biomedical Enhancement.

Introduction

Background and purpose

The coexistence of two or more chronic conditions in the same individual (multimorbid) has become increasingly common in the last few decades [1,2]. Moreover, it relates to a greater risk of safety issues as a result of fragmented care and a high level of therapeutic complexity [3–5].

For instance, polypharmacy, or the intake of more than 5 different drugs, can be seen in 85% of multimorbid patients [6]. Long-standing management of these patients is complex given the substantial risk of low therapeutic adherence, pharmacological interactions and side effects of medication [7]. Additionally, in the long term, the intake of multiple medications is associated with a lower quality of life (QoL) [8,9], a decline in the efficacy of the treatment or even the development of a new health problem [10,11]. Most of these negative consequences related to the misuse of medication could be avoided. It is the responsibility of professionals to establish programs designed to ensure the safety and efficacy of patients with polypharmacy [12,13].

Among chronic patients, solid organ transplant recipients characteristically present a greater risk of multimorbidity and polypharmacy due to chronic exposure to immunosuppressive treatment [5,14]. This type of complex therapy shows rates of up to 55% non-compliance depending on the type of organ transplant, and this is recognized as a risk factor for morbidity and mortality and negative economic outcomes after solid organ transplantation [15,16]. Thus, strategies directed at improving treatment adherence in this population need to be developed.

Furthermore, in recent decades there has been an increase in post-transplant life expectancy which has led to a change in the focus from acute to long-term patient care, aiming at new goals such as increasing morbidity-free survival and achieving acceptable QoL [17,18]. Despite this, the functional status and QoL of recipients remain lower than in the general population due to a greater complexity of this patient group [19]. As with other patients with multiple pathologies, there is a need for sharing the post-transplant patient's management with diverse professionals and levels of care [15].

Although international transplant guidelines list the main comorbidities in transplant patients [20], an increase in the mean age of these patients involves the emergence of additional comorbidities. It is estimated that 5 years after a heart transplant, 95% of the patients develop hypertension, 81% hyperlipidemia, 33% chronic renal failure and 32% diabetes. However, in the long-term (10 years after transplant) the main factors that limit survival are cardiac allograft vasculopathy (CAV) and malignancies (affecting 25-50% and 35% of patients respectively) [17,21]. In particular, CAV has been related to severe comorbidities such as long-standing high blood pressure or serum lipid profile alteration, justifying the importance of improving long-term management of cardiovascular risk in these patients [22,23].

Therefore, the solid organ transplant population is a perfect example of one with high complexity and chronicity which needs to be approached by an interdisciplinary team. In the specific case of the heart transplant group, the prevention of cardiovascular events acquires special importance because of the risk factors related to the ischemic disease present before the transplant [17,21]. This would justify implementing interventions designed to improve

therapy management, health status and QoL and, in this sense, telemedicine has been shown to have an immense potential in this population [24].

Implementing strategies for dealing with comorbidity patients taking multiple medications.

Given the scarcity of resources which often limits the quality of health care in patients with polypharmacy in our catchment area, we selected three strategies in terms of their effectiveness in clinical practice. These three strategies combined and applied to a model population in real practice should improve patient and carer support, reduce the number of complications affecting patients with polypharmacy and make the patient's healthcare experience easier.

Strategy number 1: Ensuring that patients with multiple chronic diseases, who typically experience fragmented and poorly coordinated management, receive care through a comprehensive integrated program [25–27].

Strategy number 2: Innovating in clinical practice through the development and implementation of new health technologies such as mHealth. Mobile devices have been used effectively in long-term management of comorbidity [28–32] and have been proven to increase quality of care in chronic patients and reducing costs [33–37].

Strategy number 3: Implementing effective and sustainable interventions that are provided to people during their everyday lives (i.e., in real time) and in natural settings (i.e., real world). Using mobile technology to carry them out increases patient acceptability, is effective for treating a variety of health behaviors and physical and psychological symptoms and can be successfully implemented [38,39].

The first step towards implementing these strategies in clinical practice was to establish a comprehensive healthcare program directed at this population within our hospital, followed by the development and implementation of the new software necessary for continuing the program. To this end, the DIPP-mHeart project was put into effect.

The aims of the DIPP-mHeart project

The main aim of the study is to design and Develop, Integrate and implement an mHealth tool to support monitoring of the chronic Patient with Polypharmacy (DIPP-mHeart Study) and adapt it to the cardiac transplant patient.

The secondary aim of our study is to render the development of these new technologies easier for other research groups by presenting all aspects that need to be taken into account when setting up a new app, beyond software, including our findings on the potential benefits that mHealth technology users can expect and any corresponding solutions implemented to overcome limitations.

Methods

Setting

This research study was carried out in the catchment area of a tertiary university hospital (Hospital de la Santa Creu y Sant Pau, HSCSP) in Catalonia, Spain. The study was approved by the Ethics Committee of HSCSP with the protocol code IIBSP-MHE-2014-55.

The DIPP-*mHeart* study was carried out in four stages.

Stage 1, mHeart® Prototype Design.

For 2 years (2013-2014) *mHeart*, a technological tool based on a mobile application and an Internet website, was designed as a support for the clinical follow-up of polymedicated patients. To design this *mHealth* tool, we combined different methodologies for locating guidance on how to move from a general clinical aim to a clearly defined and effective application [40].

To this end, a review of revisions, expert guidelines and descriptions of the experiences of other healthcare centers in relation to the development of modern technologies was conducted. This permitted the integration of behavioral science, design and [38,40–44]. Furthermore, we specifically took into account *mHealth* technologies or already existing websites with published results for usability, validation or implementation in clinical practice with a view to improving health impact variables (psychological support, therapeutic adherence, self-controls and bio measurements) [28,32,45,46]. The strong points in these experiences not only allowed us to base the design of the diverse functions on experiences with proven evidence, but also to consider the limitations encountered and thus prevent them.

Moreover, we evaluated the expectations of potential users, the possible impact of the technology, the authentic needs of polymedicated patients and the viability of its implementation with no added cost on the part of the health-system. To this effect, two different questionnaires were designed, one directed to patients and the other to professionals.

On the one hand, a questionnaire to be completed by chronic polymedicated patients and based on survey results published by experts was designed [47,48]. Polypharmacy was defined as more than 5 different long-term medications coexisting in a patient's electronic prescription. The aim of the face-to-face interviews was to define the actual knowledge of technology usage that these patients had and to predict whether the *mHealth* tool would be accepted or not.

On the other hand, diverse stakeholders were interviewed about the benefits and limitations of *mHealth* in our healthcare environment. The questions were drawn from information on the benefits and limitations of *mHealth* published by various institutions [33–35,49–51].

Stage 2. mHeart® Prototype Development

In order to carry out the technological development, a private firm with experience in development and integration of Health Care system applications (*mHealthCare Nabelia*) was

hired. The firm's corresponding technical team consisted of 1 analyst, 5 developers, 1 designer and 1 project leader. The HSCSP's scientific advisory team was formed by 2 information analysts, 4 pharmacists, 4 doctors, 2 nurses and 1 psychologist. The tool was designed according to the Spring framework (Spring MVC, Spring REST y Spring JPA) with a 3-layer structure. The platform has a web-based and mobile version for both Android and iOS. The development lasted from February 2014 to June 2016.

The term mHeart® prototype was used for each of the versions of the mHealth tool not clinically validated. After 3 different versions of the prototype, the final one was obtained. Each prototype version needed to be assessed in a testing environment by the developers. After this first filter, sessions for testing in a staging environment were held in the HSCSP with the participation of hospital staff and volunteer patients. The aim of such tests was to improve the usability of the platform and to detect any possible errors that might affect patient safety. Moreover, external sessions in patients' associations and organizations concerned with solid organ transplantation were previously held.

Once the final prototype had been consolidated in a staging environment, the last production preliminary test was done. This test lasted one month, with 13 professionals and 5 homebased volunteer transplant patients taking part. The idea was to simulate genuine use of the platform. With a view to recording the incidents detected and areas for improvement in usability, a grid with diverse features to be evaluated was filled in by participants.

Stage 3. mHeart® Prototype integration and implementation

When implementing and integrating the mHeart® prototype in our healthcare environment, it was necessary to consider the current resources in the catchment area. To this end, different points of reference (Catalonian Health Authorities, our Information System Centre and the analyst responsible for ensuring integration) were asked to respond to a questionnaire.

Stage 4. Quality, security and legal requirements of the mHeart® Prototype

To ensure the suitability, quality and safety of the mHeart® platform, a series of requirements need to be fulfilled (Table 1).

Table 1. Workable solutions to ensure mHeart® quality and security

1. CE marking by the Spanish Medicines Agency as a class I medical device, according to Spanish law concerning medical devices (Real Decreto 1591/2009, de 16 octubre). In order to achieve this, the mHeart® platform had to fulfill the requirements included in European legislation and follow the legal rulings regarding: medical devices software life-cycle processes: [UNE-EN 62.304 (2006)]; [UNE-EN-ISO 14.971 (2007)] and medical devices risk management and quality management systems UNE-EN-ISO 13.485 (2013).
2. Certification granted by a local institution that evaluates health apps: AppSaludable[52], App Salut[53], British[54,55], iSYS Score[56], Riezebos[47], MARS[57,58], etc.
3. Written endorsement on the part of the scientific societies and patient associations related to the group population.

Other relevant aspects to be considered in the development of a healthcare app

Processing personal data with confidentiality and security

A high level of protection of personal data was ensured through technical advice from the Department of Data Confidentiality in the HSCSP. All the legal documents, the developers' security and quality guarantees, user guides for the platform, etc. were checked and approved by a specialist in this field.

The HSCSP was responsible for the patients' data files and authorized the developers to process the data. To this end, the company contractually committed to applying the security measures stipulated for high-level processing of personal data files, as specified in Spanish law concerning data protection (Real Decreto 1720/2007); (LOPD) 15/1999. The platform Data Center, which is situated in Germany, hosts the data protected by data protection law (Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data). On the other hand, certification was granted by TÜV SÜD in accordance to ISO 27001 standard.

The developers must necessarily bear security in mind both from the regulatory and technical perspective and must annually undergo an audit so as to assess compliance with data protection and use of secure connections based on Secure Socket Layer (SSL) for demographic data integration. The Transport Layer Security (TLS) protocol is also employed to guarantee security when remitting reports to the HIS (Hospital Information System).

To join the platform, patients must sign a non-disclosure agreement. Their username and password are confidentially sent via an automated email. The first time they access the website or app, they should accept the conditions of use, which should always be available for possible consultation.

Legal advice regarding the technological development

As a result of outsourcing, support was provided by an expert in intellectual and industrial property who was specialized in the field of medical technology. With a view to regulating the collaboration with the developers' private firm, a contract of "Commercial Exploitation of Technology" between the Research Institute at HSCSP and the company was established.

Results

Stage 1 Results. mHeart® Prototype Design

The results of this first stage are the consequence of the feedback obtained from all of those involved in the design and development of the app.

Results of interviews with the main stakeholders, the patients

We interviewed 133 chronic polymedicated patients taking an average of 13 (\pm SD 10.4) different medications to treat 2.8 (\pm SD 2.2) comorbidities. Out of the total, 89 were men with an average age of 58 (\pm SD 14). Their knowledge of technology usage and their general acceptance of an mHealth tool are shown in Table 2.

Table 2. Patient's knowledge of technology usage and general acceptance of an mHealth tool.

	N=133
Technology availability	
Number of gadgets per patient; mean (SD)	2 (0.9)
Patients that have 2 or more mobile devices available to them; N (%)	105 (78.9)
Patients that have access to the internet on their device; N (%)	101 (75.9)
Frequency of technology use; N (%)	
Often	84 (63.2)
Sporadically	26 (19.5)
Never	11 (8.3)
Purpose of technology usage; N (%)	
Leisure	103 (77.4)
Work	27 (20.3)
Health	46 (34.6)
Internet usage for health-related purposes; N (%)	
Often	33 (24.8)
Sporadically	47 (35.3)
Never	40 (30.1)
Interested in recommendations on reliable resources on the Internet; N (%)	
Interested only in mobile apps; N (%)	37 (27.8)
Interested in mobile apps and websites; N (%)	60 (45.1)
mHeart® initial personal assessment N (%)	
Not very useful	25 (18.1)
Useful	76 (55.1)
Very useful	17 (12.3)
Does not know/does not answer	1 (0.7)
Initially requires a tutor to use the platform; N (%)	30 (22.6)

Results of interviews with professionals and other stakeholders

26 stakeholders were interviewed about the potential benefits and limitations of mHealth in polymedicated patients (Figure 1). The results of the questionnaires are shown in Tables 3 and 4.

Figure 1. Stakeholders' participation in the mHealth benefits and limitations questionnaire.

26 stakeholders answered the questionnaire, 16 of them were professionals who attend to such patients (6 doctors, 3 nurses, 5 pharmacists and 2 psychologists), together with 2 technology analysts, 5 key representatives of the local and regional health authorities and 3 experts in mHealth.

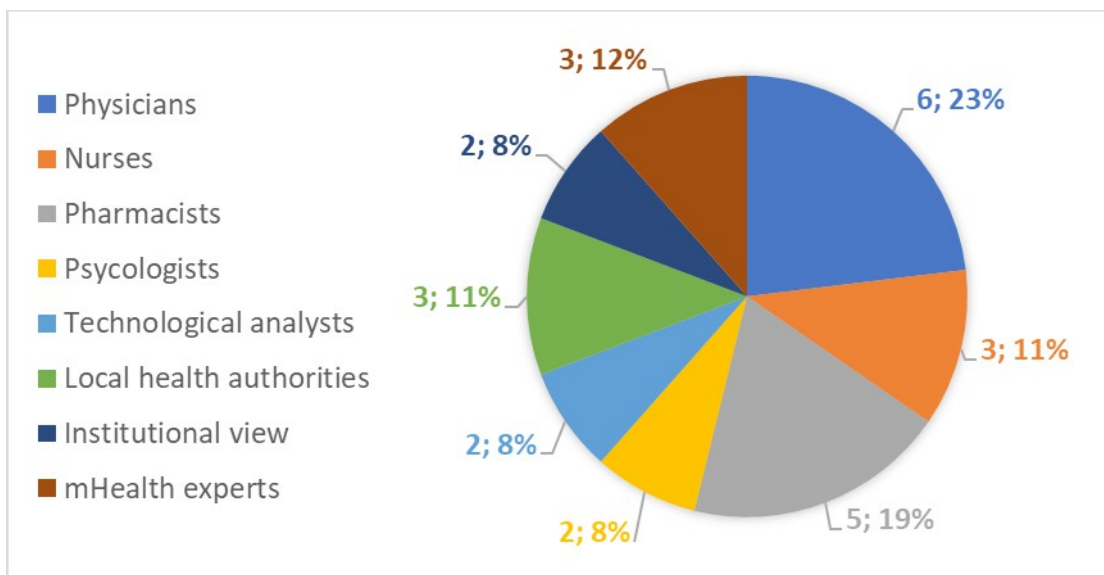


Table 3. Interview results showing the opinions of different professionals on possible benefits of mHealth in the polymedicated patient in our area

Benefits according to > 15% of those surveyed.	N (%)
Improves knowledge of therapy, management and compliance with drugs for patients at home.	23 (88%)
Improves the continuity of care and the flow of information between professionals and levels of care.	21 (81%)
Allows for patients to be empowered to actively intervene in the control of their disease and treatment.	20 (77%)
Resolves patient and caregiver queries from home thanks to the bidirectional clinical-patient communication.	20 (77%)
Detection of symptoms and adverse effects to drugs, thereby improving their management.	17 (65%)
Focus on health promotion and prevention, reducing the number of acute events.	17 (65%)
Increases the cost-effectiveness of resources by reducing scheduled visits, as well as urgent ones due to decompensation.	17 (65%)
Facilitates innovation in health and documentation of evidence that translates into measurable health outcomes.	17 (65%)
Reduces inequalities in access to the health system due to traveling difficulties or lack of resources.	10 (38%)
Improves patients' experience because of closeness to professionals.	4 (15%)

Table 4. Interview results showing the opinion of different professionals on possible limitations of mHealth in the polymedicated patient in our area

Limitations according to > 15% of those surveyed.	N (%)
Increase in workload for staff.	15 (58%)
Lack of institutional guidelines for the development and accreditation of mobile applications in healthcare.	14 (54%)
Risk of not sharing the patient's registered information with other levels of care or with other apps (used to manage other health conditions).	13 (50%)
Risk of not protecting the patient's confidential data.	6 (23%)
Risk of creating inequalities regarding patient care due to the digital divide [59].	6 (23%)
The long-term economic sustainability of research projects for innovative technologies and companies that develop them is sometimes not granted.	4 (15%)

As a result of patient and professional feedback, the HSCSP's scientific advisory team designed the mHeart® application with the main challenge of detecting and improving non-adherence to medications. Two of the main sub-functions of the developed application were to solve patients' questions about their treatment, and to empower patients, enabling them with self-control and management of their clinical situation.

Stage 2 Results. mHeart® Prototype Development

Prototype test

The results of the prototype 1 and 2 test, permitted greater functionality and the solution of usage problems. The improvements identified in the prototype 3 test (developed in a production or real environment) were incorporated if they represented an upgrade in patient safety. The cooperation of different patient associations enabled us to either include new functionalities in prototype 3 or take them into account in other phases of the development. The main points expressed by them during the piloting of the prototype are shown in Table 5. This process resulted in the final prototype, or mHeart® prototype (Figure 2).

Figure 2. mHeart mobile application.
Application's main screen.



Table 5. Patient associations' feedback gathered in external sessions to improve Prototype 3

The patient associations showed great interest in the use of mHealth in the management of their chronic conditions.
They highlighted the interest in the use of bi-directional messaging with the clinician.
The patients compared the tool with other free downloadable ones in the Store emphasizing as an additional value the fact that mHeart® was adapted to their condition and provided the clinician's feedback.
They also showed great interest in the reinforcement of patients' communication by demanding a patients' chat room and a patient-professional teleconference module.

Functionalities of the mHeart® prototype

The mHeart® prototype is a home-based mobile phone app and website application for use by patients as a kind of diary. Professionals use it via web as an aid in their clinical practice; it allows them to consult the different variables recorded by the patients. Access to the tool is multiplatform (Smartphone, tablet, computer) and it can be used simultaneously on different devices. It is available in Castilian Spanish. It is compatible with Android (Google) and iOS (Apple) and can be downloaded for free from the Store under the name “mHeart”. The supporting web page can be accessed through the link v3-salud.nabelia.es [60].

Functionalities of the patient profile.

At a functional level, it provides patient access to a private profile which is structured in modules. These modules are equally visible in the app (Figure 3) [Multipmedia appendix 1: mHeart application demo] and on the web (Figure 4) via a menu.

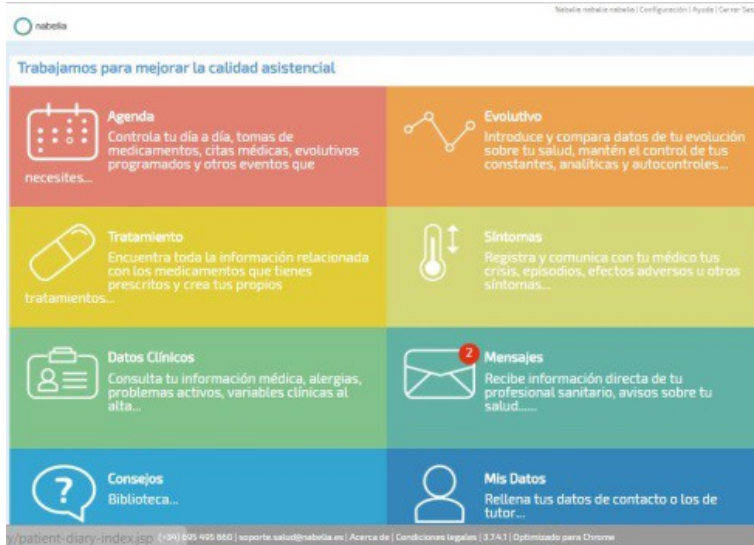
Figure 3. mHeart App Menu.

The different App modules are displayed: Treatment, Agenda, Self-control, Symptoms, Messaging, Health Education and Advice, Personal and Clinical Data.



Figure 4. mHeart Website Menu.

The different Web modules are displayed: Treatment, Agenda, Self-control, Symptoms, Messaging, Health Education and Advice, Personal and Clinical Data.



Treatment Module

In consultation mode, patients can view lists of drugs prescribed by professionals as well as inactive medication. (Figure 5) Moreover, they can add other therapies, over the counter medications (OTC) and Complementary Health Approaches (CHA) [61] to consult with the health professional about interactions with their current prescription. The recommendations can be viewed graphically in the form of traffic light signals linked to a written recommendation if necessary. (Figure 6)

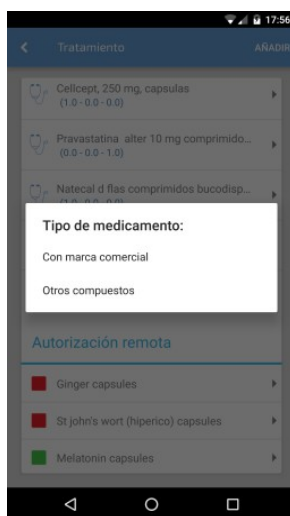
Figure 5. mHeart App Treatment Module: active treatment.

When the professional adds active treatment, a figure of a stethoscope appears in front of the drug whereas if a patient adds a new therapy, once validated by the professional, a figure of a person appears in front of the drug.



Figure 6. mHeart App Treatment Module: consultation on compatibility between active treatment and new therapies.

When adding a new therapy, the patient will choose whether it is a drug or another type of Complementary Health Approach (CHA) (e.g. ginger capsules). The new therapy will show pending until validation by the professional. If the combination is not recommended, it will appear in red, in orange if it is associated with a recommendation and in green if it is accepted without comments.



Agenda Module

Here the content of diverse modules is uploaded, enabling the patient to find on the platform all programmed activities (Table 6), which are shown in different colors and generate a Push text alert on the patient mobile phone. (Figure 7)

Table 6. Distinct kinds of activities scheduled on the mHeart® agenda

<i>Medication schedule</i>	The patient can visualize the medication schedule, receive alerts for due drug doses and record drug intake of a single drug or several drugs at the same time. (Figure 8) If a dose is canceled, the reason for it will need to be added. (Figure 9) Patients can graphically view their compliance.
<i>Bio measures</i>	Bio measures (e.g. blood pressure) can be registered by the patient directly from the agenda if they have already been programmed. (Figure 8 and 10) Frequency will be set by the patient or the professional in the self-control module.
<i>Adherence tests</i>	The patient can answer the adherence test programmed by the professional (Figure 11 and 12).
<i>Personal agenda</i>	The patient can add personal events and reminders.

Figure 7. mHeart App Agenda: scheduled tasks

The different tasks are shown in different colors in the monthly calendar and in the list of daily tasks: personal events, blood tests, visits, others. These tasks could be introduced by the patient or professional.

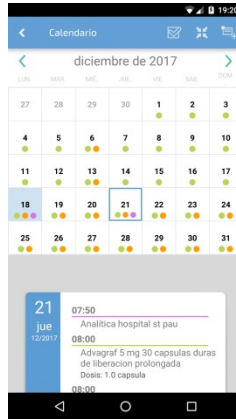


Figure 8. mHeart App Agenda: drug intake confirmation.

The patient can confirm or "validate" the intake of a drug individually or several drugs at the same time.

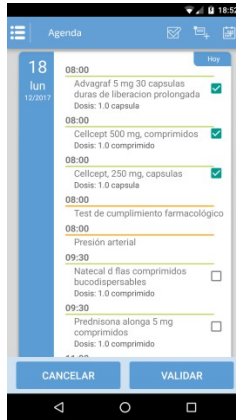


Figure 9. mHeart App Agenda: reason for non-adherence.

The patient can specify the reason for not complying with therapy: forgetfulness, insufficient information about the dosing schedule and / or illness, demotivation, side effects or fear of suffering them, complex and / or uncomfortable dosing schedules; others.

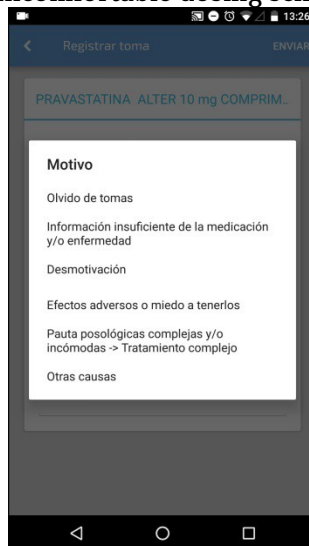


Figure 10. mHeart App Agenda: scheduled self-controls.

The patient can record self-controls (e.g. blood pressure) straight from the agenda if they have been previously programmed.



Figure 11. mHeart App Agenda: modified Haynes-Sackett adherence test.

Patients can answer the programmed adherence test directly from the agenda. If the patient answers that there are difficulties with adherence, a reason must be stated.

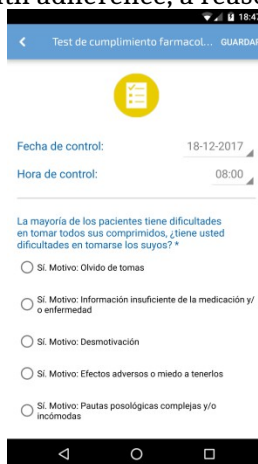


Figure 12. mHeart App Agenda: Morisky Green adherence test.

Patients can answer the programmed adherence test directly from the agenda.



Self-control Module

The self-control module allows the patient to record vital signs (e.g. blood pressure) and bio measurements (e.g. weight). (Figure 13) Recording can be done manually (Figure 10) or automatically by using wearables. When the patient enters values, which are not within reasonable limits, a message indicating “Invalid format” appears. In the case of some bio measurements, limit values emit the warning “contact your healthcare team via the platform”. The records can be viewed in graphic form through the app and in graphic and table form on the WEB. (Figure 14 and 15)

Figure 13. mHeart App Self-controls Module Menu.

This module has been adapted for heart transplant patients: diet, exercise, general wellness, cardiac frequency, glycaemia, weight and blood pressure.

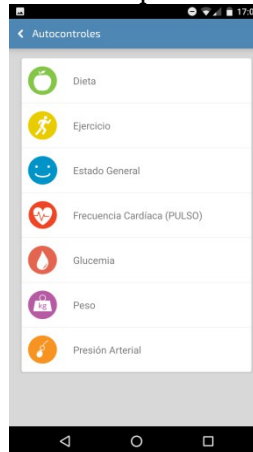


Figure 14. mHeart App Self-controls: graphics.

Patients can check their progress through a graphic (e.g. blood pressure data), introduce a new register or program a test on their agenda.

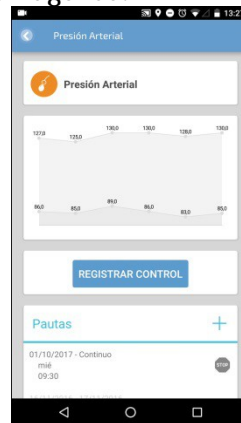


Figure 15. mHeart App Self-controls: general wellness follow-up graphic.

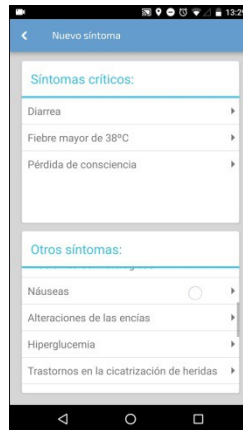


Symptoms Module

Just as if they had self-care diaries, patients will be able to select symptoms or adverse side effects derived from their medication from a list provided. They will indicate the starting date, the finishing date and relevant comments. Some of these symptoms generate an alert for the clinician. (Figure 16)

Figure 16. mHeart App Symptoms Module.

Patients may register symptoms or side effects related with medication.



Teleconsultation and Messaging Module

A two-way videoconference or chat for patient-professional communication. Files can be attached. (Figure 17)

Figure 17. mHeart App Messages Module.

Patients may send and receive messages from professionals. An opened or closed envelope symbol appears, indicating whether the patient has read the email or not.



Health Education and Advice Module

Updated healthy lifestyle and health promotion information is available. Texts, photographs or multimedia files are incorporated in accordance with this population's needs.

Personal and Clinical Data Module

Through the platform patients can consult their sociodemographic data, documented allergies, relevant past medical history and contact professionals.

Functionalities of the Professional Profile

Professionals gain access through the web, are able to organize their list of patients according to various criteria and filter by rapid search fields or systems. Within each patient profile, the same modules are viewed but with broader editing rights; patient registration, prescription and therapy monitoring, programming self-control tests, initiating communications with patients. (Figure 18)

Figure 18. mheart website Professional Profile.

The professional can create a new patient, visualize the complete list of patients, use the messaging module or access each patient's profile. Within each patient profile, there will be a summary of the data entered by patients.

Mar Gomis Pastor | Configuración | Ayuda | Cerrar Sesión

nabelia Lista de Pacientes Mensajes

Nabela nabela nabela (nabelaTC)

Fecha Nacimiento: 26/03/1993 Edad: 24 Persona de Contacto:
 Nº historia: 456456 Diagnóstico: Estado de trasplante de corazón Fecha de última actividad: 18/12/2017
 Nº CIP: 456456 Tutor: No

D. Personales D. Clínicos Tratamiento Evolutivo Síntomas Mensajes Agenda Consejos

Tratamiento Nuevo tratamiento

Tratamientos activos

Prescrito por	Nombre	Principio activo	Adherencia
	AMLODIPINO ALTER 10 mg COMPRIMIDOS EFG (1-0-0)	AMLODIPINO BESILATO	<div style="width: 100%; height: 10px; background-color: #ccc;"></div>

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Registration of New Patients

When new patients are registered, their sociodemographic data is automatically uploaded from the HIS. This information must be verified and completed with the patients' or carers' contact details.

Prescription Module

Professionals prescribe from a drop-down list of drugs imported and automatically updated from the Spanish National Formulary. Other therapies can be added to a patient's prescription in free-form data entry (e.g. relaxation exercises prescribed by a psychologist). Each prescription can be accompanied with personalized comments (e.g. "Anti-rejection treatment. It is recommended that you take this on an empty stomach"). From this module possible drug interactions can be addressed.

Messaging and Video Consultation Module

When professionals wish to text patients, an alert in the form of a Push-up message is generated in the patients' devices. Professionals can check whether the message has been read. This module permits messages to be sent to groups of patients selected in accordance with demographic data or a common drug. Moreover, preventative health promotions can be set for specific periods of time (e.g. a reminder about flu vaccination programmed for October; a reminder for patients on corticoids to avoid sugar in their diet).

Consultation Regarding Therapeutic Adherence

Identification of a non-adherent patient by professionals is achieved by the combination of diverse mHeart® functions as detailed in Table 7.

Table 7. Consulting adherence to therapy in mHeart®

The patient's drug intake registrations.
Type of information registered by the patient: <ol style="list-style-type: none">1. Doses taken versus total of doses prescribed.2. Reasons for non-adherence (drop-down list).
Professionals can see adherence information from 2 different perspectives: <ol style="list-style-type: none">1. A traffic light system alerts the professional of a drop in the patient's weekly adherence in the main patient list module.2. Adherence presented graphically and through data tables in the treatment module.
Adherence tests included in the mHeart® platform.
The professional sets up the frequency. Test results are shown graphically: <ol style="list-style-type: none">1. Haynes-Sachett test [62,63] (adapted to include reasons for non-adherence). (Figure 11)2. Morisky Green test [64] (Figure 12)

Stage 3 Results. mHeart® prototype integration and implementation in clinical practice

Considering the information supplied by the Catalan Health Authorities and our hospital's Information System Department, and considering the available resources in our healthcare system (table 8), the integration pathways were separated into local or institutional solutions depending on the phase that was being dealt with (table 9).

Table 8. Questionnaire sent to the Catalan Health Authorities and other points of reference.

1. Taking into account the technological resources available, how would you ensure that the sociodemographic, clinical and therapeutic patient data is not being manually entered by the professionals in the mHeart® prototype?
2. Regarding the transversality of the information recorded by the patient on the platform: <ul style="list-style-type: none"> • How could we ensure the addition of this information to the HSCSP patient's electronic medical record (i.e. HIS)? • How could we share this information with other care levels (e.g. Primary Care)?

Table 9. Solutions adopted as a result of the questionnaire sent to the Catalan Health Authorities and other points of reference.

Stage 1. Local solutions.	mHeart® has been integrated bi-directionally with the HSCSP's HIS. A patient's demographic data can be imported from HIS when creating a new patient in mHeart® Figure 19.
	HIS receives from the mHeart® platform a weekly report that contains all information provided by the patient (e.g. blood pressure, adverse effects, etc.), available on the clinical work station for consultation by the health team Figure 20.
Stage 2. Institutional solutions.	We are working on uploading the weekly patient report into the Catalan integrated electronic clinical record (HC3). HC3 is a health data repository which to share records between centers and clinical professionals. With this report, any professional could easily monitor patients at any point in time or at any care level.
	In 2017, the Catalan healthcare system made mHeart® app available to patients from La Meva Salut (LMS), a patient health website through which patients interact with the regional healthcare system.

Regarding the introduction of mHeart® in clinical practice, a phone and email Help Center for patients and professionals was hired, thus allowing them to solve both technical and functional problems. This call center service is formed by two professionals from the developer company who are specialized in remote technical assistance. Apart from dealing with incidents, the developer call center actively participates in the initial training of users, as well as in the follow-up of their first few weeks of activity.

Figure 19. Local solution for integration: demographics Integration.

A patient's demographic data can be requested in two different situations: when a new patient is created in mHeart, and when mHeart force an update of a patient's data. A demographic request is mandatory in order to create and update a new patient, in this way mHeart guarantees the veracity of data. The request of demographics consists in a synchronous HL7 messages patient query through SOAP Web service. HL7 standard is widely used in health exchange data between parties.

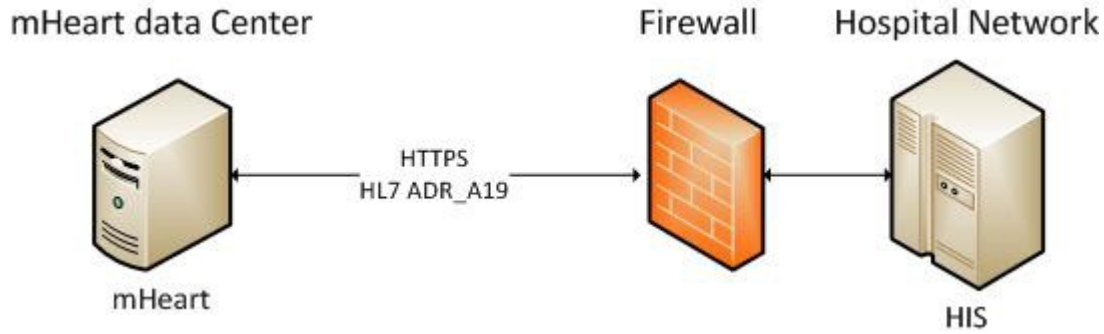
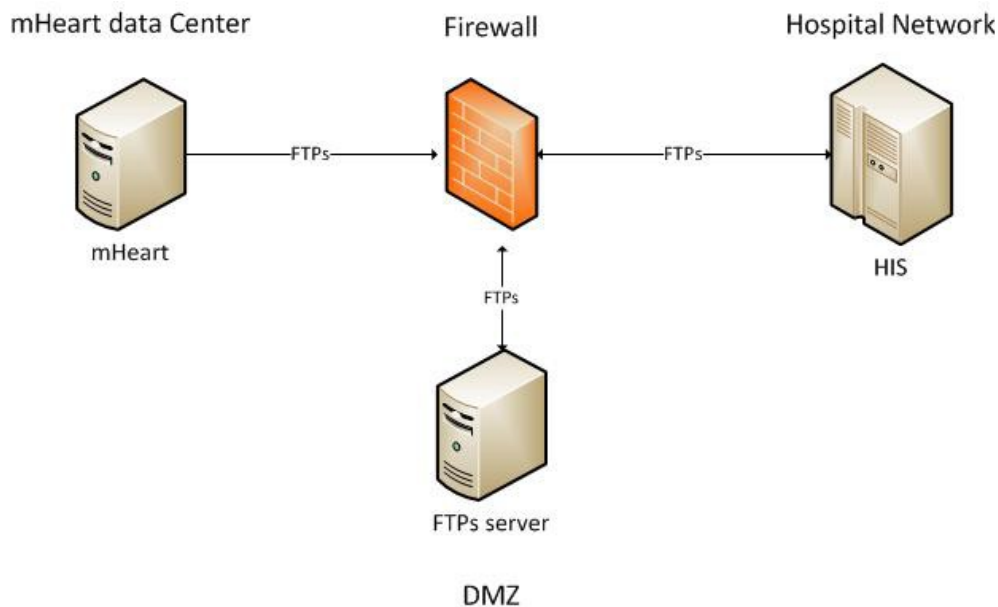


Figure 20. Local solution for integration: the patient report integration.

Once weekly, mHeart uploads an evolutionary report for each patient in the system in an implicit FTP over TLS server. A security process identifies the report and assigns it to the patient in HIS. Only the latest report can be consulted on the Clinic workstation as a clinical document.



Stage 4. Quality, security and legal requirements of the mHeart® Prototype

The requirements finally fulfilled are shown on Table 9.

Table 9. Workable solutions to ensure mHeart® Quality and security

<p>1. According to the law concerning medical devices, since mHeart® registers symptoms, side effects, vital signs and adherence to medication, it enables professionals to intervene in response to these data. For this reason, the mHeart® platform was required to obtain the CE marking as a class I medical device.</p>
<p>2. Institutional support: - Written endorsement by Catalan Transplant Organization (OCATT) and the Catalan</p>

Transplant Society (SCT). - La Meva Salut (LMS) certification.
3. Representatives for the cardiac transplant patient support groups (written endorsement): Clinic Hospital (" Club de la Cremallera") and Bellvitge Hospital ("Cors Nous").

Discussion

The DIPP-mHeart project resulted in the development of a technological tool that is extremely useful as a support for carrying out integral healthcare for patients with polypharmacy. Not only was this platform designed and developed, but its safety and quality, its implementation in our environment and its continued use in the long term were also ensured. When the design of the platform first began in 2013, the potential benefits and limitations of mHealth described by different institutions had not been sufficiently endorsed in real clinical practice. [33–35,49–51] Therefore doubts arose about whether the platform could combine clinical and technical aspects and address many other relevant ones related with an eHealth development.

In this regard, the opinion of healthcare professionals and health managers made it possible to create an mHealth platform adapted to the potential benefits expected and real needs of professionals. At the same time, having information in advance on the real limitations of mHealth in our setting allowed us to search for new functionalities and to correct them with the resources and technology available to us. Moreover, as a result of the interviews completed by patients, a knowledge of real usage of technology, acceptance of the new tool and the requirements of polymedicated patients was acquired. Thus, reinforcing the idea of the acceptance and potential impact in our environment of an mHealth Project aimed at patients of high complexity.

Once the prototype structure had been built, it was adapted for the follow-up of solid organ transplant patients, providing both patients and professionals with a version that fulfills the clinical needs of that specific population. Interventions via mobile technology have proven to be more successful when adapted to the patient's environment [30,38,39,65,66].

Furthermore, ensuring that the prototype structure is easily adaptable to any other chronic health condition has led other Spanish healthcare centers to use the mHeart® tool as a basis to obtain a version adapted to their needs (e.g. MedPlan+, e-OncoSalud, ePrematur, Entrena EII, Gerar).

Combining behavioral science, design and engineering to create a new tool to improve polymedicated patients' care

The combination of both conductual and engineering strategies for achieving the clinical aims established, provided us with diverse mHeart® functionalities with the potential of improving patient care.

Improving management and adherence to therapy

A broad consensus of the professionals surveyed showed that an improvement in the management of polytherapy could be the main benefit of mHealth due to the significant effect on patient health outcomes [67]. In this sense, the key functionalities mHeart® has to offer

are: identifying non-adherent patients and the corresponding explanation for their behavior; successfully intervening on an individual basis; identifying potential interactions and adverse effects; improving patients' knowledge and management of their therapy; reinforcing patients' training and sense of co-responsibility in their treatment.

Given that low adherence jeopardizes the therapeutic success of a treatment, special emphasis was placed on this functionality. It is shown that mHealth could improve treatment adherence through the combination of different educational and motivational content together with customized interventions [28]. This is why we prioritized functionalities which made the identification of non-adherent patients and adherence limiting factors possible [68,69], as well as those which allow professionals to carry out targeted interventions.

Another point to consider is the growing demand in our environment for the co-responsibility of patients in the management of their therapy [68], in the sense that professionals reach an agreement with patients on the most adequate drug treatment regimen adapted to both their timetables and lifestyles [70–73]. On this account, the platform medication schedule was designed to be programmed in accordance with this agreement and included individualized reminders adapted to a patient's environment and specific difficulties (e.g. "Remember to take this anti-rejection drug on an empty stomach").

Furthermore, the growing use of CHA shows this increasing autonomy of patients with regard to their therapy and the need to create patient-friendly spaces in which they can ask questions and consult any doubts [74,75]. In order to accomplish this, the treatment consultation module was designed for dealing with different kinds of therapies which could interfere with the success of a treatment.

Promoting integral healthcare

Improving the flow of information between professionals and levels of care is the second greatest potential benefit of mHealth in our environment. Chronic polymedicated patients require clinical monitoring shared between various levels of care and by a multidisciplinary team which usually use information systems that are not interconnected within the same health area.

First of all, it was crucial that mHeart® should ensure that clinical information is shared with a patient's whole environment. Hence, the summary report (adherence to treatment, self-control records and critical symptoms) has been made visible to all the professionals involved in the patient's care at all levels.

On the other hand, the Teleconference module among professionals was incorporated as a tool for interdisciplinary communication and shared decision-making. Without forgetting that the module Treatment of the platform allows us to include non-pharmacological treatments (e.g. relaxation practice according to psychological prescription), integrating the recommendations of all the members of the interdisciplinary team.

Improving professional-patient communication

It has been demonstrated that communication between professionals and home-based patients through mHealth is more effective than the conventional kind, as it acts in real time and in a patient's usual environment [39]. This new means of intervention may lead to behavioral changes or reinforce interventions performed from the hospital [38]. mHeart

texting offers personalized feedback on patients' platform records, but also permits the programming of large-scale interventions, thereby saving professionals' time.

In addition, the Mobile Teleconference Module allows for the reinforcement of interventions in a cost-effective manner, avoiding the need to travel for patients without resources or living far away from their care center.

From the patient's perspective, written messaging is a channel for solving problems within a usual setting, where doubts about their therapy and its management will arise. It also allows patients greater freedom, for example, if they enjoy travelling but feel too afraid to be far from their healthcare providers. And also, if patients feel more accompanied by their healthcare providers, a better care experience will be ensured.

Empowering patients suffering from chronic diseases

mHeart® also has huge potential with respect to empowering patients [35,49,51]. With this purpose in mind, the platform functionalities have been aimed at maintaining patients well-informed so that they actively intervene and follow the progress of their self-care and therapy in a proactive way.

On the one hand, the Self-control Module was created, hence facilitating the recording of hygiene and dietary habits, as well as bio measurements. These variables, were chosen if they had shown long-term survival impact in patients [76]. The programming of these self-control alerts in the calendar could be another chance to customize interventions. Furthermore, according to published experiences, viewing diagrams of patients' recorded data (validation of dosages or information on self-control) allows them to become aware of the effects that changes in their lifestyle have [65,77–80].

On the other hand, early detection of certain symptoms via tablet computers has shown impact on survival and quality-adjusted survival in a recent clinical trial among 766 outpatients receiving chemotherapy for advanced solid tumors [32]. This was made possible through active participation on the part of the patients. The mHeart® Symptoms Module combined with the multimedia Advice Module and the health campaigns could achieve greater impact on health prevention.

Real limitations of the implementation of a new eHealth tool and corresponding solutions

Having prior knowledge of the limitations that may be expected when implementing a new eHealth tool in real practice and learning about practical solutions would have been extremely useful in the preliminary stages of the project. To this end, in what follows we share our own experience with the aim of anticipating possible limitations that may arise during the first stages of eHealth tool designs while offering workable solutions.

Communication between the tool and the healthcare environment

Integration allowed us to improve the flow of information between levels of care and to overcome the potential limitation of mHeart® being isolated from the system. This was one of the greatest challenges we encountered. There was scarce evidence available to us of mHealth developments that had been integrated with the environment at the time of the platform's

design, added to the fact that each health information system functions differently and they are not interconnected.

On this matter, the opinion of the relevant Health Authorities and the IT systems team enabled us to find solutions and finally, in all the settings, achieve the integration of the platform patient records with the health information systems. Moreover, the connection of mHeart® with our HIS allowed the inclusion of patients' data automatically onto the platform whenever they were registered. This improves safety in mHeart®, since transcription errors are avoided, and the time dedicated to this task is reduced.

Investment of time and the healthcare burden

The development and implementation of mHeart® entailed a significant initial investment of time on the part of the clinical team. According to Heron & Smyth [38] and to our experience, this was due to the need for coordinating the user-friendly design, assuring quality and safety and implementing the new real-time support for patients in everyday clinical practice.

So that the increase in the burden of care does not imply a limitation, different measures should be considered. On the one hand, it is necessary to set up an efficient technical support service that is responsible for both training and resolution of queries or doubts inherent to the use of the application, so that healthcare professionals do not spend time on these issues. On the other hand, the professional's daily routine should include time for patient follow-up using the tool. In this sense, the possibility of consulting a summary of patient records directly on HIS makes it easier for the user.

Digital divide.

The results of the patient interviews showed that some of them could need reinforcement in the use of the technology. If that support was not granted then it could lead to inequalities as a consequence of the digital divide [59]. To overcome this limitation, the figure of the tutor (a caregiver or a close family member) was included in the design of the platform, as well as the technical support service.

Although the age of those interviewed could have been an obstacle as far as technology usage was concerned, the patients stated that they had different devices and that they frequently used technology for health-related purposes. Furthermore, half of the patients said they would like to have a website associated to the app. So, the initial design was modified from including only an app to also including a website for use on the PC or Tablet.

Sustainability and cost of an mHealth solution

At present, health authorities will only cover the costs of mHealth solutions if evidence of positive impact on health with minimal impact on resources is generated. Thus, mHeart® should be easily implementable in clinical practice and should be extendable to other populations of polymedicated patients assuming the lowest economic burden possible for the system or the patient.

For this reason, we made the app compatible with most mobile phones on the market, thus allowing patients to use their own devices. Besides this, the platform not only allows the use of wearables to perform bio measures (which send the result automatically from the device to the app), but also manual entry.

Finally, medical devices such as mHeart® should be clinically validated ensuring that there is no need for extra costs on reference methods to confirm the data accuracy (e.g. electronic pill dispensers or medication event monitoring systems to measure treatment adherence).

Quality and security of an mHealth solution

The search for viable solutions to certify the suitability, quality and safety of the mHeart® prototype, showed the lack of uniformity and institutional guidelines. For instance, local institutions follow different guidelines with the purpose of certifying the quality of apps. Even though each guideline provided us with a minimum standard, no guideline can be considered a golden standard/rule as they all presented advantages and disadvantages. Nevertheless, the only compulsory certification for medical devices is the CE marking, which safeguards confidentiality of data, risk analysis and preventative actions during the software life cycle.

Moreover, the endorsement of different scientific societies and patient associations related to heart transplant, reinforce the quality of the content of the adapted version of the platform (table 5). Moreover, having the feedback from the clinical team that is working with the mHeart App has proven to be an additional value that other apps on the market do not have.

Tips for new eHealth developments

In the case of DIPP-mHeart, the design and development were carried out from scratch, with scarce information about other experiences published, and with little guidance from national and international institutions. Failure to take into account some initial considerations, extended the development period of the app by a year. Having this information beforehand would have made it easier to reach the final version of the mHeart® prototype that meets the standards of quality and safety that patients deserve. Therefore, we offer a summary of a series of key points to be considered when conceiving this type of project.

- Our experience tells us that the selection of the technology developing company must be based on objective criteria. It is paramount to check that the company complies with quality and safety standards according to the country's regulations; demonstrates previous experience in the development of healthcare applications that have been tested in real clinical practice and have an excellent customer service.
- From our point of view, the most efficient way to approach a new development is to evaluate the tools available up-to-date in the market and choose the one that meets the requirements as a starting point. The fact that the platform has already been used in real practice will help allocate the costs to new functionalities, compliance with the project calendar and achieve the expected quality.
- Moreover, from the start of the project, the integration of the tool into the different levels of care and the project continuity needs to be planned in advance.
- It is important to allocate part of the initial resources towards having an intellectual property consultant specialized in the field of medical technology. These aspects must be defined in the contract between the developer and the institution.
- The limited experience of professionals in regard to data protection entails an excess of concern about confidential data of mHealth users. Having a specialist to advise on this matter (the CE marking and the patient's consent) deals with this limitation.
- The initial time investment in the project justifies assigning a part-time project coordinator, who provides scientific advice to developers, coordinates the pilot tests, as well as the relationship with third parties (legal advice, etc.).

- During the pilot tests, new and innovative functionalities emerged. The incorporation of these new ideas that significantly affect the usability and quality of the platform in a first tool version is recommended. Addressing other improvements in the next phases of the technological development.
- Joining forces with patient associations and scientific societies during the developing process of the tool allows one to gauge whether it has been adapted to the diverse realities in the various healthcare institutions.
- From our point of view, health technology must be adapted to a target population and enable patients and the multidisciplinary team to suggest any technical adjustments required according to their changing needs. This dynamism will improve its usability and persistence over time and will mark the difference in regard to other health apps available on the market.

Future challenges for mHeart®

The description of new improvements planned for mHeart® that we are currently working on could be embraced by future developers and the ideas incorporated into their initial design.

- Automatic answers to the consultations regarding interactions with concomitant therapies.
- Connecting the mHeart® platform with the hospital's electronic agenda to activate appointment reminders on the app.
- Setting up a discussion forum for patients.
- Programming periodical changes to the type of mHeart® questionnaires (e.g. adherence or general condition). This will prevent the patient from responding in a routine manner and the system from losing sensitivity in identifying the non-adherent patient.
- Translating the platform into other languages to make the tool usable in other countries.
- It is our future aim to develop a decision support system based on artificial intelligence algorithms (patterns and prediction rules) thanks to the data obtained using the mHeart® platform in real clinical practice.

Furthermore, our future challenge is to carry out the m-Heart prototype validation study (*Val-mHeart Study*), a clinical validation of the medical device in real practice. This will be followed by a long-term clinical trial looking at the impact on health and economic outcomes of a multidisciplinary ambulatory care program with the support of an mHealth tool in chronic polymedicated patients (Clinicaltrials.gov ID NCT02554578 *mHeart*).

Conclusions

We have developed a new eHealth tool as the first step towards implementing an innovative holistic polymedicated patient care program. The opinion of different stakeholders, scientific societies and patients has made it possible to provide a version that fulfills the clinical needs of organ transplant patients, which is easily adapted to other chronic diseases.

One of the major strengths of this tool is that it allows the multidisciplinary team to intervene in a sustainable way and in real time in a patient's habitual context, empowering patients through clinician feedback. Moreover, not only has the design of this tool mainly focused on

improving the management of polytherapy, but also on enhancing the flow of communication between patients and professionals, including different care levels.

Our experience could be a valuable guide to other professionals not only in optimizing the development of a new eHealth tool, but also in successfully integrating the software into the healthcare system and implementing it in real clinical practice.

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Authors' contributions.

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Astellas Pharma has contributed to the financing of the development of the mHeart® platform.

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Conflicts of Interest

None declared.

Abbreviations

QoL: Quality of Life

mHealth: mobile health.
eHealth: use of information and communication technologies for health.
App: mobile application.
HTxR: heart transplant recipients.
HSCSP: Hospital de la Santa Creu i Sant Pau.
HIS: hospital information system.
IT: information analyst.
SSL: secure socket layer.
TLS: the transport layer security.
LOPD: Spanish law concerning data protection (Ley Orgánica de Protección de Datos Personales).
ISO: International Organization for Standardization.
CHA: complementary health approaches.
OTC: over the counter.

Multimedia Appendix 1:

mHeart application demo

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