DECISION MAKING IN DIGITAL HEALTH:

Usage of the cost-effectiveness analysis to improve the sustainability of the healthcare system

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“Um, yes, well. Not exactly. You see, the Wheel of Time weaves the Pattern of the Ages, and the threads it uses are lives. It is not fixed, the Pattern, not always. If a man tries to change the direction of his life and the Pattern has room for it, the Wheel just weaves on and takes it in. There is always room for small changes, but sometimes the Pattern simply won’t accept a big change, no matter how hard you try. You understand?”

Rand nodded. “I could live on the farm or in Emond’s Field, and that would be a small change. If I wanted to be a king, though…” He laughed, and Loial gave a grin that almost split his face in two. His teeth were white, and as broad as chisels.

“Yes, that’s it. But sometimes the change chooses you, or the Wheel chooses it for you. And sometimes the Wheel bends a life-thread, or several threads, in such a way that all the surrounding threads are forced to swirl around it, and those force other threads, and those still others, and on and on. That first bending to make the Web, that is ta’veren, and there is nothing you can do to change it, not until the Pattern itself changes. The Web—ta’maral’ailen, it’s called—can last for weeks, or for years. It can take in a town, or even the whole Pattern. Artur Hawkwing was ta’veren. So was Lews Therin Kinslayer, for that matter, I suppose.”

Robert Jordan – The Wheel of Time (Chapter 36)

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Abstract

Healthcare systems worldwide are facing a number of challenges that are conjunctural to the historical moment and are somehow reshaping a discipline as traditional as medicine. The five major challenges that are defining the future landscape of healthcare practice can be classified into: 1) Demographic change, 2) Urbanization, 3) Deliver patient-centric care, 4) Move the focus from reactive to proactive medicine and 5) Adoption of digital health technologies.

The healthcare sector has been particularly slow in the adoption of digital technologies. When this Ph.D. project started in year 2017, many barriers were preventing the implementation at-scale of digital health. Among those, the lack from evidence-base and proper economic studies around their implementation were the two biggest issues.

Governments, health systems and health provider organizations struggle on how best to allocate their finite resources. A strategy followed by most has historically been targeting their investments on the areas causing the biggest burdens in terms of health and economic impacts. Worldwide, noncommunicable diseases (NCDs) are the main source of mortality for both men and women, and account for 41 million deaths per year, equivalent to 71% of all deaths globally. Most NCDs are of chronic nature and its development is the result of the combination of physiological, genetic, environmental, and behavioral factors. The global economic burden of chronic diseases is posing a major challenge for the sustainability of health and social care systems because of the high direct and indirect costs associated to them. Due to the huge impacts in individuals and societies, preventing and controlling chronic diseases is in all policy agendas. Policymakers, product developers and other stakeholders within the healthcare ecosystems around the world have focused on the design and implementation of digital health solutions that can be integrated into health systems and facilitate the management of chronic diseases.

Acknowledging the abovementioned challenges, the main aim of this Ph.D. thesis was to assess the cost-effectiveness of digital health solutions designed to support the management of major chronic conditions that can be implemented within the Catalan health system. To address this aim, three research questions were formulated considering three types of digital tools in three different areas related to major chronic conditions.

First, we hypothesized that a mHealth intervention for the prevention and control of cardiovascular diseases would improve the utility of individuals (quality of life) decreasing the cost comparing to usual care (Do CHANGE project). Second, we hypothesized that the provision of information and communication technology–enhanced integrated care services that encompass health and social care in the setting of domiciliary care would improve health outcomes and reduce health system costs (BeyondSilos project). Moreover, we hypothesized that an Internet-based Cognitive Behavioral Therapy intervention for the treatment of depression would improve the utility of individuals (quality of life) decreasing the cost comparing to usual care (MasterMind project).

The three interventions analyzed in the framework of this project proved to be cost-effective. Overall, we concluded the implementation of digital health solutions aimed to support the management of major chronic conditions within the Catalan health system can provide cost-effective results. Moreover, we envisaged that barriers towards the implementation are non-technological and relate to other aspects such as the organizational structure, governance and professionals' culture.

Resum

Els sistemes sanitaris de tot el món s'enfronten a diversos reptes que són conjunturals del moment històric i que, d'alguna manera, estan reformant una disciplina tan tradicional com la medicina. Els cinc grans reptes que defineixen el futur panorama de la pràctica sanitària es poden classificar en: 1) Canvi demogràfic, 2) Urbanització, 3) Prestar atenció centrada en el pacient, 4) Passar el focus de la medicina reactiva a la medicina proactiva i 5) L'adopció de tecnologies de salut digital.

El sector sanitari ha estat especialment lent en l'adopció de tecnologies digitals. Quan aquest projecte de doctorat va començar l'any 2017, moltes barreres impedien la implementació a escala de la salut digital. Entre aquestes, la manca d'evidència sobre l'efectivitat i d'estudis econòmics adequats al voltant de la seva implementació van ser identificats com els dos problemes més importants.

Els governs, els sistemes de salut i les organitzacions proveïdores de salut lluiten per la millor manera d'assignar els seus recursos finits. Històricament, l'estratègia seguida per la majoria s'ha centrat en posicionar les seves inversions en les àrees que provoquen la major càrrega en termes d'impactes econòmics i sobre la salut. A tot el món, les malalties no transmissibles (MNT) són la principal font de mortalitat tant per a homes com per a dones i representen 41 milions de defuncions anuals, el que equival al 71% de totes les defuncions a nivell mundial. La majoria de les MNT són de naturalesa crònica i el seu desenvolupament és el resultat de la combinació de factors fisiològics, genètics, ambientals i de comportament. La càrrega econòmica mundial de les malalties cròniques suposa un desafiament important per a la sostenibilitat dels sistemes sanitaris i d'atenció social a causa dels elevats costos directes i indirectes que s'hi associen. A causa dels enormes impactes en les persones i les societats, la prevenció i el control de les malalties cròniques es troba en totes les agendes polítiques. Els responsables polítics, els desenvolupadors de productes i altres grups d'interès dels ecosistemes sanitaris de tot el món s'han centrat en el disseny i la implementació de solucions de salut digital que es puguin integrar als sistemes de salut i que facilitin la gestió de malalties cròniques.

Reconeixent els desafiaments abans esmentats, l'objectiu principal d'aquesta tesi doctoral va ser avaluar el cost-efectivitat de diferents solucions de salut digital dissenyades per donar suport a la gestió de les principals malalties cròniques, de manera que es poguessin implementar al sistema sanitari català. Per abordar aquest objectiu, es van formular tres preguntes de recerca considerant tres tipus d'eines digitals en tres àrees diferents relacionades amb afeccions cròniques importants.

En primer lloc, vam plantejar la hipòtesi que una intervenció de mHealth per a la prevenció i el control de malalties cardiovasculars milloraria la utilitat dels individus (qualitat de vida) disminuint el cost en comparació amb l'atenció habitual (projecte Do CHANGE). En segon lloc, vam plantejar la hipòtesi que la prestació de serveis d'atenció integrada amb el suport de les tecnologies de la informació i la comunicació que englobessin l'atenció sanitària i social en l'àmbit de l'atenció domiciliària millorarien els resultats en salut i reduirien els costos del sistema sanitari (projecte BeyondSilos) A més, vam plantejar la hipòtesi que una intervenció de teràpia cognitiva conductual basada en Internet per al tractament de la depressió milloraria la utilitat dels individus (qualitat de vida) disminuint el cost en comparació amb l'atenció habitual (projecte MasterMind).

Les tres intervencions analitzades en el marc d'aquest projecte van resultar ser cost-efectives. En general, vam concloure que la implementació de solucions de salut digital destinades a donar suport a la gestió de les principals malalties cròniques del sistema sanitari català poden proporcionar resultats cost-efectius. A més, vam preveure que les barreres a la implementació no són tecnològiques i es relacionen amb altres aspectes com són l'estructura organitzativa, la governança i la cultura dels professionals.

Resumen

Los sistemas de salud en todo el mundo se enfrentan a una serie de desafíos que son coyunturales al momento histórico y que, de alguna manera, están remodelando una disciplina tan tradicional como la medicina. Los cinco desafíos principales que están definiendo el panorama futuro de la práctica de la salud se pueden clasificar en: 1) Cambio demográfico, 2) Urbanización, 3) Brindar atención centrada en el paciente, 4) Cambiar el enfoque de la medicina reactiva a la proactiva y 5) Adopción de tecnologías sanitarias digitales.

El sector de la salud ha sido particularmente lento en la adopción de tecnologías digitales. Cuando este proyecto de doctorado fué iniciado en el año 2017, muchas barreras impedían la implementación a escala de la salud digital. Entre ellos, la falta de evidencia sobre la efectividad y estudios económicos adecuados en torno a su implementación fueron los dos problemas más importantes.

Los gobiernos, los sistemas de salud y las organizaciones proveedoras de servicios de salud luchan por encontrar la mejor manera de asignar sus recursos limitados. Históricamente, una estrategia seguida por la mayoría ha sido focalizar sus inversiones en las áreas que causan las mayores cargas en términos de impactos económicos y de salud. A nivel mundial, las enfermedades no transmisibles (ENT) son la principal fuente de mortalidad tanto para hombres como para mujeres, y representan 41 millones de muertes por año, lo que equivale al 71% de todas las muertes a nivel mundial. La mayoría de las ENT son de naturaleza crónica y su desarrollo es el resultado de la combinación de factores fisiológicos, genéticos, ambientales y de comportamiento. La carga económica mundial de las enfermedades crónicas plantea un gran desafío para la sostenibilidad de los sistemas de atención sanitaria y social debido a los altos costos directos e indirectos asociados a ellas. Debido a los enormes impactos en las personas y las sociedades, la prevención y el control de las enfermedades crónicas está en todas las agendas políticas. Los políticos, los desarrolladores de productos y otras partes interesadas dentro de los ecosistemas de atención médica de todo el mundo se han centrado en el diseño y la implementación de soluciones de salud digital que puedan integrarse en los sistemas de salud y facilitar la gestión de enfermedades crónicas.

Reconociendo los retos antes mencionados, el objetivo principal de esta tesis doctoral fue evaluar el coste-efectividad de las soluciones sanitarias digitales diseñadas para apoyar la gestión de las principales enfermedades crónicas y que pudiesen implantarse en el sistema sanitario catalán. Para abordar este objetivo, se formularon tres preguntas de investigación considerando tres tipos de herramientas digitales en tres áreas diferentes relacionadas con las principales enfermedades crónicas.

Primero, planteamos la hipótesis de que una intervención de mHealth para la prevención y el control de enfermedades cardiovasculares mejoraría la utilidad de los individuos (calidad de vida) disminuyendo el costo en comparación con la atención habitual (proyecto Do CHANGE). En segundo lugar, planteamos la hipótesis de que la provisión de servicios de atención integral mejorados por las tecnologías de la información y la comunicación que abarquen la atención social y de salud en el contexto de la atención domiciliaria mejoraría los resultados de salud y reduciría los costos del sistema de salud (proyecto BeyondSilos). Además, planteamos la hipótesis de que una intervención de terapia cognitivo-conductual basada en Internet para el tratamiento de la depresión mejoraría la utilidad de los individuos (calidad de vida) disminuyendo el costo en comparación con la atención habitual (proyecto MasterMind).

Las tres intervenciones analizadas en el marco de este proyecto resultaron coste-efectivas. En general, llegamos a la conclusión de que la implementación de soluciones de salud digital destinadas a apoyar la gestión de las principales enfermedades crónicas dentro del sistema de salud catalán puede proporcionar resultados coste-efectivos. Además, contemplamos que las barreras para la implementación no son tecnológicas y se relacionan con otros aspectos como la estructura organizacional, la gobernanza y la cultura de los profesionales.

List of main contributions associated with the thesis

The validation of the research questions has been carried out throughout the publication of three original articles. The published articles are the main outcome of several years of research in three different European-funded projects in which I was involved as principal investigator of the project partner. My contribution to these projects included the obtention of the competitive funding, the design of the different studies, the piloting phase (including data collection), the analysis and interpretation of the experimental results, and the publication of the scientific outcomes.

The list of main contributions to this Ph.D. thesis is as follows:

	Title	Journal	Impact Factor*	Quartile	Authorship position
1	Changing the Health Behavior of Patients With Cardiovascular Disease Through an Electronic Health Intervention in Three Different Countries: Cost-Effectiveness Study in the Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE) 2 Randomized Controlled Trial	Journal of Medical Internet Research	5,034	Q1: Medical Informatics Q1: Health Care Sciences & Services	1
2	BeyondSilos, a Telehealth-Enhanced Integrated Care Model in the Domiciliary Setting for Older Patients: Observational Prospective Cohort Study for Effectiveness and Cost-Effectiveness Assessments	JMIR Medical Informatics	2,577	Q2: Medical Informatics	1
3	Guided Internet-Based Cognitive Behavioral Therapy for Depression: Implementation Cost-Effectiveness Study	Journal of Medical Internet Research	5,034	Q1: Medical Informatics Q1: Health Care Sciences & Services	1

(*) Impact factor according to InCites Journal Citation Reports for year 2019.

Other scholarly contributions within the same thematic area and period but not included as main contributions to this thesis can be found in Appendix I.

Preamble

The work presented in this Ph.D. project is the result of nearly seven years of effort in the design, implementation, and evaluation of digital health solutions within the Catalan healthcare system.

My research interest on innovation, research, and digital health grew early in my professional career while working as a software engineer in Badalona Serveis Assistencials (BSA). BSA is a health and social care provider with a target population of nearly 450,000 inhabitants and 17 centers covering all health levels and spread across the cities of Badalona, Montgat and Tiana (Catalonia, Spain). Back in year 2003, the City Council of Badalona entrusted the provision of the social services to BSA, thus enabling a health organization that was already vertically integrating primary, secondary, and tertiary health levels to also integrate the social care delivery into a unique provision.

During that period, we implemented the Electronic Medical Record, developed the Social Care Record, and worked on the integration between both. The work we conducted these times changed my view forever because it made me see the huge potential the digital transformation to improve the quality of care and the sustainability of the health and social care systems.

In 2005, after many failed attempts, I got my first European-funded project as principal investigator. By then, the smartphones had not yet hit the market, nor the Bluetooth protocol, but we were already implementing telemonitoring solutions at patients' home, even though we had to wire all the household. Projects such as Home Sweet Home, Persona, Aladdin, or ReAAL were some of the frontrunners in the field of digital health in Europe.

Personally, I am very proud I was able to be part of them and contribute to the development of the field in Europe. All in all, it has been a long journey where Badalona and BSA proved to be the perfect test site to carry out the research described in this doctoral thesis.

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List of Abbreviations and Acronyms

BSA – Badalona Serveis Assistencials
CAD – Coronary Artery Disease
CE – Cost-effectiveness
CVDs – Cardiovascular Diseases
DHI - Digital Health Intervention
DT - Digital Transformation
HF – Hear Failure
HIT - Health Information Technology
HT - Hypertension
HTA – Health Technology Assessment
iCBT - Internet-based Cognitive Behavioral Therapy
ICT - Information and Communication Technology
IT - Information Technology
MAFEIP – Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing
MAST - Model for ASsessment of Telemedicine Applications
NCDs - Noncommunicable Diseases
QALY - Quality-adjusted life-years
RCTs – Randomized controlled trials
WTP – Willingness-to-pay

1. INTRODUCTION

1.1 Background

Healthcare systems worldwide are facing a number of challenges that are conjunctural to the historical moment and are somehow reshaping a discipline as traditional as medicine. The five major challenges that are defining the future landscape of healthcare practice can be classified into:

Demographic change: The re-shaping of demographic profiles is a common denominator worldwide, regardless of the industrialization or economic status (e.g., developed or developing) of the country. Advances and better access to health services, public health gains, and improved standards of living are causing a sustained increase in life expectancy worldwide [1]. At the same time, most societies are facing a reduction in birth rates. All together is causing a significant shift in population pyramids and is leading to older communities or what is commonly known as aging [2,3]. A direct consequence of aging is the increasing prevalence of chronic diseases [4], sometimes linked to unhealthy behaviors (i.e., unhealthy diet, smoking, sedentarism, and harmful use of alcohol), which results in higher demands for health and social care services [5,6]. This, together with the sustained increase of the older population, is causing the health and social care costs to skyrocket and is posing a great challenge for the sustainability of health and social care systems worldwide [7,8].

Urbanization: The second major global trend is the intense concentration of population in cities, also known as urbanization. Urban growth is associated with a country's technological and economic development. Currently, more than half of the global population (54%) live in cities, with this figure set to rise to 66% by 2050 [9,10]. Cities are a place for opportunities but also the primary source of tremendous challenges, such as isolation and mobility barriers found by older people, intensification of inequalities, and increasing insecurity, particularly for more than 500 million people aged 65 years or more who live in cities [11]. Those are full of physical, social, and economic barriers that prevent old dwellers from fully exercise their rights and living in dignity and safety. As a direct consequence of urbanization, the rural areas are becoming empty. The lack of opportunities in small villages is causing young people to flee to cities in search of a better future. At the same time, services (including health) are concentrating in cities, which increases the difficulties to access them for the remaining citizens who live in rural areas [12].

Deliver patient-centric care: Third, a number of structural changes are taking place, which are affecting the way health services are provided. One of the most remarkable changes is the transition from a paternalistic system, in which the overall responsibility was from the healthcare professional to a shared decision-making paradigm, in which patients are ceasing to be passive subjects to become active subjects in making decisions regarding their health. To a large extent, thanks to all the available information they now have, and which is no longer exclusive to the doctor, a fact that some authors today speak of as the great fall of the ivory tower of traditional medicine [13]. Another important change is the shift towards integrated care models, where the importance of interaction between providers operating at different levels of care is paramount [14]. Care coordination is only effective when all the actors involved have information about what is happening at any point in the care continuum. This data must be provided in real-time, with enough quality, incorporate all the views of the agents involved in the care process, and be available at any point in the system [15].

Move the focus from reactive to proactive medicine: Healthcare systems worldwide are trying to shift from reactive to proactive systems. In other words, the intention is to move the focus from systems which were used to just treat the sick and move towards the so called four Ps medicine (i.e., predictive, preventative, personalized, participatory) [16]. It has never been so possible to prevent a disease as it is nowadays. Scientific advances in genomic medicine and the whole world that has opened thanks to the development of biometric sensors has led to situations never thought of. Overall, the idea is to improve health outcomes and reduce costs [17,18].

Adoption of digital health technologies: Digital health is the application of information and communication technology (ICT) as a tool to improve health services and systems. It is considered an umbrella term including a broad range of different technologies such as telehealth and telemedicine, mobile health (mHealth), wearable devices, advanced data services, and clinical decision support tools (i.e., Artificial Intelligence, Machine Learning, Natural Language Processing and Predictive Modelling), amongst others [19]. For many years, digital health solutions have been seen as the vehicle to improve health outcomes, reduce the associated travel burdens to receive specific treatments for both patients and caregivers, and reduce the costs for all stakeholders within the healthcare ecosystem [20]. Therefore, the adoption of digital health technologies must be seen as both a challenge and an enabler to provide an answer to the other four challenges healthcare systems are facing.

But where do we stand in terms of the digital transformation of the healthcare sector?

Digital transformation (DT) should be understood as *"a process that aims to improve an entity by triggering significant changes to its properties through combinations of information, computing, communication, and connectivity technologies"*

[21]. DT processes are never straightforward and by any means an end by themselves. From an organizational perspective, such transformative processes may last for years of consecutive adaptation to each new cycle of innovation. It is not possible – not even for the ones leading the transformation process – envisaging the final picture which is, by default, continuously changing. A DT process must be seen as the addition of multiple disruptive efforts that require the participation of both business and Information Technology (IT) leaders. The perception of true transformation will not be noticed after many years have gone by and will require some perspective on the journey [22].

While the ongoing DT is disrupting all business and social sectors, it is also true that the level of penetration of the digitalization has varied across industries in terms of reach and implementation [23].

We are currently amid the second wave of DT which is a bit trickier than the first one because it encompasses traditional settings where the physical dimension will always be relevant, and the added value provided by technology must be found when achieving a successful symbiosis between the two worlds. In here, we are talking about a wide scope of industries including transportation, agriculture, or healthcare. All of them are traditional sectors with their own characteristics and dynamics that have started their transition towards digital but at a completely different pace than the first wavers. Within these sectors, the concept of digitally enhanced process or functionality is the predominant [24].

The healthcare sector has been particularly slow in the adoption of digital technologies [25]. In 2015, a study on digital maturity ranked healthcare within the lowest third of industries [26]. Research shows that barriers for the adoption of digital solutions in the healthcare sector are mainly nontechnological and relate to culture, governance, and organizational structures [27–31].

Healthcare is formed by a complex ecosystem of stakeholders with varying preferences and interests [32]. Among the actors conforming the health landscape, physicians are the most influential collective and one of the main sources of resistance to the adoption of health information technology (HIT) [33]. In fact, very little has changed over the years in the way medical doctors are being taught; therefore, physicians are unlikely to be ready to embrace new technological advances [34,35]. Different claims arise against the implementation of HIT such as the attacks to personal autonomy (e.g., are machines going to decide for me?) [36], threats to the classical clinical encounter (e.g., should patient-related information be registered in a computer by administrative staff instead of a physician?) [37–39], aversion to technology and change (e.g., key opinion leaders advocating against HIT) [33,40], security, privacy, and safety issues (e.g., what if the information system is providing wrong health-related information about a certain patient?) [41–44], and being the cause of stress and burnout for professional staff (e.g. physicians reporting stress and burnout due to HIT usage) [45]. Despite all the previous barriers, the main source of physicians' reluctance is the lack of evidence regarding the (cost-) effectiveness of HIT [46,47].

Due to the extensive costs associated with healthcare delivery, health systems are organized as an insurance-based industry [48]. Globally, the overall expenditure in health reaches around 10% of the gross domestic product and, in some developed countries, it is the biggest budget chapter [49,50]. Either public or private, all the stakeholders involved in healthcare provision follow strict governance regulations that ensure the quality of care and the access to services [51–53]. Another barrier towards the adoption of HIT is the complexity and regulatory frameworks that have led to a sector which is characterized by information systems fragmentation, thus hampering interoperability and collaboration among stakeholders [54–56]. Such heterogeneity of proprietary systems is also having a great impact in leveraging the full usage of patient-related data and lowering the adoption of advanced data analytics or artificial intelligence systems [57].

Organizational structures adapt to financing schemes which, in most healthcare systems are old-fashioned, hence do not foster the systematic implementation of HIT [58]. Consequently, health technology infrastructure is lagging behind other industrial sectors and continuously increasing its already deep technical debt [59].

1.2 Justification of research interest

When this Ph.D. project started, many barriers were preventing the implementation at-scale of digital health. But which were the most important? Which of those would greatly improve the adoption if removed? Both questions did not (and still do not) have empirical answers, thus it was important to find a proxy that could serve the purpose of deciding where it would be most useful to put the focus of this thesis.

In year 2016, the American Medical Association (AMA) conducted a survey among its large membership about the motivations and requirements for the systematic adoption of digital health solutions [60]. The results of the study showed the main requirements could be allocated into one of the following four categories:

- Does it work?
- Will I receive payment?
- Will I be liable?
- Will it work in my practice?

From a scientific perspective, these findings were very interesting because the answers to each question can be found in different branches of science as depicted in Table 1.1.

Table 1.1 Relationship in between the requirements categories from the 2016 AMA survey and the branches of science.

Requirement category according to AMA's survey	Rephrased categories by the author	Branch of science
Does it work?	What is the evidence-base?	Health services research: clinical effectiveness
Will I receive payment?	What is the business model?	Health services research: economic models
Will I be liable?	Which is the legal framework?	Health services research: ethics and bioethics
Will it work in my practice?	Which is the implementation strategy?	Health services research: implementation research

The first category relates to the essence of the digital health interventions. Understanding the health-related benefits of those is mandatory and the first requirement before deciding the implementation in routine care [61]. Once the first question has been solved, it is necessary to understand the costs associated with the deployment of such solutions. Some of them can provide relatively small gains in terms of health outcomes but great savings for healthcare systems, while others may provide great health benefits at a cost impossible to afford.

On the other hand, the third and fourth categories could be considered instrumental, and solved throughout laws providing coverage to such practices, proper training and recommendations to professional staff, change management work, and tailored implementation strategies.

While there is a common agreement about the possibilities offered by the technologies of digital transformation to reshape the current healthcare systems, digital health solutions tend to stay in pilot initiatives and not scale-up into routine care [62,63]. Notwithstanding, public and private investors have spent massive amounts into the digitalization of the healthcare sector with the expectation to achieve a substantial impact and return on investment [64,65].

Governments, health systems and health provider organizations struggle on how best to allocate their finite resources. A strategy followed by most has historically been targeting their investments on the areas causing the biggest burdens in terms of health and economic impacts, even though this approach presents different issues [66].

Worldwide, noncommunicable diseases (NCDs) are the main source of mortality for both men and women, and account for 41 million deaths per year, equivalent to 71% of all deaths globally. Most NCDs are of chronic nature and its development is the result of the combination of physiological, genetic, environmental, and behavioral factors.

Cardiovascular diseases (CVDs), cancers, chronic respiratory diseases, and diabetes are amongst the most prevalent NCDs [67]. This group of NCDs are commonly associated with mental disorders such as depression and anxiety disorders, and are known as one of the major contributors to the NCDs burden. Among the mental health conditions, depression is the leading cause of disability worldwide, with 264 million people of all ages impaired by the disease [68].

The prevalence of chronic diseases is rising globally, driven by the combination of a fast growth of ageing populations and a higher prevalence of major risk factors such as the strong presence of unhealthy behaviors (i.e., unhealthy diet, smoking, sedentarism and harmful use of alcohol) and environmental factors (i.e., air pollution, poverty, urban structures and climate change). Populations in low- and middle-income countries are disproportionately affected by NCDs and account for more than 75% of global deaths (31.4 million) and 85% of premature deaths (15 million) yearly [67].

The global economic burden of chronic diseases is posing a major challenge for the sustainability of health and social care systems because of the high direct and indirect costs associated to them. For example, the Centers for Disease Control and Prevention estimated that 90% of the United States healthcare expenditure is linked to the management of chronic conditions and mental health management [69].

Due to the huge impacts in individuals and societies, preventing and controlling chronic diseases is in all policy agendas. The multifaceted nature of the risk factors associated with the development of chronic conditions requires a comprehensive answer involving multiple sectors (e.g.., education, transportation, industry, urban planning, agriculture, health, among others) [70]. Providing an answer to each of the risk factors is not easy because some of them are linked to policies associated with the economic development of certain regions (e.g., the pollution associated to the industrial development of emerging economies), thus very difficult to change.

Providing interventions aimed at prevention and screening, diagnosis, treatment, and long-term care of chronic diseases is a mainstay for improving the quality of life of patients and avoid further expensive treatments [70]. Policymakers, product developers and other stakeholders within the healthcare ecosystems around the world have focused on the design and implementation of digital health solutions that can be integrated into health systems and facilitate the management of chronic diseases.

1.3 Aim and objectives

The main aim of this Ph.D. thesis was to assess the cost-effectiveness of digital health solutions designed to support the management of major chronic conditions that can be implemented within the Catalan health system. To address this aim, three research questions were formulated considering three types of digital tools in three different areas related to major chronic conditions:

1) Research question #1: In adult patients with cardiovascular disease managed in the outpatient setting, would a mHealth-driven intervention for behavioral life-style change increase the patients' quality of life in a cost-effective manner compared with usual care?

We hypothesized was that a mHealth intervention for the prevention and control of cardiovascular diseases would improve the utility of individuals (quality of life) decreasing the cost comparing to usual care.

2) Research question #2: In complex chronic patients managed in an integrated care domiciliary setting, would a telehealth and telecare intervention be cost-effective when compared to usual care?

We hypothesized that the provision of information and communication technology–enhanced integrated care services that encompass health and social care in the setting of domiciliary care would improve health outcomes and reduce health system costs.

3) Research question #3: In adult patients with Major Depressive Disorder managed in the primary care setting, would an Internet-based Cognitive Behavioral Therapy intervention be cost-effective when compared to usual care?

We hypothesized that an Internet-based Cognitive Behavioral Therapy intervention for the treatment of depression would improve the utility of individuals (quality of life) decreasing the cost comparing to usual care.

1.4 Methods

This thesis was conducted within the framework of three European-funded projects managed by the Research and Development Unit from Badalona Serveis Assistencials (Badalona, Spain). Even though each of the projects included an international consortium of partners, for the purpose of this Ph.D. thesis we only considered the results of the Badalona pilot site. Each project aimed to provide an answer to each research question.

Below, a brief description of the three projects, their relationship to the research questions and associated manuscripts is included:

The Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE project)

Start date: 01/03/2015 - **End date:** 28/02/2018

Brief project description and objective: The overarching goal of the Do CHANGE project was to develop, implement and evaluate a digital health ecosystem for integrated disease management of individuals with hypertension (HT), coronary artery disease (CAD) or heart failure (HF) chronic conditions. The work presented in this thesis aimed at assessing the cost-effectiveness of the intervention in the Badalona pilot site.

Manuscript #1:

Piera-Jiménez J, Winters M, Broers E, Valero-Bover D, Habibovic M, Widdershoven JWMG, et al. Changing the Health Behavior of Patients With Cardiovascular Disease Through an Electronic Health Intervention in Three Different Countries: Cost-Effectiveness Study in the Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE) 2 Randomized Cont. J Med Internet Res. 2020;22(7):e17351. PMID: 32720908

Learning from integrated eCare practice and promoting deployment in European regions (BeyondSilos project)

Start date: 01/02/2014 - **End date:** 28/02/2017

Brief project description and objective: The BeyondSilos project proposed an ICT-enhanced integrated care intervention (i.e., telehealth and telecare) aimed to support older Europeans to live independently within their own social environments. The ecosystem proposed by the project also included third sector care providers (i.e., volunteer organizations) to be involved within the provision of care. The work presented in this thesis aimed at assessing the cost-effectiveness of the intervention in the Badalona pilot site.

Manuscript #2:

Piera-Jiménez J, Daugbjerg S, Stafylas P, Meyer I, Müller S, Lewis L, et al. BeyondSilos, a Telehealth-Enhanced Integrated Care Model in the Domiciliary Setting for Older Patients: Observational Prospective Cohort Study for Effectiveness and Cost-Effectiveness Assessments. JMIR Med Informatics. 2020;8(10):e20938.

MAnagement of mental health diSorders Through advancEd technology and seRvices – telehealth for the MIND (MasterMind project)

Start date: 01/03/2014 - **End date:** 28/02/2017

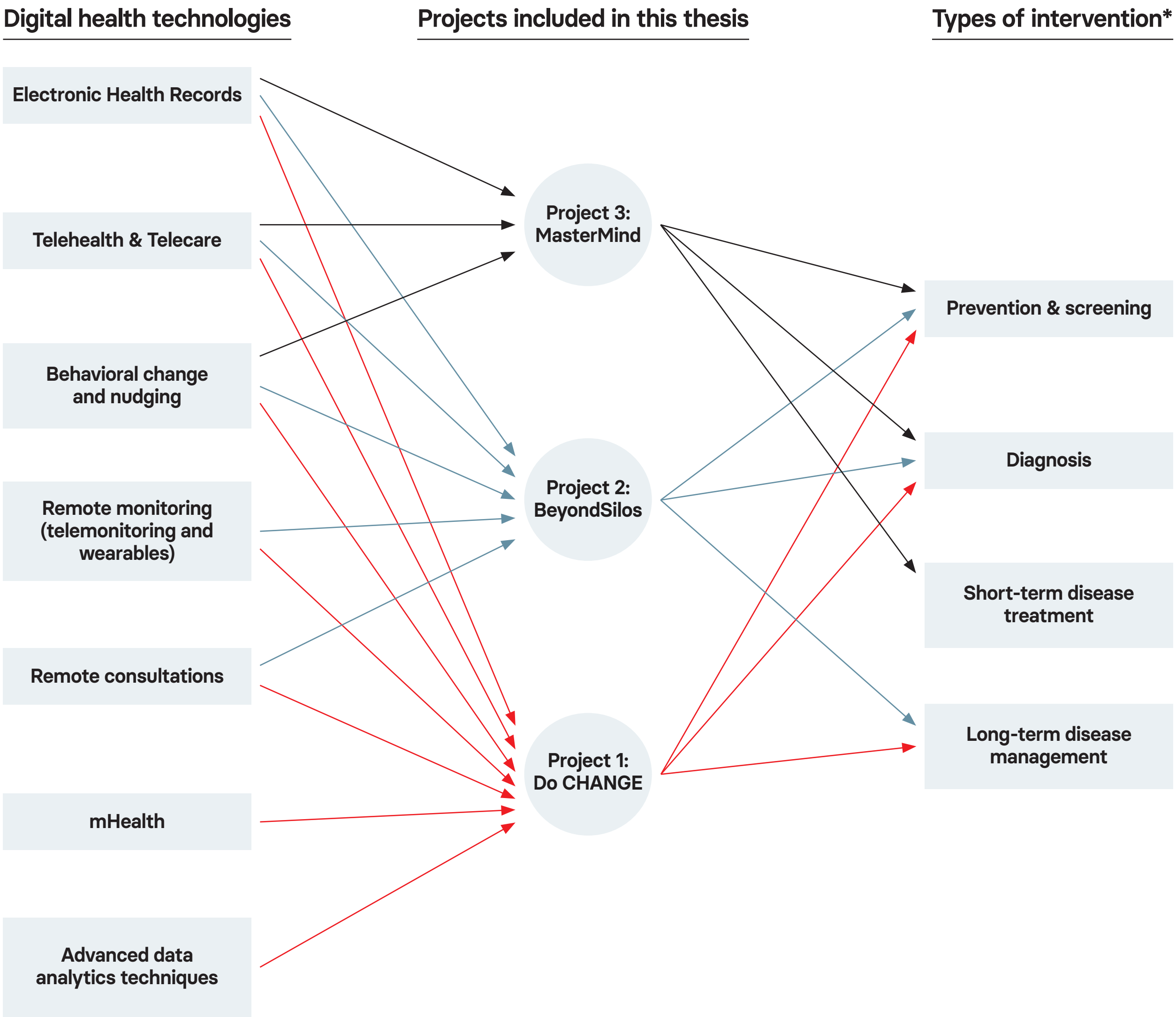
Brief project description and objective: The MasterMind project deployed Internet-based Cognitive Behavioral Therapy (iCBT) services for depression at-scale across 15 regions in Europe and beyond for more than 5,000 patients. The work presented in this thesis aimed at assessing the cost-effectiveness of the implementation of the “Super@ tu depresión” program in the Badalona pilot site.

Manuscript #3:

Piera-Jiménez J, Etzelmueller A, Kolovos S, Folkvord F, Lupiáñez-Villanueva F. Guided Internet-Based Cognitive Behavioral Therapy for Depression: Implementation Cost-Effectiveness Study. J Med Internet Res. Canada; 2021;23(5):e27410. PMID: 33973857

Each Project put in place a different set of digital health technologies that were involved in delivering different types of interventions (Figure 1.1).

Figure 1.1 Relationship in between the different studies forming this thesis, the implemented digital health technologies and the types of intervention delivered.



(*) Working Group on Digital Health. The Promise of Digital Health: Addressing Non-communicable Diseases to Accelerate Universal Health Coverage in Low- and Middle-Income Countries, September 2018.

Overview of the characteristics of each study

Table 1.2 summarizes the key methodological aspects of each study included in this thesis.

Table 1.2 Overview of the characteristics of the three trials included in this thesis

Trial	Do CHANGE	BeyondSilos	MasterMind
Aim	Improving lifestyle by promoting behavioural change	Better controlling patients through an ICT-enabled integrated care intervention	Treatment of depression through psychotherapy
Sample	Patients primarily diagnosed with HT, CAD or HF	Complex chronic patients	Patients diagnosed with depression
Study design	Randomized controlled trial	Quasi-experimental design (cohort study)	Pragmatic
Intervention	mHealth, innovative wearable technology, advanced analytics, telemonitoring solution and real-time nudging	Telemonitoring solution (telehealth and telecare) including domotic devices, health education and real-time alarms	Telemedicine solution delivering Internet-based cognitive behavioral therapy
Ecological context	Intervening on real-time	Intervening on real-time	Passive way of intervening
Outcome measures	- Patient-reported outcomes (behavioral flexibility, lifestyle promoting behavior, quality of life, satisfaction and usability) - Real-time objective measurements (step-count, physical activity, sleep efficency, blood pressure, weight and electrocardiogram)	- Primary outcome measures were related to the health status of study participants (Barthel Index, Instrumental Activities of Daily Living and Geriatric Depression Scale) - Real-time objective measurements (blood pressure, weight and electrocardiogram)	- Reach of the interventions - Perceived acceptability by patients and healthcare professionals of cCBT and ccVC - Perceived appropriateness of cCBT and ccVC to address patients' and healthcare professionals' needs - Implementation costs - Intended sustained use of the interventions in routine practice by the organisation

This section provides an overview of the methodological approach. Each of the manuscripts presented within the next chapters present a detailed description of the methods used.

The Model for ASsessment of Telemedicine applications (MAST) [71] came as an outcome from the MethoTelemed project [72]. It was developed in 2010 by MedCom and the Norwegian Centre for Integrated Care and Telemedicine in association with the University of Stirling & Norwegian Knowledge Centre for the Health Services. MAST framework provides a systematic and multidisciplinary assessment of the effectiveness and contribution to quality of care of integrated telemedicine services.

The overall framework is founded on a broad view and analysis of the factors and areas to consider when introducing and implementing telemedicine in an existing healthcare setting. The assessment of telemedicine solutions is based on the following seven domains: 1) the health problem and characteristics of the application, 2) safety, 3) clinical effectiveness, 4) patient perspectives, 5) economic aspects, 6) organizational aspects, 7) socio-cultural and ethical aspects and legal aspects.

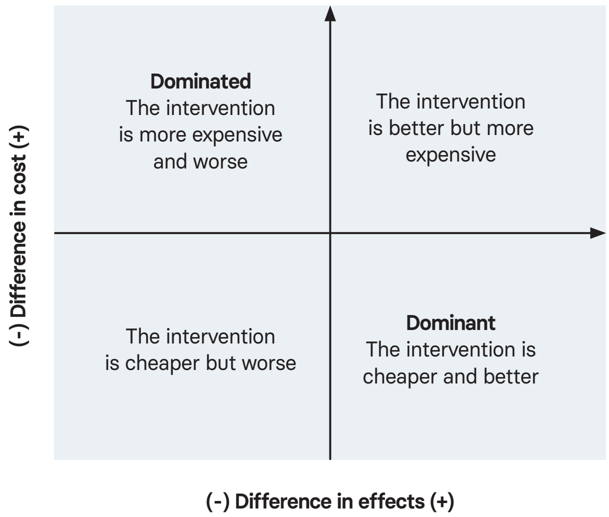
The framework has three dimensions: 1) the value network, 2) the assessment domains, and 3) the use-cases corresponding to the new digital health intervention. The value network includes all the stakeholders around the new solution for whom some assessment domains are applicable at different stage. Different actors have different goals and perspectives; therefore, for each combination of stakeholder and domain a set of indicators needs to be defined. Finally, the third dimension allows to define different use-cases for different patient profiles, implying a different usage of the technological solutions proposed by the new technology. Consequently, not all indicators are necessarily relevant for assessing all use-cases. The overall idea is to provide a comprehensive evaluation covering all possible perspectives.

The model was first used and consequently validated by the 9 large scale pilots participating in the RENEWING HEALTH project and, since then, it has been used in many other EU funded initiatives, such as the SmartCare and the CareWell projects. Later, the MAST framework was subjected to some modifications to be adapted to the Ambient Assisted Living reality in the ReAAL project. MAST was also the evaluation framework used to design the assessment strategies and the data collection for the three projects used as a basis to develop this Ph.D. thesis.

Health Technology Assessment (HTA) is a process for assessing the clinical, social, and economic impacts of health technologies. Within that context, the term health technology must be understood broadly and can include medicinal products, public health programs, procedures and pathways or devices [73]. HTA considers aspects such as efficiency, effectiveness, safety, cost-effectiveness, among others [74]. HTA's main objective is to support health policy and decision makers in coherent and rational decision-making for technologic incorporation in health and social care systems [75].

Among the different modelling techniques used in HTA, Decision Analytic Modelling has gained attention to compile the costs, outcomes and cost-effectiveness of health interventions and programs when compared to standard care [76]. The cost-effectiveness of an intervention can be estimated based on the relationship of three core elements: 1) the clinical and economic outputs of a given intervention, 2) the costs of the intervention (including savings and expenses in front of the alternative), and 3) the payer's willingness-to-pay threshold. Owing to its visual nature, the cost-effectiveness plane provides a straightforward way to interpret the results of a cost-effectiveness analysis (Figure 1.2).

Figure 1.2 The cost-effectiveness plane.



The standard of care is on the center of the cost-effectiveness plane. The intervention under study will occupy different positions in the graph depending on the health outcomes and costs when compared to standard care. Interventions that fall into the dominant quadrant will always be accepted whereas the ones falling into the dominated quadrant will never be accepted. For interventions falling within the two other quadrants, the decision will be made according to the cost-effectiveness (CE) ratio and the willingness-to-pay (WTP) threshold (see below).

The cost-effectiveness ratio is calculated by:

$$\textbf{CE ratio} = \frac{Cost\_new - Cost\_reference}{Effects\_new - Effects\_reference}$$

The WTP threshold represents the amount a certain individual or health system is willing to pay for the health gains. Even though decision around this may be controversial and are linked to the wealth of the region where those evaluations are taking place, most local HTA authorities have defined a range of acceptable thresholds. Therefore, interventions falling outside the dominated and dominant quadrants will be accepted when they CE ratio is positioned below the WTP threshold.

Among the different types of cost-effectiveness studies, cost-utility studies are the most prevalent when introducing new technologies within the health care sector. Cost-utility studies calculate the health effects of a certain intervention by measuring the individual preference for different health states, such as quality-adjusted life-years (QALY).

The cost-effectiveness of the three interventions conforming this Ph.D. thesis were calculated using the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) [77]. MAFEIP was designed to help assessing the different innovations developed under the European Innovation Partnership on Active and Healthy Ageing. It is a web-based tool implementing the principles of DAM through a classical Markov model commonly used in economic evaluations of healthcare interventions.

1.5 Thesis outline

Each research question is answered in a separate chapter in this thesis. Chapter 2 investigates the cost-effectiveness of an advanced mHealth intervention for behavioral change (the Do CHANGE project). A detailed description of the results of a telehealth and telecare integrated care intervention can be found in Chapter 3 (the BeyondSilos project). In Chapter 4 we investigate the outcomes of the implementation of an Internet-based Cognitive Behavioral Therapy (the MasterMind project). The answers to the research questions can be found in Chapter 5, which also includes the recommendations for further research. Finally, Appendix I includes all the different scholar contributions performed during the same development period of this Ph.D. thesis.

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2. MANUSCRIPT #1

ORIGINAL PAPER

Changing the Health Behavior of Patients With Cardiovascular Disease Through an Electronic Health Intervention in Three Different Countries: Cost-Effectiveness Study in the Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE) 2 Randomized Controlled Trial

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Abstract

Background: During the last few decades, preventing the development of cardiovascular disease has become a mainstay for reducing cardiovascular morbidity and mortality. It has been suggested that interventions should focus more on committed approaches of self-care, such as electronic health techniques.

Objective: This study aimed to provide evidence to understand the financial consequences of implementing the "Do Cardiac Health: Advanced New Generation Ecosystem" (Do CHANGE 2) intervention, which was evaluated in a multisite randomized controlled trial to change the health behavior of patients with cardiovascular disease.

Methods: The cost-effectiveness analysis of the Do CHANGE 2 intervention was performed with the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing tool, based on a Markov model of five health states. The following two types of costs were considered for both study groups: (1) health care costs (ie, costs associated with the time spent by health care professionals on service provision, including consultations, and associated unplanned hospitalizations, etc) and (2) societal costs (ie, costs attributed to the time spent by patients and informal caregivers on care activities).

Results: The Do CHANGE 2 intervention was less costly in Spain (incremental cost was –€2514.90) and more costly in the Netherlands and Taiwan (incremental costs were €1373.59 and €1062.54, respectively). Compared with treatment as usual, the effectiveness of the Do CHANGE 2 program in terms of an increase in quality-adjusted life-year gains was slightly higher in the Netherlands and lower in Spain and Taiwan.

Conclusions: In general, we found that the incremental cost-effectiveness ratio strongly varied depending on the country where the intervention was applied. The Do CHANGE 2 intervention showed a positive cost-effectiveness ratio only when implemented in Spain, indicating that it saved financial costs in relation to the effect of the intervention.

Trial Registration: ClinicalTrials.gov NCT03178305; https://clinicaltrials.gov/ct2/show/NCT03178305
(J Med Internet Res 2020;22(7) :e17351) doi: 10.2196/17351

KEYWORDS
Cost-effectiveness; randomized controlled trial; RCT; eHealth; cardiovascular disease; engagement; behavior change; digital health.

Introduction

Background

In the last few decades, prevention at both population and individual levels in patients with established cardiovascular disease (CVD) has become a mainstay for reducing cardiovascular morbidity and mortality [1]. However, CVD remains the leading cause of death globally [2].

One of the cornerstones of CVD prevention is the promotion of lifestyle changes, including physical activity, a healthy diet, and avoidance of unhealthy behaviors such as smoking and drinking alcohol [1]. However, providing patients with relevant information regarding the importance of lifestyle habits seems to be insufficient to prompt these changes and maintain them over time [3]. Instead, it has been suggested that the preventive paradigm should shift from passive to more committed approaches of self-care based on the following three core elements: self-care maintenance, self-care monitoring, and self-care management [4-6].

The emergence of solutions based on information and communication technologies (ICTs), such as telemedicine, has greatly contributed to filling some of the gaps of effective self-care. One of the most classical ICT solutions has been the use of self-monitoring devices in patients with high cardiovascular risk to facilitate successful blood pressure (BP) control [7]. The expansion of mobile apps and their peripheral devices has raised the number of ICT-based interventions aimed at improving not only self-monitoring but also behavior changes in various patient profiles, including older people with high cardiovascular risk [8-10]. The emergence of lifestyle data-driven apps illustrates the increasing interest in this approach in various health care areas [11].

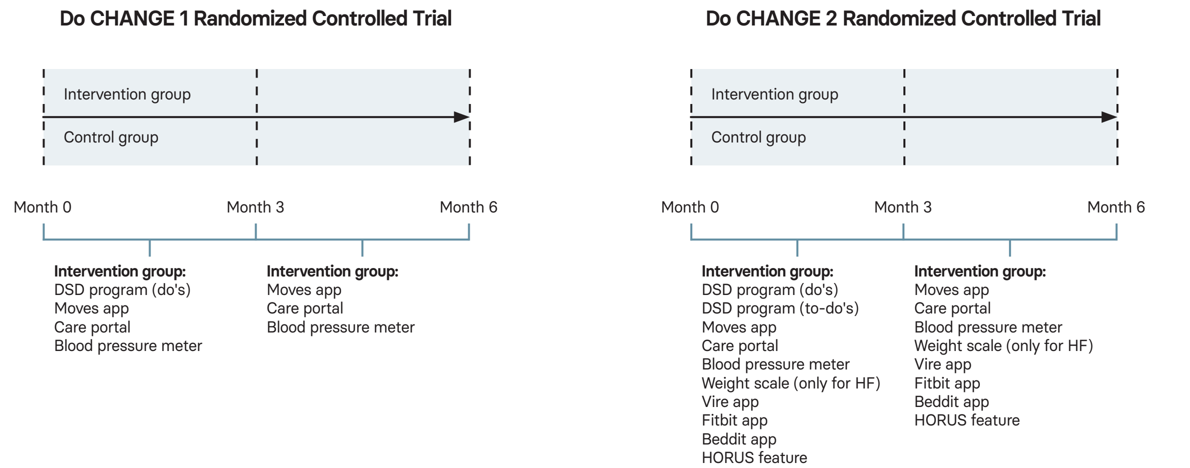
To date, evidence regarding the efficacy of these interventions is still evolving. Clinical guidelines for the prevention of CVD highlight that cost-effectiveness data from randomized controlled trials (RCTs) are scarce, and most data regarding the cost-effectiveness of cardiovascular prevention strategies combine clinical evidence with simulation approaches [1,12,13]. Simulation modeling is currently used to address important issues in clinical practice and health policy that have been very difficult to study within high-quality clinical trials but provide necessary insights for making health care decisions. Nonetheless, assumptions and personal choices are required to conduct simulation modeling, leading to potentially biased outcomes. Transparency in decision-making is therefore critical to adequately understand the observed outcome [14]. In this regard, there is a need for providing the various stakeholders, particularly policy makers, with evidence from nonsimulated research trials to understand the financial consequences of scaling up ICT solutions for health care systems [15]. In this study, we aimed to determine whether the Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE) 2 preventive intervention is a cost-effective alternative for patients with CVD in Spain, the Netherlands, and Taiwan.

The Do CHANGE Project

The Do CHANGE program was developed as an ICT-based alternative for providing health education, which leads to behavioral changes in care recipients [16,17]. The Do CHANGE program consists of a 6-month intervention with a set of devices that include self-monitoring tools and the Do Something Different (DSD) behavior change program (only available during the first 3 months of the intervention), which has been shown to be effective in changing health behaviors in previous studies targeting different populations [18]. The Do CHANGE program included the following two phases: Do CHANGE 1 and Do CHANGE 2, which were assessed in two consecutive RCTs (Figure 1).

Patients included in the Do CHANGE 1 study received the DSD behavior change program, which was provided via text messages on patients' mobile phones. Behavioral flexibility is associated with a broad range of behavioral repertoires, making people more open to experience and adopt new behaviors [19]. This is achieved by disrupting patients' daily behavioral routines for a short period (eg, a few seconds) with behavioral prompts (referred to as "do's") delivered through patients' mobile phones. These messages challenge patients to do something different and get out of their comfort zone. Do's have been developed by a multidisciplinary team including cardiologists and psychologists, ensuring that they apply to the target population and are thus related to daily behaviors or needs. Patients received a total of 32 do's during the 3-month intervention period (2-3 do's per week). The program was tailored to the cardiac population with slight differences in the program depending on patients' primary diagnosis (coronary artery disease, heart failure, and hypertension), as the preferred health behaviors may vary depending on the diagnosis [20]. In order to obtain objective measures on patients' physical functioning, all participants received a BP monitor, the Moves app (Facebook Inc; to register GPS location), and the Careportal (Docobo Ltd, home monitoring device measuring daily symptoms and an electrocardiogram).

Figure 1. Do CHANGE 1 and 2 randomized controlled trial design including intervention details. Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem; DSD: Do Something Different; HF: heart failure.



The main additional features of the Do CHANGE 2 compared with the Do CHANGE 1 trial were the greater number of devices for self-monitoring and collecting behavioral information, and the capacity of the DSD program to tailor the behavioral prompts to the actual behavior of the care recipient, thus allowing for a personalized approach. Do CHANGE 2 integrates the principle of theory-driven behavioral change techniques, which can guide behavior change, within the offered interventions [21]. As a natural evolution from the Do CHANGE 1 trial, the second phase aimed to increase the ability of a person to express behavior in a more context-dependent way [22], thus being more open to experience and increasing the likelihood of adopting new behaviors [19].

Care recipients perceived the Do CHANGE 1 program as helpful and easy to use; however, it failed to prompt relevant lifestyle changes (measured with the Health Promotion Lifestyle Profile-II questionnaire) compared with treatment as usual (TAU) [20]. The Do CHANGE 2, based on a more personalized approach, resulted in a relevant change in lifestyle behavior over time in the intervention group. In addition, the intervention was perceived as useful and feasible by patients and health care professionals [23]. In order to provide a broader perspective of the effects of this program, we present herein the results of the cost-effectiveness analysis of the Do CHANGE 2 compared with TAU.

Methods

Trial Design and Patients

This was a multisite RCT to assess the cost-effectiveness of an ICT-based program to change behavior in patients with CVD compared with TAU. Local clinical specialists and research assistants recruited adult patients treated in the following three hospitals in three different countries: *Badalona Serveis Assistencials* (Spain), *Elisabeth TweeSteden Ziekenhuis* (the Netherlands), and *Buddhist Tzu-Chi Dalin General Hospital* (Taiwan). The planned sample size based on the available project resources was 75 patients for Spain, 75 for the Netherlands, and 100 for Taiwan. Once accepted to participate in the study, patients at each study site were randomized to receive either the TAU or the Do CHANGE 2 intervention. The primary outcomes were lifestyle change and quality of life. Additionally, behavioral flexibility was considered a mediator variable in this relationship. As the project aimed to provide proof of concept and examine the feasibility of the intervention, no sample size calculation was performed a priori. Recruiting a comparable number of patients across the countries was considered relevant to provide proof of concept. The details regarding the study patients and trial design are described in the report by Habivovic et al [16].

The most remarkable changes from the original study protocol (Do CHANGE 1) were the changes in the DSD program (moving from predefined messages according to the patient psychological profile to nudges tailored according to their behavior as gathered by the measurement devices), the addition of two new wearable devices (Beddit [Apple] and Fitbit [Fitbit Inc]), and the Vire app (Do CHANGE app). Considering the importance of weight in heart failure (HF), patients with this diagnosis also received a weight scale.

Inclusion Criteria

Participants were screened from adult patients (aged 18-75 years) who had been primarily diagnosed with either hypertension (ie, systolic BP [SBP]/diastolic BP [DBP] r140/90 mmHg in two consecutive measurements), coronary artery disease (ie, occurrence of myocardial infarction or angina pectoris, or previous percutaneous coronary intervention and/or coronary artery bypass graft surgery), or symptomatic HF (ie, New York Heart Association class I-IV). Patients also had to have two or more of the following risk factors: increased cholesterol, smoking, diabetes, sedentary lifestyle, and psychosocial risk factors. The presence or absence of each of the risk factors was assessed following the local guidelines in each participant country. For HF patients, additional inclusion criteria were a diagnosis of systolic or diastolic HF and the presence of HF symptoms (eg, exhaustion, shortness of breath, and chest pain). Other general inclusion criteria were an adequate level of the native language, access to the internet at home, having a smartphone compatible with the apps used in the study, and having the skills necessary to use a personal computer and a smartphone.

Exclusion Criteria

Patients with life expectancy less than 1 year, life-threatening comorbidities, a history of psychiatric diseases other than anxiety and depression, and relevant cognitive impairments and those on the waiting list for heart transplantation were excluded from the study.

The reasoning for establishing the exclusion criteria was to prevent the inclusion of patients whose disease severity may critically increase during the intervention. These patients may perceive participation as an extra burden, are more likely to drop out due to illness-related complaints or early mortality, and may be less likely to benefit from a lifestyle intervention owing to severe comorbidities. Patients with mental illness were also excluded because the intervention might become stressful and trigger symptoms in these patients. The selected exclusion criteria are in line with the DO CHANGE 1 trial, safeguarding that the study is not perceived as a burden and meets patients' needs as much as possible.

Intervention

The Do CHANGE 2 program implemented in this trial was similar to that described by Broers et al for Do CHANGE 1 [20]. Patients randomized to the intervention group received devices for measuring key clinical parameters needed for monitoring their CVD, such as a BP monitor, weight scale (in HF patients only), and the Careportal, which allowed monitoring of daily symptoms and an electrocardiogram. The patient's location was monitored by the Moves app. In addition to the aforementioned ICT solutions (also used in the Do CHANGE 1 program), the Do CHANGE 2 program included the Vire app, a purpose-designed app to integrate the input from all the monitoring devices, so that the patient could interact with a unique easy-to-use source of information. The app integrates the information coming from the following apps: the Beddit app (provided with the device under the mattress cover sheet) aimed at monitoring sleep efficiency, the Fitbit app (with the wristband) aimed at measuring physical activity through step count, and the HORUS feature embedded in and aimed at collecting pictures of the different meals of the patients in order to provide diet recommendations. Study participants in the Do CHANGE 2 intervention group were also provided with leaflets (Multimedia Appendix 1) and multimedia resources explaining the use of the Do CHANGE environment.

Like in the Do CHANGE 1 program, patients in the intervention group received a 3-month behavior change program. The program was based on providing care recipients with short messages aimed at disturbing daily routines. Messages were delivered through their mobile phones and suggested them to "do something different." However, unlike the Do CHANGE 1 program, in the Do CHANGE 2 program, behavioral nudges were not only predefined according to the patient's personality profile but also tailored to the patient's behavior, as recorded by the monitoring devices. These behavior-driven messages called to-do's were delivered to the patients based on their current functioning. Patients receive their do's and to-do's through the Careportal or the Vire app, or via SMS, depending on patients' preferences [16].

The GPS data from the Moves app and activity data from the Fitbit device were used to calculate higher abstraction scores called *activity, variety,* and *social opportunities.* The to-do's were tailored based on the trends of these scores over time (eg, a patient with declining activity would receive a message that focuses on increasing activity). The granularity of this system is not restricted to one score; alternatively, new scores are calculated for each update of data, and the system determines whether the score is a "target" for a message. Multiple combinations of targets are possible; therefore, a to-do can tackle both variety and social opportunities if needed based on the scores. A detailed description of the construction process of to-do's can be found in previously published work [23,24].

Besides receiving personalized prompts (eg, based on activity levels), patients were contacted each week by the research assistant to check how everything was going and to provide dietary coaching. This might have greatly contributed to the high adherence rate during the first 3 months, as they received personalized feedback. After this period, patients were not contacted in person anymore; however, they were allowed to keep all the devices (eg, Fitbit, Beddit, etc) in order to monitor their behavior for the remaining 3 months.

Cost-Effectiveness Analysis

The cost-effectiveness analysis of the Do CHANGE 2 RCT was conducted using the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) tool [25]. The MAFEIP tool performs a cost-utility analysis through a web app that analyzes incremental costs and effects. The cost-effectiveness estimates are based on the principles of decision analytic modeling and Markov models that assess the impacts that health-related innovations have in terms of health outcomes and resource usage. For Do CHANGE 2, we parametrized the tool on a Markov model of five health states from the perspective of the three service providers (Figure 2) [26].

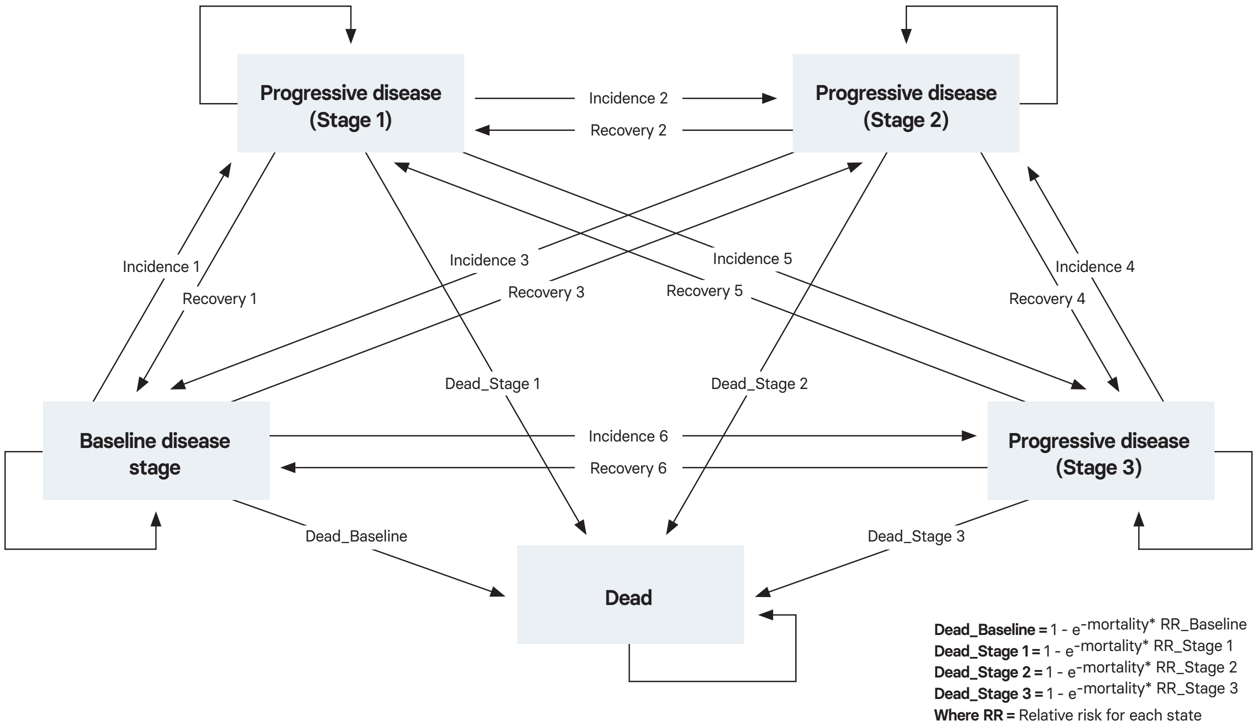


Figure 2. Markov model of five health states applied for the Do CHANGE cost-effectiveness analysis. Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.

The MAFEIP tool requires the user to provide the following three main types of inputs: (1) the health states and the corresponding transition probabilities between them, (2) the costs, and (3) the utility, for which the EuroQol five-dimension three-level (EQ-5D-3L) questionnaire was used as recommended by the National Institute for Health and Care Excellence [27].

In order to estimate the incremental health gain from a particular intervention delivered, the defined model needs to be run twice. Once with parameter estimates for the respective intervention under assessment (ie, Do CHANGE 2), and once with parameters corresponding to the standard care scenario (ie, TAU). In the model, these two scenarios may differ in terms of transition probabilities (disease incidence, recovery, and mortality), as well as the utility weight and health care and societal costs related to the health states. When the model simulates a hypothetical cohort of patients moving between these health states over time, the differences in survival, utility, and cost accumulate until reaching an estimate of the incremental costs (C) and health effects (E) that can be expected from the intervention under evaluation. Therefore, the tool can be used to estimate the incremental cost-effectiveness ratio (ICER= C/ E) or the incremental net monetary benefit (E×λ– C) of one intervention compared with another, where is defined as the willingness-to-pay (WTP) threshold for an additional unit of health gain.

Besides the transition probabilities among health states, the utility, and the cost, the tool allows the user to include the relative risks for mortality, the discount rates, and the time horizon for the analysis (cycle length). The parameters included in this analysis and their assessments during the study are explained in detail below.

Definition of Health States

The first stage in the construction of a Markov model is defining the different states of the disease in relation to the important clinical and economical effects of the disease. Evidence suggests that high BP is the predominant risk factor for CVD [28]. Following the scientific evidence and for the purpose of the Do CHANGE assessment, the health states were established based on SBP and DBP, according to the classification of the American Heart Association [29] as follows: baseline disease stage (SBP <120 mmHg and DBP <80 mmHg), progressive disease stage 1 (SBP 120-129 mmHg and DBP <80 mmHg), progressive disease stage 2 (SBP 130-139 mmHg or DBP 80-89 mmHg), progressive disease stage 3 (SBP r140 mmHg or DBP r90 mmHg), and death. On a side note, the latest stage was not included, as it is considered to be a hypertensive crisis (SBP >180). The transition probabilities were calculated based on the changes between the initial health states (at baseline) and those at 3 months. These transitions can be of incidence (ie, the annual probability for an individual to move from baseline to eachprogressive stage of the disease) and recovery (ie, the annual probability of improving).

Cost Estimate

The following two types of costs were considered for both study groups: (1) health care costs (ie, costs associated with the time spent by health care professionals on service provision, including consultations, unplanned hospitalizations, etc) and (2) societal costs (ie, costs associated with the time spent by patients and informal caregivers on care activities).

The data collected by the research team in each country were provided in local currency units (Euro for both Spain and the Netherlands and New Taiwan Dollars for Taiwan). Taiwan prices were converted into a common basis of 2018 Euros using simple exchange rate conversion factors, reflecting the average market exchange rate between New Taiwan Dollars and Euros during the year in question (NT $1=€0.02862). A currency exchange rate of €1=US $1.12 is applicable (average exchange rate for 2018).

For computing the time spent by health care professionals, we considered an average duration of 15 minutes and 25 minutes for a visit to a general practitioner and specialist, respectively. The personnel cost was established based on the average cost for one full-time employee, including employer contributions to social security. The average hourly costs were €29.23 (Spain), €59 (the Netherlands), and €16.88 (Taiwan) for a general practitioner; €20.79 (Spain), €40 (the Netherlands), and €6.33 (Taiwan) for a nurse; and €34.81 (Spain), €113.50 (the Netherlands), and €84.91 (Taiwan) for a specialist. The estimations of cost per bed-day for hospitalizations were €733.56 (Spain) and €1853.57 (the Netherlands), which were obtained by dividing the expenditure for inpatient curative care in hospitals by hospital bed-days for services of curative care (both publicly available) [30]. The corresponding costs for Taiwan were calculated by dividing the average expenses of hospitalization by the number of hospital days, which was €342.50 [31].

Societal costs differed according to the study group. For patients allocated to the control group, we considered the extra travel time spent by patients and caregivers in usual care compared with Do CHANGE 2, whereas for those allocated to the intervention group, we considered the time spent by patients using the service.

Additionally, for patients in the Do CHANGE group, the following costs were added: time spent by professionals in service development and training (4 hours per professional, divided by the number of randomized subjects), time spent by nurses in training patients (30 minutes per participant) and installing the Do CHANGE service ecosystem (45 minutes per patient), and the cost of the devices (including taxes). Data are provided in Euro (2018).

Utility Calculation

Utility was estimated using the EQ-5D-3L tool [32]. The EQ-5D is a standardized questionnaire-based measure of self-rated health-related quality of life developed by the EuroQol Group to provide a simple and generic measure widely used for both clinical and economic appraisals. In the case of the Do CHANGE 2 project, we used the EQ-5D-3L version, which was administered at baseline and at 3 and 6 months.

The resulting scores of the questionnaire were weighted using the trade-off method previously described for Spain [33], the Netherlands [34], and Taiwan [35]. The EQ-5D health states, defined by the EQ-5D descriptive system, were subsequently converted into a single summary index by applying specific weights to each of the levels in each dimension of quality of life. The index was calculated by deducting the appropriate weights from 1, which was the value assigned to full health. In the case of the cost-effectiveness analysis of the Do CHANGE intervention, our interest was to measure the change over time, rather than the absolute values. Therefore, we calculated the changes in utility for each of the five health states and for each of the study conditions and added a common initial measure for the whole sample to each of them. The MAFEIP requires EQ-5D utility scores combined with time indicators to compute quality-adjusted life-years (QALYs) automatically.

Relative Risks of Mortality, Discount Rates, and Time Horizon

The MAFEIP tool allows mortality rates to be internally calculated by using the all-cause mortality rates (age- and sex-dependent) extracted from the Human Mortality Database. The relative risk of mortality is a measure that estimates the mortality in a specific population (eg, people who participated in the Do CHANGE 2 study) compared with (ie, divided by) the mortality in a reference population or condition (in this case, from the Human Mortality Database). The reference condition considers CVD mortality for the population of the specified country (ie, Spain, the Netherlands, and Taiwan).

The discount factors for costs and effects are used to estimate outcomes while taking into account the future costs and health effects, that is, adjusting for differences in the timing of costs (expenditure) compared with health benefits (outcomes). Therefore, adequately applied discount factors express future costs or benefits at today's equivalent value. In Do CHANGE 2, we followed the recommendations from the Health Technology Assessment authorities in each country [36-40]. The discount factors for costs and health outcomes applied in Do CHANGE 2 were 3% for both costs and health outcomes in Taiwan and Spain, and 4% for costs and 1.5% for health factors in the Netherlands.

Finally, the MAFEIP framework allows specifying the number of cycles that the model will run, which represents the timeframe in which the impact of the intervention will be evaluated. Markov models are used to simulate both short-term and long-term processes (ie, CVDs) [41]. In the case of Do CHANGE 2, we wanted to see estimates of the incremental costs (and effects) of the intervention in a time horizon of 5 years. The cycle length we selected is not in line with CVD's etiology (ie, a long disease development process) [41] but considers the nature of the intervention and the maximum time frame it can be sustained in light of the deprecation of the wearable and medical device technology that was used.

WTP Threshold

The balance between the economic benefit and clinical effectiveness varies and is entirely dependent on the relationship between the ICER and the threshold value the society is willing to pay at a specific point of time, which is known as the WTP threshold. The fact that WTP thresholds can be specified after the ICER is calculated raises concerns about researchers selecting WTP thresholds that suit their hypothesis, hence compensating for technology of relatively lower value [42].

While there is an agreement about CVDs being preventable to a certain extent, there has also been a discussion as to whether prevention interventions offer good value for money. Previous research has shown a positive relation between lower lifetime risk for CVD mortality and increased survival and quality of life [43]. Prevention strategies can bring relevant benefits at lower costs relative to most treatment options provided that their cost-effectiveness value is almost always below the accepted societal WTP [44].

For the Do CHANGE 2, we selected a WTP threshold of €15,000/QALY for the three countries, not corresponding to the value recommended by local Health Technology Assessment guidelines. The WTP threshold is lower in all cases. We set a lower WTP threshold in order to avoid the concerns mentioned above and to fit the results of the technology, and considering comparisons with other preventive interventions.

Data Collection and Analysis

The questionnaires, as defined in the study protocol, were loaded into the web tool LimeSurvey [45] and collected by local research assistants. Data from the medical devices (built-in electrocardiogram monitor, blood pressure meter, and weight scale) were collected through the Careportal. The data generated by the wearable devices (Fitbit and Beddit) were continuously monitored and integrated through the Vire app. Information regarding resource consumption (eg, hospitalization costs) was collected by local research assistants from the local electronic medical records.

IBM SPSS Statistics for Windows Version 21.0 (IBM Corp) was used to perform the statistical analyses of the effectiveness study, and R (R Core Team 2018) and RStudio (RStudio Team 2016) were used to calculate the transition probabilities and utilities. We used the MAFEIP tool to perform the cost-effectiveness analysis.

Results

Study Participants

Figure 3 shows the overall flow chart of participant recruitment in the Do CHANGE 2 project. Of the 4540 patients assessed for eligibility at all three sites, 238 were enrolled in the study (120 in the intervention group [Do CHANGE] and 118 in the control group).

Owing to relevant differences in patient recruitment strategies between sites, most patients screened in Spain and the Netherlands agreed to participate, whereas many patients in Taiwan refused to participate. Based on retrospective investigation, it appeared that all inclusion criteria in Taiwan were checked after the patients were approached for participation. Hence, the number of patients that were approached appeared to be much higher. In Spain and the Netherlands, patients who fulfilled the basic inclusion criteria were offered to participate. If the same strategy was applied in Taiwan, the refusal rate would have been much lower. Both Spain and the Netherlands met the target number of participants as defined in the project plan, whereas Taiwan did not reach the planned number of participants.

Eighteen patients dropped out before the end of the 6-month follow-up, demonstrating a very high adherence rate. Owing to the personalized nature of the intervention (eg, relevant behavioral prompts and personalized feedback), we expected the adherence to be high. We believe that the nature of the 3-month intervention, where blended and personalized care was provided, combined with the monitoring devices after that period contributed to the high adherence. Patients were engaged in their health management, and therefore, they might be more willing to proceed with monitoring.

Of the 114 participants who were in the program for at least 3 months, 72 (60%) claimed to have carried out all the nudges provided by the DSD and 86 (72%) reckoned the program was useful. Reasons for not adhering to the program were mainly having no time (8/84, 6.7%), not feeling like it (2/84, 1.7%), and falling ill (2/84, 1.7%). One of the participants who quit the program disclosed that being confronted with the illness on a daily basis became too stressful. Moreover, in some cases, the confrontation for some partners to deal with the illness of their husband or wife caused anxiety.

Table 1 summarizes the main demographic characteristics of the three participating countries. None of the variables collected showed relevant systematic differences between study conditions at baseline, except for Spain, with participants in the Do CHANGE 2 group being younger (Do CHANGE 2 group vs TAU group: mean 53.8 years, SD 15.8 years vs mean 67.4 years, SD 7.5 years), having a higher education (mean 14.5 years, SD 6.3 years vs mean 9.1 years, SD 5.5 years), and showing a higher employed proportion (17/37, 45.9% vs 4/37, 10.8%). Multimedia Appendix 2 presents the clinical characteristics of the study sample, medication, and psychological symptoms. The only significant difference at baseline was observed in psychotropic medication for participants in the TAU group in Spain (P=.03), which is consistent with the population in the control group being older.

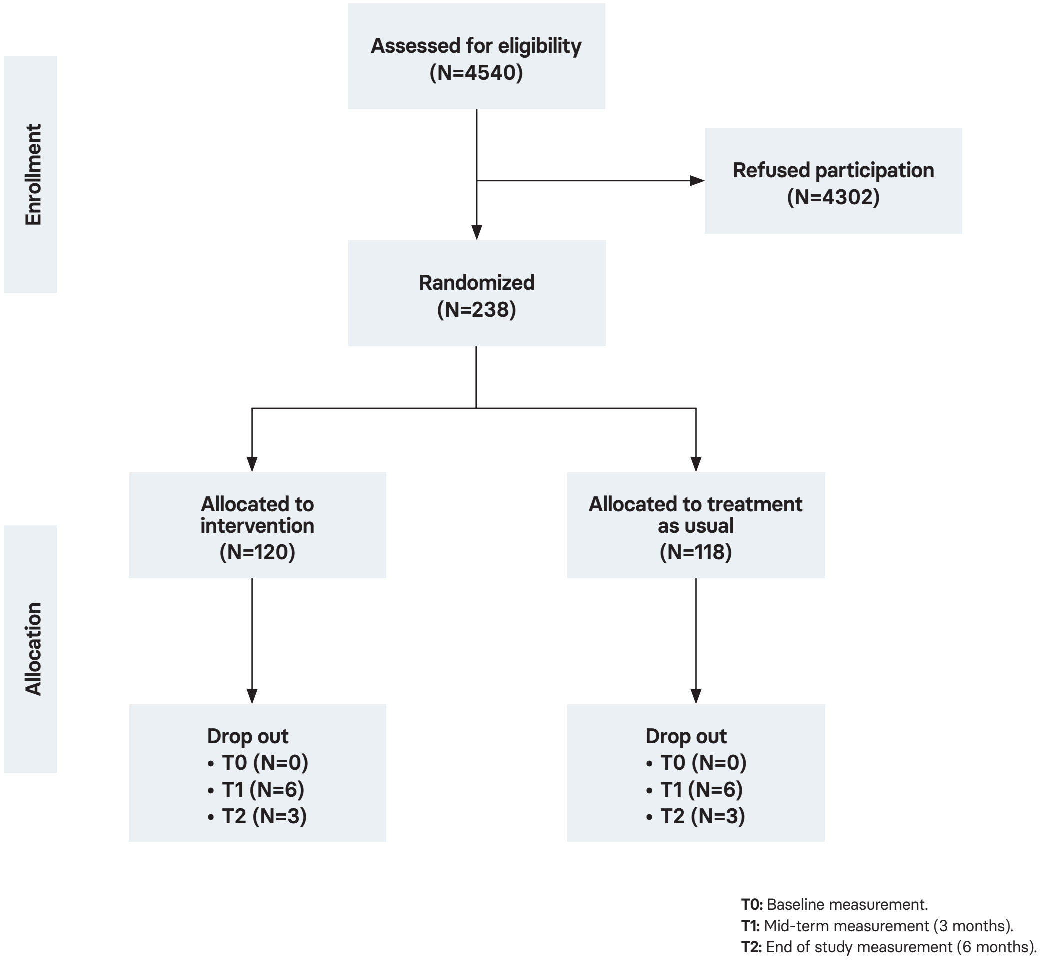


Figure 3. Flow chart of participant recruitment (aggregated numbers for Spain, the Netherlands, and Taiwan).

Table 1. Demographic baseline characteristics of the total sample (N=238).

Characteristic	Spain (N=75)	The Netherlands (N=75)	Taiwan (N=88)	Total (N=238)
Sample size, n (%)				
Do CHANGE[a] 2	38 (50.7)	38 (50.7)	44 (50.0)	120 (50.4)
TAU[b]	37 (49.3)	37 (49.3)	44 (50.0)	118 (49.6)
Total	75 (100.0)	75 (100.0)	88 (100.0)	238 (100.0)
Age (years), mean (SD)				
Do CHANGE 2	53.8 (15.8)	63.0 (9.2)	58.2 (9.9)	58.3 (12.3)
TAU	67.4 (7.5)	63.9 (7.4)	56.7 (9.1)	62.3 (9.2)
Total	60.5 (14.1)	63.4 (8.3)	57.5 (9.5)	60.3 (11.1)
Gender (male), n (%)				
Do CHANGE 2	27 (71.1)	32 (84.2)	30 (68.2)	89 (74.2)
TAU	19 (51.4)	29 (78.4)	38 (86.4)	86 (72.9)
Total	46 (61.3)	61 (81.3)	68 (77.3)	175 (73.5)
Education (years), mean (SD)				
Do CHANGE 2	14.5 (6.3)	12.9 (5.1)	14.9 (5.5)	14.1 (5.7)
TAU	9.1 (5.5)	13.16 (7.9)	16.4 (5.0)	13.1 (6.9)
Total	11.8 (6.5)	13.0 (6.6)	15.7 (5.3)	13.6 (6.3)
Marital status (partner), n (%)				
Do CHANGE 2	27 (71.1)	34 (89.5)	39 (88.6)	100 (83.3)
TAU	27 (73.0)	33 (89.2)	42 (95.5)	102 (86.4)
Total	54 (72.0)	67 (89.3)	81 (92.0)	202 (84.9)
Working status (paid job), n (%)				
Do CHANGE 2	17 (45.9)	13 (34.2)	26 (59.1)	56 (46.7)
TAU	4 (10.8)	16 (43.2)	28 (63.6)	48 (40.7)
Total	21 (28.0)	29 (38.7)	54 (61.4)	104 (43.7)
Smoking (yes), n (%)				
Do CHANGE 2	7 (18.4)	3 (7.9)	2 (4.5)	12 (10.0)
TAU	5 (13.5)	7 (18.9)	4 (9.1)	16 (13.6)
Total	12 (16.0)	10 (13.3)	6 (6.8)	28 (11.8)

[a]Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.
[b]TAU: Treatment as usual.

Model Input

The model input for the MAFEIP tool included data regarding the health states (and transition probabilities) of study participants, the costs associated with each study group, and the utility estimate. Table 2 summarizes the distribution of study participants across the MAFEIP health states at study start, as well as the transition probabilities between these states, computed by considering data recorded at month 3. Table 3 summarizes the total health care and societal costs for each group and each state. The detailed amounts for each type of health care and societal cost are provided in Multimedia Appendix 3. The specific costs associated with the implementation of the Do CHANGE environment are presented in Table 4. The utility values calculated from the EQ-5D-3L scores and the estimated utility computed by adding the initial common measure are described in Table 5. No systematic differences were observed between study conditions at baseline. The utility values for the whole study sample in Spain, the Netherlands, and Taiwan were 0.897, 0.842, and 0.854, respectively.

Table 2. Frequency and percentage of patients across the various health states (N=207).

Variable	Do CHANGE 2[a,b] (N=92)			TAU[b,c] (N=115)		
	Spain (n=27)	The Netherlands (n=29)	Taiwan (n=36)	Spain (n=36)	The Netherlands (n=37)	Taiwan (n=42)
Health states at study start, n (%)[d]						
Baseline disease stage	5 (19.4%)	4 (14.3%)	9 (25.0%)	5 (13.5%)	5 (13.3%)	8 (18.6%)
Progressive disease stage 1	3 (11.1%)	1 (2.9%)	0	1 (2.7%)	2 (6.7%)	3 (7.0%)
Progressive disease stage 2	10 (36.1%)	9 (31.4%)	15 (40.9%)	17 (46.0%)	10 (26.7%)	19 (44.2%)
Progressive disease stage 3	9 (33.3%)	15 (51.4%)	12 (34.1%)	14 (37.8%)	20 (53.3%)	13 (30.2%)
Transition probabilities, %						
Incidence 1 (baseline disease stage to progressive disease stage 1)	14.3%	0.0%	18.2%	80.0%	25.0%	12.5%
Recovery 1 (progressive disease stage 1 to baseline)	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%
Incidence 2 (baseline disease stage to progressive disease stage 2)	14.3%	20.0%	0.0%	20.0%	0.0%	37.5%
Recovery 2 (progressive disease stage 2 to baseline)	7.7%	0.0%	5.6%	17.7%	0.0%	10.5%
Incidence 3 (progressive disease stage 1 to stage 2)	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%
Recovery 3 (progressive disease stage 2 to stage 1)	38.5%	0.0%	11.1%	29.4%	12.5%	10.5%
Incidence 4 (baseline disease stage to progressive disease stage 3)	14.3%	0.0%	0.0%	0.0%	50.0%	12.5%
Recovery 4 (progressive disease stage 3 to baseline)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Incidence 5 (progressive disease stage 1 to stage 3)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Recovery 5 (progressive disease stage 3 to stage 1)	0.0%	0.0%	0.0%	0.0%	0.0%	7.7%
Incidence 6 (progressive disease stage 2 to stage 3)	38.5%	27.3%	16.7%	5.9%	0.0%	47.4%
Recovery 6 (progressive disease stage 3 to stage 2)	50.0%	5.6%	33.3%	42.9%	0.0%	30.8%

[a]Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.
[b]Distribution of study participants at study start and the corresponding transition probabilities (in percentage).
[c]

[d]Baseline disease stage: systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg; Progressive disease stage 1: SBP 120-129 mmHg and DBP <80 mmHg; Progressive disease stage 2: SBP 130-139 mmHg or DBP 80-89 mmHg; Progressive disease stage 3: SBP ≥140 mmHg or DBP ≥90 mmHg.

Table 3. Total health care and societal costs for each of the study groups (N=207).

Variable	Do CHANGE 2 [a,b] (N=92)			TAU [b,c] (N=115)		
	Spain (n=27)	The Netherlands (n=29)	Taiwan (n=36)	Spain (n=36)	The Netherlands (n=37)	Taiwan (n=42)
Health care costs[d]						
Baseline disease stage	299.90	489.82	156.94	646.08	343.97	114.25
Progressive disease stage 1	729.25	166.43	244.96	1284.41	88.76	71.45
Progressive disease stage 2	942.39	240.36	161.58	2381.76	313.00	93.44
Progressive disease stage 3	2176.32	240.36	138.67	3484.41	88.76	114.94
Societal costs[d]						
Baseline disease stage	309.61	512.90	158.94	648.48	367.43	113.35
Progressive disease stage 1	737.38	198.51	247.90	1289.75	76.53	70.71
Progressive disease stage 2	953.98	277.55	163.44	2386.12	323.81	93.06
Progressive disease stage 3	2198.96	287.20	140.62	3485.76	73.47	115.09

[a]Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.
[b]Data are presented in € (2018; €1=US $1.12). The detailed costs of each category are provided in Multimedia Appendix 3.
[c]

[d]Baseline disease stage: systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg; Progressive disease stage 1: SBP 120-129 mmHg and DBP <80 mmHg; Progressive disease stage 2: SBP 130-139 mmHg or DBP 80-89 mmHg; Progressive disease stage 3: SBP ≥140 mmHg or DBP ≥90 mmHg.

Table 4. Costs associated with the implementation of the Do CHANGE 2 intervention (N=92).

Variable	Spain[a] (n=27)	The Netherlands[a] (n=29)	Taiwan[a] (n=36)
Time spent by professionals[b] (overhead of 18%)	50.02	99.79	19.19
Time spent by specialists (service development, receiving training, and adaptation)	1.86	7.12	4.53
Time spent by nurses (service development, receiving training, and adaptation)	1.39	2.67	0.42
Time spent by nurses on training provision to patients	25.99	50	7.91
Time spent by nurses on installation of the Do CHANGE[c] ecosystem	20.79	40	6.33
Cost of the set of devices included within the Do CHANGE ecosystem	748.99	748.99	748.99
Total	799.01	848.78	768.18

[a]Data are presented in € (2018; €1=US $1.12).
[b]For the personnel cost, we use the average cost for one full-time employee including employer contributions to social security. The average hourly costs are as follows: €29.23 (Spain), €59 (the Netherlands), and €16.88 (Taiwan) for a physician; €20.79 (Spain), €40 (the Netherlands), and €6.33 (Taiwan) for a nurse; and €34.81 (Spain), €113.50 (the Netherlands), and €84.91 (Taiwan) for a specialist.
cDo CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.

Table 5. Calculation of utility (N=207).

Disease stage[a] and assessment	Spain (N=63) Do CHANGE[b] 2 (N=27)	TAU[c] (N=36)	*P* value[d]	The Netherlands (N=66) Do CHANGE 2 (N=29)	TAU (N=37)	*P* value[d]	Taiwan (N=78) Do CHANGE 2 (N=36)	TAU (N=42)	*P* value[d]
Baseline disease stage									
M0[e]	0.896	0.869	.74	0.854	0.936	.40	0.875	0.638	.01
M3[f]	0.900	0.950	.49	0.931	0.904	.83	0.911	0.847	.59
[g]	0.004	0.081		0.077	−0.032		0.036	0.209	
Progressive disease stage 1									
M0	0.871	0.719	—[h]	0.861	0.807	—	0.726	1	—
M3	0.853	0.898	.57	0.861	0.904	—	0.726	1	.19
	−0.018	0.179		0	0.097		0	0	
Progressive disease stage 2									
M0	0.912	0.875	.49	0.896	0.821	.23	0.877	0.895	.75
M3	0.938	0.853	.07	0.886	0.825	.42	0.841	0.883	.56
	0.026	−0.022		−0.010	0.004		−0.036	−0.012	
Progressive disease stage 3									
M0	0.964	0.889	.09	0.805	0.843	.42	0.832	0.870	.62
M3	0.944	0.866	.21	0.852	0.872	.64	0.766	0.838	.32
	−0.020	−0.023		0.047	0.029		−0.066	−0.032	

[a]Baseline disease stage: systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg; Progressive disease stage 1: SBP 120-129 mmHg and DBP <80 mmHg; Progressive disease stage 2: SBP 130-139 mmHg or DBP 80-89 mmHg; Progressive disease stage 3: SBP ≥140 mmHg or DBP ≥90 mmHg.
[b]Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem.
[c]TAU: treatment as usual.
[d]A P value <.05 is considered significant.
[e]M0: baseline assessment.
[f]M3: assessment at 3 months.
[g]Δ: M3 – M0.
[h]Not enough data to calculate a *P* value.

Cost-Effectiveness

After cleaning the data, 207 participants were included in the cost-effectiveness analysis (92 in the intervention group and 115 in the control group). The Do CHANGE 2 intervention was less costly in Spain (incremental cost was −€2514.90) and more costly in the Netherlands and Taiwan (incremental costs were €1373.59 and €1062.54, respectively). Figure 4 shows the cost-effectiveness plane for the three countries. The cost-effectiveness plane plots the incremental cost of the intervention on the y-axis and the incremental health outcome (measured in QALYs) on the x-axis. The diagonal line represents the WTP per additional QALY gained, which is the maximum amount that the society is willing to give in exchange for a better quality of life. Different thresholds may also be selected. Depending on the location of the ICER point in this plane, one would be able to interpret whether an intervention is cost-effective. When the ICER point is within the lower-right quadrant, it means the intervention is accepted (it is more effective and cheaper), and when it is within the upper-left quadrant, it means that the intervention is not accepted (it is less effective and more expensive). If the ICER point lies in the other two quadrants, then the intervention may or may not be accepted depending on the ICER and WTP threshold values.

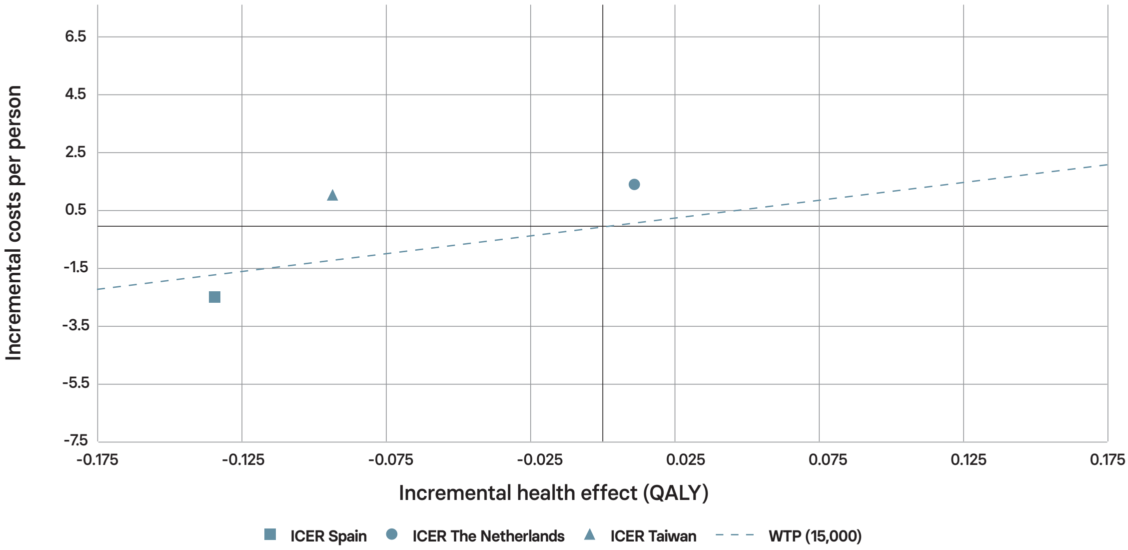


Figure 4. Cost-effectiveness plane for the Do CHANGE intervention in Spain, the Netherlands, and Taiwan. The dotted line shows the willingness-to-pay threshold of €15,000 per QALY. Do CHANGE: Do Cardiac Health: Advanced New Generation Ecosystem; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year; WTP: willingness to pay.

Compared with usual care, the effectiveness of the Do CHANGE 2 program in terms of QALY gains was slightly higher in the Netherlands (incremental effect of 0.011) and lower in Spain and Taiwan (incremental effects of –0.134 and –0.094, respectively). Even though the Do CHANGE program was more effective than usual care in the Netherlands, the relative costs for gained utility (€124,489.27 per QALY) were too high to accept this intervention. Taken together, the Do CHANGE intervention would only be accepted in Spain, where it would help save €18,769.05 per QALY.

We also calculated the incremental cost and health-related quality of life for every age-gender combination in the specified target population. The data are presented in Multimedia Appendix 4.

Discussion

Principal Findings

In this cost-effectiveness analysis of an ICT-based intervention to change the health behavior of patients with CVD (the Do CHANGE program) assessed in a multicenter RCT, we found that the ICER strongly varied depending on the country where the intervention was applied. The Do CHANGE 2 program was slightly more effective than usual care in the Netherlands only, albeit at an incremental cost too high to accept the intervention at the selected WTP threshold (€15,000 per QALY). The same intervention was less effective but less costly than usual care in Spain. In Taiwan, the intervention resulted in the dominated option (less effective and more expensive). Therefore, implementation of the Do CHANGE 2 intervention is only recommended in Spain, where it could allow saving financial costs taking into account the costs and effects of the intervention. We further tested the results with higher WTP thresholds (ie, €30,000 per QALY), with results remaining in the same line.

Contextualization With Previous Work

There is a large body of evidence showing that ICT solutions, including mobile-based telemonitoring, improve the quality and outcomes of care in patients with CVD [46]. Unfortunately, the cost-effectiveness assessment is often disregarded, and many studies reporting cost information do not meet a quality standard high enough to determine the cost-effectiveness or cost-utility of the intervention [46,47].

Regardless of the quality in reporting of individual studies, evidence on the cost-effectiveness of ICT-based lifestyle interventions is rather controversial, and many authors have acknowledged difficulties in drawing strong conclusions in this regard [48-50]. Overall, cost-effectiveness evaluations of secondary and tertiary prevention strategies for patients with CVD are challenged by the multiple factors influencing the outcomes and costs, such as baseline cardiovascular risk, the cost of drugs or other interventions, reimbursement procedures, and implementation of preventive strategies [1]. In the case of telemedicine approaches, it has been recognized that cost-effectiveness depends largely on local aspects of the individual service (and care as usual) being evaluated, and a service may be highly cost-effective in one context but highly ineffective when transferred to another context [47]. This was the case in our analysis, which yielded controversial results regarding the cost-effectiveness of the intervention in the different countries involved. Importantly, the success of an ICT-based lifestyle intervention strongly depends on the willingness of individuals to adopt the intervention, which is likely to be associated with cultural constraints and, therefore, to be country specific.

These differences were particularly pervasive between the Netherlands and Taiwan, where the cost-effectiveness planes showed an almost opposite profile, although the same intervention was implemented. We associate this situation with the majority of patients recruited in Taiwan having hypertension as the primary diagnosis and medical consultations involving health care professionals (ie, physicians) in the Netherlands being too expensive for them to devote time to a prevention intervention that could perhaps be conducted by nurses. This finding supports the need to evaluate the cost-effectiveness of these types of interventions within each context in order to provide the various stakeholders with evidence to understand the financial consequences of scaling up ICT solutions for health care.

Limitations

The main limitation of our trial was the sample size, which was constrained by budget restrictions. The discrepancy between the target and the actual sample size was mainly due to technical difficulties in recruiting participants, who had to enroll in the trial for a minimum duration of 6 months. The low sample size might have constrained the representativeness of the results and made them more sensitive to biases associated with patients with extreme behaviors (ie, outliers). Actually, the extremely low number of participants within, for instance, the states "baseline" and "progressive disease stage 1," might explain the unrealistic utilities of these patients before the intervention (eg, 0.962 and 1, respectively, for the control group), which were considerably higher than the average reported in larger RCTs involving HF (utility 0.84) [51]. Another example associated with this limitation is the relevant differences for patients allocated to the intervention group in Spain, who were younger and had higher education.

Second, an acknowledgment must be made regarding the limitation associated with the heterogeneous characteristics of the study sample for the primary diagnosis and cultural setting (ie, Spain, the Netherlands, and Taiwan), which may have contributed to the heterogeneous results across countries.

Unlike other cost-effectiveness analyses, we did not consider the contribution of medication to the health care costs. Although this might have increased the accuracy of the absolute costs, from a clinical point of view, it is unrealistic that the prescribed medicines would change throughout a 3-month time lapse. Since our main interest was assessing the change in costs rather than describing the actual values, we considered that it was more appropriate to exclude this concept from the cost-effectiveness analysis.

Finally, although RCTs are considered the gold standard for assessing cost-effectiveness, some authors criticize that they might miss information regarding how the intervention fits into routine practice [15].

Conclusions

Our results suggest that the Do CHANGE 2 environment may help reduce health care costs associated with the management of patients with CVD in certain settings. However, changing health behavior and assessing the impact of this change on health care and societal costs remain big challenges. In line with previous research in this field, our assessment does not allow drawing strong conclusions in this regard. Irrespective of the specific cost-effectiveness of the Do CHANGE 2 program, our results highlight the high heterogeneity that ICT-based interventions might show depending on the country where they are implemented and stress the need for assessing each intervention in all areas before scaling up implementation.

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Authors' Contributions

JPJ, JWMGW, MH, EB, and DVB contributed to the study design and data collection. JPJ, MW, and DVB conducted the statistical analyses. JPJ drafted the manuscript. All authors critically revised and approved the final version of the manuscript. FLV and FF supervised the study.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Do CHANGE leaflet.
[PDF File (Adobe PDF File), 796 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Clinical characteristics of the study sample, medication, and psychological symptoms.
[PDF File (Adobe PDF File), 179 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Health care and societal costs.
[XLSX File (Microsoft Excel File), 17 KB-Multimedia Appendix 3]

Multimedia Appendix 4

Incremental costs and effects (age and gender specific) per pilot site.
[PDF File (Adobe PDF File), 674 KB-Multimedia Appendix 4]

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Abbreviations

BP: Blood Pressure.
CVD: Cardiovascular Disease.
DBP: Diastolic Blood Pressure.
DSD: Do Something Different.
Do CHANGE:
Do Cardiac Health: Advanced New Generation Ecosystem.
EQ-5D: EuroQol five Dimensions.
HF: Heart Failure.
ICER: Incremental Cost-Effectiveness Ratio.
ICT: Information and Communication Technology.
MAFEIP: Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing.
QALY: quality-Adjusted Life-Year.
RCT: Randomized Controlled Trial.
SBP: Systolic Blood Pressure.
TAU: Treatment As Usual.
WTP: Willingness To Pay.

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3. MANUSCRIPT #2

ORIGINAL PAPER

BeyondSilos, a Telehealth-Enhanced Integrated Care Model in the Domiciliary Setting for Older Patients: Observational Prospective Cohort Study for Effectiveness and Cost-Effectiveness Assessments

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Abstract

Background: Information and communication technology may provide domiciliary care programs with continuity of care. However, evidence about the effectiveness and cost-effectiveness of information and communication technology in the context of integrated care models is relatively scarce.

Objective: The objective of our study was to provide evidence on the clinical effectiveness and cost-effectiveness of the BeyondSilos project for patients enrolled in the Badalona city pilot site in Spain.

Methods: A quasi-experimental study was used to assess the cost-effectiveness of information and communication technology–enhanced integration of health and social care, including the third sector (intervention), compared to basic health and social care coordination (comparator). The study was conducted in Badalona between 2015 and 2016. Participants were followed for 8 months.

Results: The study included 198 patients: 98 in the intervention group and 100 in the comparator group. The mean Barthel index remained unchanged in the intervention group (mean change 0.14, 95% CI −4.51 to 4.78; P=.95) but decreased in the comparator group (mean change −3.23, 95% CI −5.34 to −1.11; P=.003). Instrumental Activities of Daily Living significantly decreased in both groups: mean changes of −0.23 (95% CI −0.44 to −0.02; P=.03) and −0.33 (95% CI −0.46 to −0.20; P<.001) in the intervention and comparator groups, respectively. No differences were found in the Geriatric Depression Scale (intervention: mean change 0.28, 95% CI −0.44 to 1.01, P=.44; comparator: mean change −0.29, 95% CI −0.59 to 0.01, P=.06). The intervention showed cost-effectiveness (incremental cost-effectiveness ratio €6505.52, approximately US $7582).

Conclusions: The information and communication technology–enhanced integrated domiciliary care program was cost-effective.
The beneficial effects of this approach strongly rely upon the commitment of the professional staff involved.

Trial Registration: ClinicalTrials.gov NCT03111004; http://clinicaltrials.gov/ct2/show/ NCT03111004
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KEYWORDS
Integrated care; telemedicine; telecare; digital health; cost-effectiveness; clinical effectiveness; chronic disease.

Introduction

Background

Domiciliary care programs are increasingly used to deliver health care to patients—particularly older patients and those with chronic conditions—who are unable to go to a primary care center due to their medical condition or disability, thus improving their health and functional independence, while reducing hospitalizations [1-4]. Among domiciliary care programs, integrated care models prioritize continuity in the sense that the same care provider supports the patient both at home and the primary care center. However, the need for integration with social care is often undervalued [5]. The relevance of social care is not limited to the role of social workers, but also that of stakeholders in the third sector, which in some areas may strongly contribute to day-to-day welfare of these patients [6].

Regardless of the involvement of stakeholders from the social domain, integrated domiciliary care models face the challenge of being efficient enough to absorb the rapidly rising number of care recipients in this setting, likely prompted by social and demographic shifts [7]. In fact, the current overloaded schedule of primary care teams involved in integrated domiciliary care programs has been already identified as a significant drawback of this care model [8,9].

Among the interventions designed to increase the efficiency of health care systems, the use of information and communication technologies have shown promising results in various areas, including the management of older people with chronic diseases [10-12]. Besides integrating all patient information and facilitating the coordination of the various professionals involved, information and communication technology provides domiciliary care with telemonitoring solutions, which may bring patients and professionals closer [13]. However, the evidence regarding the cost-effectiveness of these solutions in the context of integrated care models is scarce and heterogeneous in terms of quality [7,14,15].

The BeyondSilos Project

BeyondSilos aimed to promote community-based, independent lives by providing domiciliary care with information and communication technology solutions capable of crossing through domain boundaries that typically separate social and health care providers [16]. One of the key areas of integration (frequently referred as to horizontal integration) was for the common access of all cross-sectorial care teams, including those of the third sector, to telehealth platforms in order to improve coordination and promote continuity of care.

To overcome the traditional boundaries separating social and health care, information and communication technology solutions of the BeyondSilos project went hand-in-hand with innovative organizational designs. This approach was based on the assumption by Urošević and Mitić, who pointed out that "Successful service integration in policy and practice requires both technology innovation and service process innovation being pursued and implemented at the same time [17]." Because information and communication technology–based services are typically delivered within sociotechnical system (ie, organizational frameworks where people interact with technology), their success often depends on the value of people applying technology. Hence, information and communication technology can effectively support well-designed care service delivery processes, but it cannot replace them because of the emotional aspects of physical meetings [18].

The first step in achieving a combined innovation approach was the development of common integrated care pathways that were to be supported by information and communication technology. For this purpose, the project adopted 2 generic service pathways of the SmartCare project which were adapted to fit local context through service process modeling techniques (Multimedia Appendix 1). The first pathway addressed needs for integrated home care during an acute episodes and immediately after hospital discharge. The second pathway was directed toward people needing integrated long-term care (eg, frail patients with multiple comorbidities).

We hypothesized that the provision of information and communication technology–enhanced integrated care services that encompass health and social care in the setting of domiciliary care would improve health outcomes and reduce health system costs. Herein, we report the clinical effectiveness and cost-effectiveness of the BeyondSilos intervention for patients enrolled in the long-term pathway in a Badalona city pilot site (Spain).

Methods

Study Design, Setting, and Participants

As part of the BeyondSilos project, an observational prospective cohort study was carried out to assess the implementation of an information and communication technology–enhanced integrated care model in the setting of domiciliary care in Badalona Serveis Assistencials (BSA), a public provider of health and social care services to the City Council of Badalona, the most populated suburban area to the north of Barcelona, Spain with a reference population of 433,175 inhabitants. BSA has recently been shifting toward integrated care models [19-30].

In Spain, the health and social care systems are centrally managed by the Ministry of Health, Consumerism, and Social Services, which provides the basic regulations and guidelines. The political control and jurisdiction over the organization and provision of health and social services are transferred to the 17 regional governments (autonomous communities). The health system is based on a Beveridge model, characterized by universal coverage, funded by the government through tax, and delivered by an extensive network of public and private health providers. The regions have the main responsibility for social services provision, together with municipalities [31,32]. Third-sector organizations (voluntary and nonprofit) play an essential role in responding to many and different social needs of the general population that are beyond the reach of the scarce public resources (eg, volunteer care and accompaniment of those at risk of social exclusion and isolation) [33].

Care recipients assessed for eligibility were involved in a domiciliary care program as described by Burgos-Díez et al (study condition) [19] and were recruited among care recipients managed from 6 primary care centers. Centers acting as intervention and comparator were paired 1-to-1 for similar socioeconomic status in their area of influence. To this end, candidate sites were stratified into 3 categories of socioeconomic status of the catchment area (2 primary care centers per category). The information and communication technology–enhanced integrated care model (intervention) was first introduced in 1 center in each category; the remaining centers were used as comparators. The first care recipient was enrolled March 3, 2015, and the last care recipient exited the project October 20, 2016.

Eligibility Criteria

The main inclusion criteria were age ≥65 years, special health needs due to the presence of chronic diseases (ie, heart failure, stroke, diabetes, or chronic obstructive pulmonary disease plus at least 1 additional chronic disease included in the Charlson Comorbidity Index [34]), and the need for social care based on Barthel Index of Activities of Daily Living [35] and Instrumental Activities of Daily Living. To be assessed for eligibility, patients were not require to have an active internet or mobile contract but had to have reliable 4G coverage at home (required by the telehealth solution provided). Participants with an active cancer or AIDS diagnosis, in a terminal state, those who had undergone an organ transplant, or who were on dialysis before enrolment were excluded from the study.

Ethics

The study protocol was approved by the Independent Ethics Committee of the *Hospital Germans Trias i Pujol*, and all participants provided informed consent before entering the study.

Intervention

Participants from both groups received health and social care, integrated through a corporate enterprise resource planner which was used as a facilitator for administrative coordination between BSA and the municipality (ie, management of admissions and discharges). Health and social care information were stored in 2 centralized repositories linked to each other through interoperability. Domiciliary care was coordinated using a homecare department software, which stored the Shared Care Plan, accessible for both health and social care professionals. Based on this Plan, professionals scheduled regular visits or phone contacts with care recipients.

In addition to the aforementioned common resources, participants in the intervention group were provided with a telehealth platform, the Health Insight Solutions Homecare Platform, which included the following components: security sensors (ie, fire and water detectors, behavioral movement sensors, and a cell phone with GPS tracking and fall detection), medical devices (ie, weight scale, blood pressure meter, glucometer, and oximeter), serious games, a personal diary, and a videoconferencing system (Multimedia Appendix 2). The telehealth platform was used by the participants and their close relatives to continuously track their health status following the care plan defined by their formal caregivers. Information collected within the telehealth platform was checked daily by the primary care team responsible for the patient. Exacerbation of health conditions (eg, weight increase over 20% in a 1-week period) and out-of-hours alarms (ie, fall detection, fire, or water leak) automatically triggered an alert (SMS text message) to the team on call. In the intervention group, third-sector care providers had access to basic clinical information (ie, main diagnostics and visits from other professional staff) throughout the Shared Care Plan and provided volunteer accompaniment support to patients at risk of social exclusion.

Recruitment

Potential study participants were identified in a 2-stage process. The first part of the process was conducted by the Information Systems Department of BSA and consisted of identifying possible candidates through a database search using the inclusion and exclusion criteria. The initial selection process identified 4800 possible candidates receiving both health and social care services. Applying more specific inclusion criteria, such as diagnosis-based specificities, reduced the list to 430 patients. In a second stage, research assistants in each participating center approached the individuals and asked them if they were willing to participate.

Assessments

The effectiveness of the intervention was evaluated using the Model for Assessment of Telemedicine [36]. Primary outcome measures were related to the health status of study participants and established based on the Barthel index scale, the Instrumental Activities of Daily Living scales [37], and the Geriatric Depression Scale [38]. All questionnaires were collected online by trained researchers using a purpose-designed survey built on an open-source tool

(LimeSurvey; Limesurvey GmbH) [39].

Costs were modeled and collected from both a health care and societal perspective using the ASSIST Tool [40] and were estimated in 2016 euros. For the intervention group, 2 types of costs were considered: one-off costs (ie, incurred only at implementation) and recurring costs (ie, costs derived from the service practice).

The health care costs perspective included the assessment of resource utilization and considered all characteristics regarding hospitalization (eg, number of admissions and readmissions, length of hospital stay, and type of admission) and contacts with health and social care professionals (eg, type of professional, number of contacts, and type and setting of the contact). For personnel costs, the average income for 1 full-time employee with employer contributions to social security was used. The average hourly wages were €29.23 for a physician (approximately US $34.07), €20.79 for a nurse (approximately US $24.23), and €18.19 for a social care worker (approximately US $21.20).

The societal cost perspectives considered were the health care costs plus those outside the health care sector. In this case, the costs for the intervention group included the time spent by patients using the new service. Moreover, the intervention brought savings in travel time and costs for patients and their caregivers. These were computed as a cost for the control group. The monetary equivalent for the time spent by the patients and informal caregivers was calculated using the minimal interprofessional wages for the year 2016 and resulted in an hourly wage of €6.07 (approximately US $7.07).

All costs were homogenized per patient and per year. Bed days of each group were multiplied by the estimated cost per bed–day in Spain (€733.56, approximately US $854.91).

Analyses

Categorical variables were described as frequency and percentage of available data, whereas quantitative variables were described as mean and standard deviation or median and interquartile range; 95% confidence intervals were provided for mean differences. Between-group differences regarding the proportions of each category were compared using the chi-square test, whereas quantitative variables were compared using the ***t*** test, analysis of variance, or their nonparametric counterparts (Mann-Whitney ***U*** test and Kruskal-Wallis test, respectively). Normality was assessed using the Kolmogorov-Smirnov test [41]. In all comparisons, the Piera-Jiménez et al significance threshold was set at a 2-sided α=.05. Descriptive and comparative analyses were performed using SPSS software (version 17.0; SPSS Inc).

Cost-effectiveness analysis was performed using Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) [42]. MAFEIP is a free web-based tool promoted by the European Commission aimed at performing cost-utility analysis to estimate health outcomes and resource usage of a large sample of information and communication technology–enabled health and social care innovations, developed and implemented in the context of the European Innovation Partnership on Active and Healthy Ageing [42,43]. More precisely, the cost-effectiveness estimates are based on the principles of decision analytic modeling and a generic Markov model which provides the flexibility required to be tailored to the variety of solutions promoted by the European Innovation Partnership on Active and Healthy Ageing [44-46].

Quality-adjusted life years were computed using change in the Barthel index as a proxy of utility as described by Kaambwa et al [47], and based on a 3-states Markov model: *baseline disease stage* (the patient remains in the same state or improves), *deteriorated disease stage* (the patient worsens), and dead (Figure 1). The 3 states led to the corresponding transition probabilities: *recovery* (improving or remaining the same state), *incidence* (worsening), and *death*. Mortality rates were internally calculated by the MAFEIP tool using all-cause mortality rates (age- and sex-dependent) extracted from the Human Mortality Database. Discount factors for health outcomes and costs were both set to 3% following recommendations from local Health Technology Assessment authorities. In order to estimate the incremental costs and outcomes associated with the intervention, we ran the model over a 40-year time horizon, following the proposed standardization for economic analysis of health technologies in Spain, which recommends assessing the costs and benefits on a time horizon that covers the entire lifespan of the patients affected [48-50].

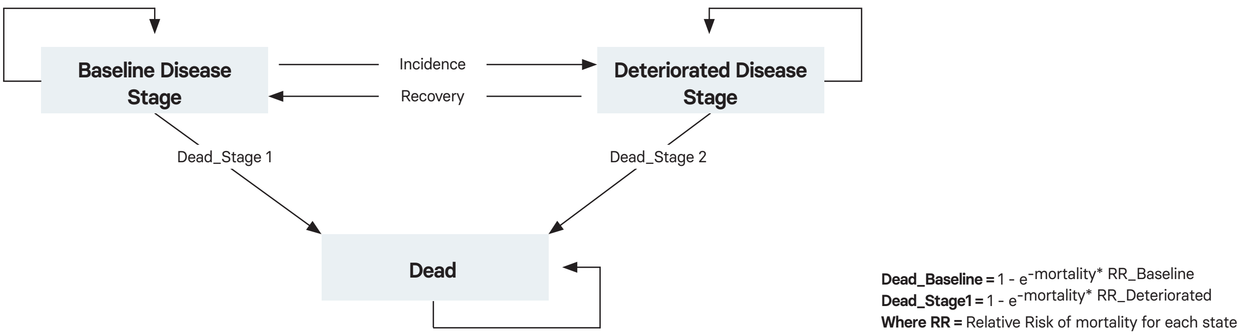


Figure 1. 3-state Markov model applied for the BeyondSilos cost-effectiveness analysis.

Results

Participant Characteristics

Of the 268 individuals considered for eligibility, 70 were excluded, resulting in a study sample of 198 patients: 98 (49.5%) were managed within the BeyondSilos project (intervention group) and 100 (50.5%) were managed according to usual care (comparator group) (Figure 2).

Figure 2. Flowchart of participant recruitment for the BeyondSilos project.

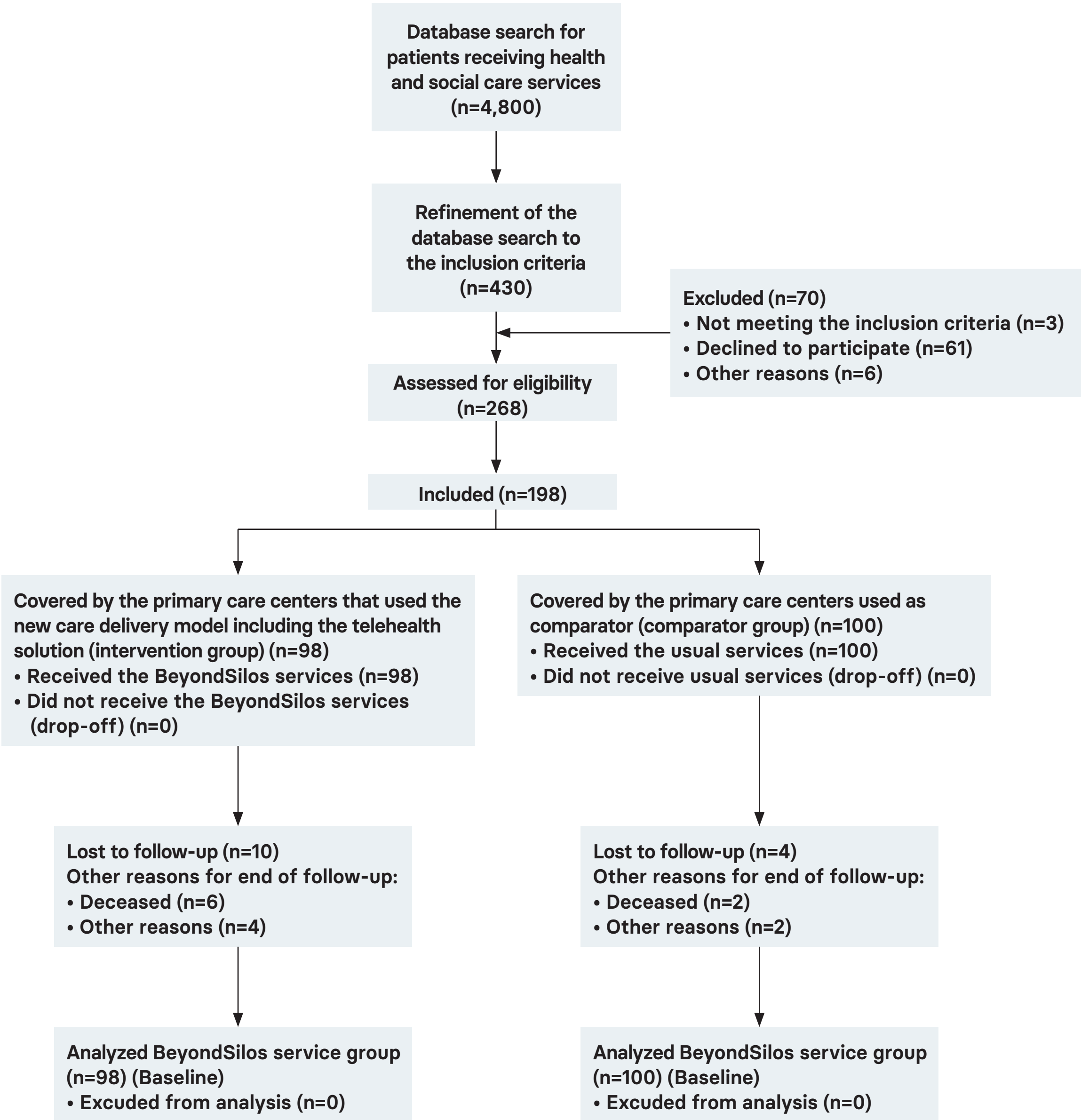


Table 1 summarizes the sociodemographic characteristics of study participants. Participants in the 2 study groups were balanced regarding education level and household income, but the intervention group tended to be overrepresented by older, female, and widowed individuals.

Table 1. Demographic baseline characteristics of the total sample (N=198).

Characteristics	Intervention group (n=98)	Comparator group (n=100)	*P* value
Gender, n (%)			.02
Male	26 (26)	43 (43)	
Female	72 (74)	57 (57)	
Age (years), median (IQR)	85.5 (7.3)	82.8 (8.3)	.01
Age group (years), n (%)			.003
<65	1 (1.0)	0 (0)	
65-75	7 (7.1)	24 (24.0)	
>75	90 (91.8)	76 (76.0)	
Marital status, n (%)			.053
Never married	2 (2.0)	3 (3.0)	
Currently married	30 (30.6)	47 (47.0)	
Separated	0	3 (3.0)	
Divorced	2 (2.0)	1 (1.0)	
Widowed	63 (64.3)	46 (46.0)	
Cohabitating	1 (1.0)	0 (0)	
Education level, n (%)			.23
Less than primary school	50 (53.2)	40 (40.8)	
Primary school	30 (31.9)	42 (42.9)	
Secondary school	5 (5.3)	10 (10.2)	
High school	7 (7.4)	4 (4.1)	
College/university	2 (2.1)	1 (1.0)	
Post graduate degree	0 (0)	1 (1.0)	
Household income (€ [a] yearly), median (IQR)			.96
0-6999	7 (13.2)	11 (14.7)	
7000-13,999	32 (60.4)	45 (60.0)	
14,000-19,999	12 (22.6)	15 (20.0)	
20,000 or more	2 (3.8)	4 (5.3)	

[a]An approximate exchange rate of €1 to US $1.17 was applicable at the time of publication.

At baseline, study participants in both groups had a median of 3 comorbidities (IQR 2-4), with no significant differences regarding either the number of comorbidities (*P*=.96) or the prevalence of each comorbidity, except malignancies, which were 2.6-fold more frequent among those in the intervention group (Table 2). The mean Charlson Comorbidity index was 4.42 (SD 2.34) and 4.31 (SD 1.81) for the intervention and comparator groups, respectively (*P*=.79). Congestive heart failure was the most prevalent comorbidity in both study groups. The intervention group had significantly lower Barthel index scores (*P*=.001) and higher Geriatric Depression Scale scores (*P*=.002). This trend was not observed for the Instrumental Activities of Daily Living (*P*=.44).

Table 2. Clinical characteristics of study participants at baseline (N=198).

Characteristics	Intervention group (n=98)	Comparator group (n=100)	*P* value
Comorbidities, n (%)			
Myocardial infarction	17 (17.3)	23 (23.0)	.32
Congestive heart failure	61 (62.2)	71 (71.0)	.19
Peripheral vascular disease	1 (1.0)	3 (3.0)	.33
Cerebrovascular disease	43 (44.3)	25 (25.0)	.004
Dementia	3 (3.1)	5 (5.0)	.49
Chronic pulmonary disease	1 (1.0)	3 (3.0)	.33
Rheumatic disease	3 (3.1)	10 (10.0)	.051
Peptic ulcer disease	19 (19.6)	16 (16.0)	.51
Mild liver disease	22 (22.7)	34 (34.0)	.08
Diabetes without chronic complication	25 (26)	27 (27.0)	.88
Diabetes with chronic complication	31 (32.0)	19 (19.0)	.04
Hemiplegia or paraplegia	28 (28.9)	37 (37.0)	.22
Renal disease	1 (1.0)	1 (1.0)	.99
Malignancies[a]	23 (23.7)	9 (9.0)	.005
Moderate or severe liver disease	3 (3.1)	4 (4.0)	.73
Metastatic solid tumor	13 (13.4)	12 (12.0)	.77
Anthropometric and laboratory exams, mean (SD)			
Body mass index (kg/m^2)	28.8 (4.8)	27.3 (5.4)	.02
Blood glucose (mg/dL)	110.8 (34.6)	116.9 (44.5)	.44
HbA_1[b](%)	6.82 (1.70)	7.45 (1.81)	.11
eGFR[c](mg/dL/1.73 m^2)	75.9 (38.1)	74.4 (43.2)	.40
Tobacco use, n (%)			.12
Never	75 (79.8)	69 (69.0)	
Former	19 (20.2)	29 (29.0)	
Current smoker	0 (0)	2 (2.0)	
E-cigarette	0 (0)	0 (0)	
Other	0 (0)	0 (0)	
Alcohol drinking (weekly drinks past 12 months), n (%)			.02
None	87 (88.8)	80 (80.0)	
<1	6 (6.1)	6 (6.0)	
1-7	3 (3.1)	14 (14)	
8-14	2 (2.0)	0 (0)	
15-21	0 (0)	0 (0)	
>21	0 (0)	0 (0)	
Assessment scores, mean (SD)			
Barthel index	44.66 (27.37)	71.58 (27.95)	.001
Instrumental Activities of Daily Living	1.45 (1.74)	2.94 (2.55)	.44
Geriatric Depression Scale	7.23 (3.47)	6.11 (3.51)	.002

[a]Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin.
[b]HbA1c: glycohemoglobin.
[c]eGFR: estimated glomerular filtration rate.

Clinical Effectiveness

The Barthel index remained unchanged throughout the follow-up period in the intervention group (mean change from enrolment to end was 0.14, 95% CI −4.51 to 4.78; *P*=.95), but decreased in the comparator group (mean change −3.23, 95% CI −5.34 to −1.11; *P*=.003). The score of the Instrumental Activities of Daily Living significantly decreased in both groups: mean change of −0.23 (95% CI −0.44 to −0.02) in the intervention group (*P*=.03) and −0.33 (95% CI −0.46 to −0.20) in the comparator group (*P*<.001). The Geriatric Depression Scale score did not significantly change in either the intervention group (mean change 0.28, 95% CI −0.44 to 1.01; *P*=.44) or the comparator group (mean change −0.29, 95% CI −0.59 to 0.01; *P*=.06). None of the deaths were deemed to be related to the intervention or likely to been preventable with the intervention.

Resource Utilization

During the 8 months of follow-up, the study participants contacted the health care or social professionals 5209 times: 2556 times in the intervention group and 2653 times in the comparator group. The contact profile of the 2 groups differed significantly regarding the type of professional, the planned/unplanned contact, and the setting of contacts (Table 3). Overall, participants in the intervention group tended to have contact more with their general practitioner and the social worker, and less with the specialists. Regarding the type of visit, participants in the intervention group tended to have more planned visits, predominantly at home, compared to those of the comparator group.

Table 3. Resource utilization of study participants (N=198).

Resource use	Intervention group (n=98)	Comparator group (n=100)	*P* value
Hospitalization			
Hospitalized patients, n (%)	32 (32.7)	45 (45.0)	.08
Length of hospital stay per admission (days), mean (SD)	5.84 (8.81)	2.3 (2.8)	.02
Length of hospital stay per patient (days), mean (SD)	12.9 (15.0)	6.36 (9.0)	.02
Time to first admission (days), mean (SD)	56.3 (57.9)	70.8 (59.3)	.31
Admissions per patient (all patients), mean (SD)	0.85 (1.61)	1.12 (2.10)	.17
Readmissions within 30 days per patient, mean (SD)	1.73 (1.78)	2.11 (2.74)	.96
Type of admission, n (%)			
Planned	24 (28.9)	36 (32.1)	
Unplanned	59 (71.1)	76 (67.9)	
Annual length of hospital stay (unplanned admissions), mean (SD)	1.58 (5.15)	0.65 (1.41)	.74
Interaction with health and social professional			
Type of professional, n (%)			
General practitioners	895 (34.2)	670 (23.3)	<.001
Specialists	116 (4.4)	225 (7.8)	<.001
Nurses	1504 (57.5)	1901 (66.1)	<.001
Other health care provider	25 (1.0)	39 (1.4)	.17
Social workers	76 (2.9)	42 (1.5)	<.001
Volunteers	N/A[a]	N/A	N/A
Type of anticipation, n (%)			<.001
Planned	1677 (93.2)	1359 (87.6)	
Unplanned	123 (6.8)	193 (12.4)	
Setting of contacts, n (%)			
Physical meeting out of home	239 (9.4)	563 (21.2)	<.001
Home visit	1089 (42.6)	687 (25.9)	<.001
Telephone	759 (29.7)	535 (20.2)	<.001
Writing (email, SMS text message, etc)	463 (18.1)	857 (32.3)	<.001
Other	6 (0.2)	8 (0.3)	.82
Annual rates for contacts, mean (SD)			
Annual contacts rate	51.0 (36.1)	53.1 (40.3)	.85
Annual unplanned contacts rate	2.4 (3.5)	3.8 (5.3)	.07
Annual physical contacts rate	24.9 (23.5)	23.4 (18.1)	.66

[a]N/A: not applicable.

Cost-Effectiveness Analysis

Table 4 summarizes the costs with transition probabilities between the 3 health states of the Markov model used as inputs for the MAFEIP tool. Although the expenditures shared by the 2 care models were very similar, the intervention group was associated with an extra cost, resulting in an incremental cost of €4755 (approximately US $5542). The increase of costs was associated to the extra home visits and general practitioner contacts associated to the training and usage of the telehealth technology (for a detailed table of costs see Multimedia Appendix 3).

The effectiveness, computed based on transition probabilities between the 3 states of the Markov model, was also higher in the intervention group, yielding an incremental

Table 4. Input used for the cost-effectiveness analysis based on the 3-state Markov model (N=198).

Input	Intervention group (n=98)	Comparator group (n=100)
Transition probabilities, %		
Incidence	34	36
Recovery	66	64
Relative risk (mortality)		
Baseline disease stage	1.005	1.005
Deteriorated disease stage	1.005	1.005
Utility after intervention		
Baseline disease stage	0.56	0.45
Deteriorated disease stage	0.3	0.33
Costs, € ($)[a]		
One-off cost per patient (intervention)	1268.89 (1484.60)	N/A[b]
Recurring cost per patient/year (intervention)	230.40 (269.57)	N/A
Health care cost—baseline disease stage	5664.89 (6627.92)	5198.62 (6082.39)
Health care cost—deteriorated disease stage	4502.89 (5268.38)	5221.69 (6109.38)
Societal cost—baseline disease stage	5953.15 (6965.19)	5259.14 (6153.19)
Societal cost—deteriorated disease stage	4791.15 (5605.65)	5282.21 (6180.19)

[a]An approximate exchange rate of €1 to US $1.17 was applicable at the time of publication.
[b]N/A: not applicable.

effect of 0.731. Overall, the incremental cost-effectiveness ratio was €6505.52 (approximately US $7582), making the intervention more effective than usual care for all willingness-to-pay thresholds above €6500 (approximately US $7575) per quality-adjusted life year (Figure 3).

The sensitivity analysis showed that a change between 0% and 5% in the utility in the baseline health for the intervention group would place the incremental cost-effectiveness ratio still below the willingness-to-pay threshold of €15,000 (approximately US $17,481)/quality-adjusted life year (Figure 4).

Similarly, a change between 0% and 5% in the health care costs would not affect the result (Figure 5).

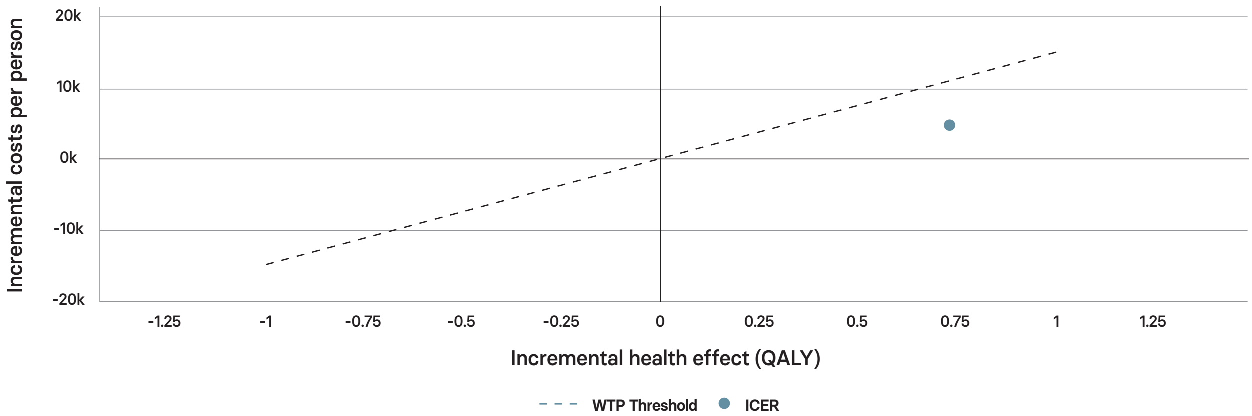


Figure 3. Cost-effectiveness plane for a willingness-to-pay of €15,000 (approximately US $17,481)/quality-adjusted life year. ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year; WTP: willingness-to-pay.

Figure 4. Sensitivity analysis showing effects between 0% and 5% change in utilities—willingness-to-pay of €15,000 (approximately US $17,481)/quality-adjusted life year. QALY: quality-adjusted life year; WTP: willingness-to-pay.

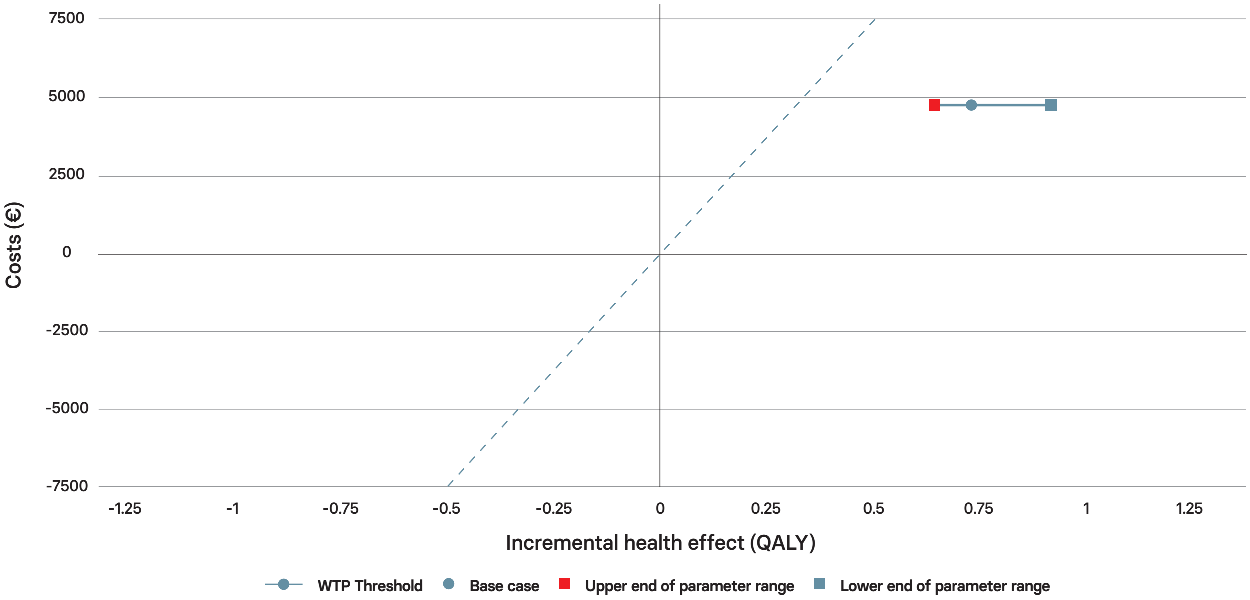
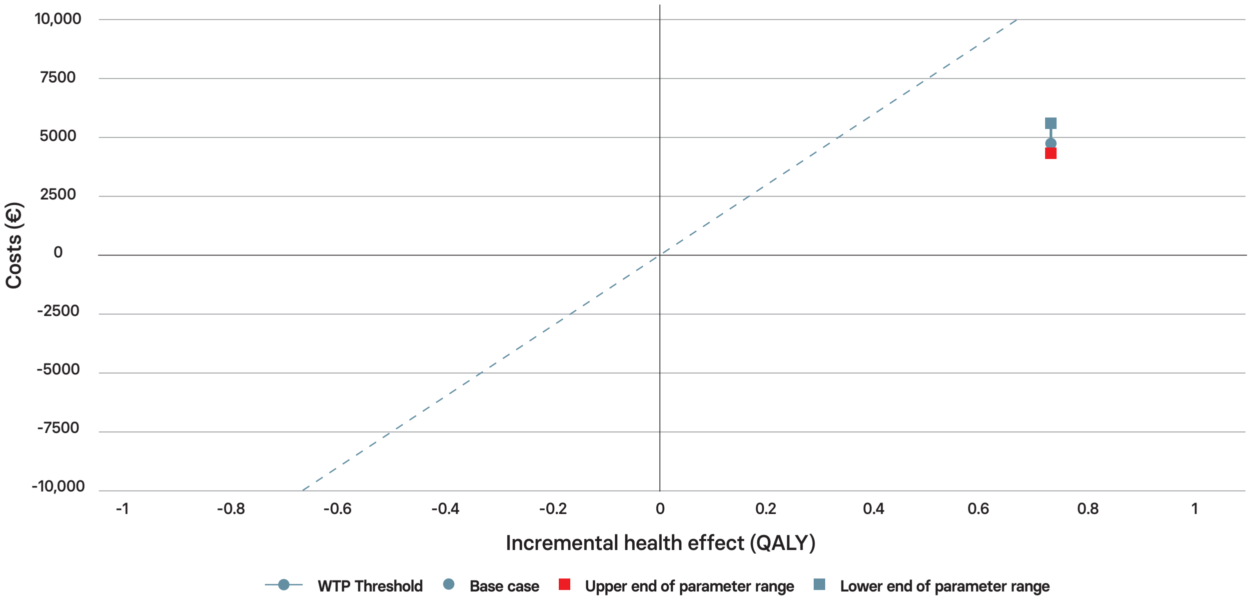


Figure 5. Sensitivity analysis showing effects between 0% and 5% change in costs—willingness-to-pay of €15,000 (approximately US $17,481)/quality-adjusted life year. QALY: quality-adjusted life year; WTP: willingness-to-pay.



Discussion

Summary of Main Results

In this observational prospective cohort study, we found that the addition of an information and communication technology solution (which also involved the third sector) to a basic integrated care model was more effective than integration only in terms of transition between health states established with the Barthel index and the Instrumental Activities of Daily Living. The superiority of the BeyondSilos intervention was confirmed by all willingness-to-pay thresholds above €6500 (approximately US $7575) per quality-adjusted life year, far below the €30,000 (approximately US $34,963) threshold traditionally considered in Spain [51].

Besides the specific context of the pilot site, these results must be interpreted by bearing in mind the challenges of assessing cost-effectiveness of a complex intervention (such as an integrated care model). First, the complexity of both the intervention and the usual care model (in this case, an integrated care framework) often blurs the different contribution of each element to costs [7,15]. This also applies to stakeholders in the third sector (volunteer care), which cannot be easily quantified. Furthermore, it is worth mentioning that quality-adjusted life years may not always be a useful indicator for decision making at the level of provider organizations, particularly when (1) the delivery of care is already constrained by decisions at national or regional level [50] and (2) additional factors such as patient and provider satisfaction need to be taken into account.

Contextualization of the Badalona Pilot Within the BeyondSilos Project

An important characteristic of projects aimed at implementing integrated care strategies is the need of tailor the overarching plan and methodology to the organizational framework of each area. Therefore, considering the expected differences between pilot sites in this regard, the original purpose was to provide a general integrated care framework so that pilot sites could tailor it to their health care environment. The most remarkable characteristic of Badalona pilot site was that, unlike other pilot sites enrolled in the BeyondSilos project, it was already delivering both health and social care services based on an integrated care approach. In this context, the BeyondSilos project added only 2 remarkable improvements compared with usual care: (1) a deeper commitment of the third-sector organizations and (2) the use of information and communication technology to enhance domiciliary care. The fact that the pilot site already operated under an integrated care approach had the advantage that the health care team was already used to integrated pathways, thus facilitating the incorporation of additional integrated care elements into the organizational model. However, this feature brought the trial to a challenging scenario in which the comparator (ie, comparator group) already included social care within the integrated care approach, thus reducing the benefits of the BeyondSilos model.

Strengths, Limitations, and Future Work

Our analysis was strengthened by the appropriate balance between the primary care centers that piloted the information and communication technology–based intervention and those acting as comparators (paired by socioeconomic status). Although this approach did not preclude baseline differences in some demographic and clinical characteristics, the study groups were balanced regarding sociodemographic characteristics that may influence attitudes toward information and communication technology, such as income and education level.

On the other hand, studies investigating the effectiveness of integrated care models have to deal with the difficulty of establishing an adequate comparator [7]. As a rule of thumb, usual care is the recommended comparator, but this had different meanings for the various pilot sites in the BeyondSilos project, with some comparing nonintegrated and integrated care models, and others—as in our pilot site—comparing 2 integrated care models with different intensities. The last approach has been increasingly used as more areas adopt integrated care approaches [52,53], although there is less room for improvement. Another challenge of the assessment of integrated care models includes patient profiles, often characterized by a multimorbid conditions, which may be rather heterogeneous [7,15]. In our study, the baseline demographic and clinical characteristics of patients in the 2 groups were similar, but patients in the intervention group tended to be female, older, widowed, more dependent, and with higher depression scores. These differences, likely because of the real-life setting, should be carefully considered when appraising the scope of our results. Specifically, the characteristics of the intervention group might be associated with a higher need of formal care and information and communication technology solutions than that in the control group, thus potentially shading the actual benefits of the intervention.

Keeping these limitations in mind, we found that the frequency of planned and home visit contacts was significantly higher in the intervention group ($P<.001$). Although this trend might be influenced by the higher complexity of patients in the intervention group, health care professionals explicitly explained that the usage of information and communication technology required more of their time and they were afraid that information and communication technology may replace their jobs. This attitude, together with the usual resistance of care recipients to losing contact with their formal caregivers [54,55], was likely to hinder the reduction of home visits that is expected with telemonitoring. Of note, the lack of differences in the estimated annual rates suggests that this phenomenon was not homogeneous throughout the follow-up period, being more pervasive during the first stages of the intervention. The temporal patterns of this attitude may reflect a certain resistance of professional staff to trust the new information and communication technology–supported integrated care model (ie, not fully taking advantage of the telemonitoring solution thus not abandoning the routine cadence of home care visits). Besides being a lesson for future implementation of information and communication technology solutions, this observation suggests that, in our study, uncontrolled factors such as the personal commitment of professionals to the project might influence the apparent cost-effectiveness of an information and communication technology solution, potentially overriding other factors such as patient characteristics. Future evaluations based on multicriteria decision analyses may provide interesting insights regarding the implementation of information and communication technology–enhanced integrated care programs [56].

Conclusion

Our study provided evidence regarding the clinical effectiveness and cost-effectiveness of an information and communication technology–enhanced integrated care model that enables telemonitoring and increases the intensity of integrated care by involving organizations of the third sector in the management of older patients in a domiciliary care setting. The cost-effectiveness analysis placed the intervention as more effective than usual care—and reasonably inexpensive. However, our findings confirm the difficulties of assessing the effectiveness of interventions and suggest that the beneficial effects of a new care model strongly depend on the commitment of health and social care professionals with the model.

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Authors' Contributions

JP-J, SD, PS, IM, SM, LL, and PC contributed to the study design. JP-J was the principal investigator locally and managed the overall trial and data collection. JP-J, SD, PS, IM SM, and PC conducted the statistical analyses. JP-J drafted the manuscript and all authors critically revised and approved the final version of the manuscript. FLV and FF supervised the cost-effectiveness study. All authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

Conflicts of Interest

The authors declare no conflicts of interest. The BeyondSilos team received 50% funding for Research and Innovation from the European Union for the project. The provider of the telehealth solution (Health Insight Solutions) is a privately-owned company which was not part of the project and was subcontracted under a public tendering process by BSA.

Multimedia Appendix 1

BeyondSilos integrated common care pathways for home care support.
[PDF File (Adobe PDF File), 460 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Telehealth solution used within the BeyondSilos project (Badalona pilot site).
[PDF File (Adobe PDF File), 472 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Tables of costs.
[PDF File (Adobe PDF File), 330 KB-Multimedia Appendix 3]

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Abbreviations

BSA: Badalona Serveis Assistencials.
MAFEIP: Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing.

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4. MANUSCRIPT #3

ORIGINAL PAPER

Guided Internet-Based Cognitive Behavioral Therapy for Depression: Implementation Cost-Effectiveness Study

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Abstract

Background: Major depressive disorder is a chronic condition; its prevalence is expected to grow with the aging trend of high-income countries. Internet-based cognitive-behavioral therapy has proven efficacy in treating major depressive disorder.

Objective: The objective of this study was to assess the cost-effectiveness of implementing a community internet-based cognitive behavioral therapy intervention (Super@, the Spanish program for the MasterMind project) for treating major depressive disorder.

Methods: The cost-effectiveness of the Super@ program was assessed with the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing tool, using a 3-state Markov model. Data from the cost and effectiveness of the intervention were prospectively collected from the implementation of the program by a health care provider in Badalona, Spain; the corresponding data for usual care were gathered from the literature. The health states, transition probabilities, and utilities were computed using Patient Health Questionnaire–9 scores.

Results: The analysis was performed using data from 229 participants using the Super@ program. Results showed that the intervention was more costly than usual care; the discounted (3%) and nondiscounted incremental cost-effectiveness ratios were €29,367 and €26,484 per quality-adjusted life-year, respectively (approximately US $35,299 and $31,833, respectively). The intervention was cost-effective based on the €30,000 willingness-to-pay threshold typically applied in Spain (equivalent to approximately $36,060). According to the deterministic sensitivity analyses, the potential reduction of costs associated with intervention scale-up would reduce the incremental cost-effectiveness ratio of the intervention, although it remained more costly than usual care. A discount in the incremental effects up to 5% exceeded the willingness-to-pay threshold of €30,000.

Conclusions: The Super@ program, an internet-based cognitive behavioral therapy intervention for treating major depressive disorder, cost more than treatment as usual. Nevertheless, its implementation in Spain would be cost-effective from health care and societal perspectives, given the willingness-to-pay threshold of €30,000 compared with treatment as usual.

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KEYWORDS
Digital health; telemedicine; eHealth; e–mental health; internet-based cognitive behavioral therapy; depression; iCBT; implementation; cost-effectiveness; cognitive behavioral therapy; CBT; cost.

Introduction

Population aging is a global trend and is expected to be one of the most significant societal challenges worldwide in upcoming years [1]. The profound impact that this aging trend is likely to cause on our societies and economies has prompted significant efforts in turning the challenges of this scenario into opportunities for rethinking the way we design and organize our society, including the delivery of health and social care services [2-5].

Depression is a significant contributor to morbidity during entire lifespans and has been among the 3 leading nonfatal causes of disability globally for nearly three decades [6]. Although often underdiagnosed, depression is the most prevalent mental health condition among adult population and across cultural settings resulting in an aggregate point prevalence of 12.9%, 1-year prevalence of 7.2%, and lifetime prevalence of 10.8% (years 1994-2014) [7-9].

The burden of depression is specifically high among the elderly, irrespective of the presence of cognitive impairment, particularly in long-term care settings [8,10,11]. Various factors may increase the risk of depression among older people, including physiological factors (eg, cardiovascular disease, diabetes, or immunological changes) and psychosocial factors (eg, low economic status, social isolation, or relocation) [12-14]. Once established, depression in older people increases the risk of suicide and may trigger dementia [10].

While the efficacy of psychotherapy in the treatment of depression has been proven [15], the availability of evidence-based interventions constitutes a persistent challenge given the lack and unequal distribution of qualified practitioners, delayed provision of treatment, and inadequacy of treatment [16,17]. Given the limitations and health care costs associated with treating depression (eg, US $7638, according to a study conducted in Singapore [18]), there is growing interest in alternative therapies to routine care. Among them, a plethora of internet-based cognitive behavioral therapies for depression treatment have been introduced, many showing efficacy in treating major depressive disorder [19-21]. Although costs associated with the implementation of these therapies have been assessed, most studies are based on descriptive approaches, and formal cost-effectiveness analysis of internet-based cognitive behavioral therapy interventions are scarce [22].

While randomized controlled trials and accompanying cost-effectiveness analysis can be considered the gold standard in exploring the cost-effectiveness of mental health interventions, the idealized and controlled nature of these trials limits the generalizability of findings to routine care populations [23-25]. Establishing the cost-effectiveness of an intervention and its implementation under routine care conditions is an important part of the evaluation before wide-scale adoption. So far, establishing the cost-effectiveness of implementation projects in routine care provides a methodological challenge.

MasterMind was a European cofunded project aimed at scaling-up the implementation of evidence-based internet interventions (eg, internet-based cognitive behavioral therapy) for the treatment of adults experiencing depressive symptoms across Europe [26]. In this study, we assessed the cost-effectiveness of the Super@ intervention as part of its implementation within the MasterMind project in a pilot site in Spain. The current analysis was performed using the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) tool, developed for monitoring the financial sustainability of initiatives for promoting a healthy lifespan of European citizens [27,28]. Provided as a free-to-access tool for economic evaluations, MAFEIP has gained relevance over the years, and its usage is expanding, particularly within the European project landscape.

Methods

Overview of Study Design

As part of the MasterMind project for implementing an internet-based cognitive behavioral therapy for treating depression, we designed a pragmatic within-group trial to assess the cost-effectiveness of the intervention [29,30]. The evaluation framework applies the Model for Assessment of Telemedicine applications [31], which helped to define the data collection tools and instruments according to 3 levels of stakeholders involved within the implementation process: (1) patients, (2) professionals, and (3) organizations.

This analysis corresponds to the experience of the MasterMind project in the BSA (Badalona Serveis Assistencials) consortium, implemented under a program named Super@ tu depresión (“Get over your depression”). The BSA consortium provides primary and specialized care to a catchment population of 433,175 inhabitants in the most densely populated suburban area of Barcelona and has a long tradition in integrated care and the adoption of digital health solutions [32-38]. The implementation and data collection process for the Badalona pilot site was carried out between March 2015 and June 2017. The outcomes and costs of the intervention were compared with those of usual care in previously published data from the same area [39].

The local study protocol was approved by the Ethics Committee of the *Hospital Germans Trias i Pujol* (reference PI-15-069), and all participants provided informed consent before entering the study.

Participants

Study candidates included health care recipients and were screened for eligibility after general practitioner referral in the primary care setting. All consecutive patients who visited their general practitioners during the study period and met the selection criteria were offered the opportunity to participate in the Super@ program. Patients included in the study were adults (ie, 18 years or older) diagnosed with mild, moderate, or severe major depressive disorder based on the Patient Health Questionnaire 9 (PHQ-9; with score cutoffs of 10, 15, and 20 for mild, moderate, and severe major depressive disorder, respectively), living in Badalona and who, according to their general practitioner, had a certain level of technological literacy and internet connection. The main exclusion criteria were having comorbidities that may interfere with the treatment, having a nonpsychiatric disease that could explain depressive symptoms, receiving structured face-to-face psychological therapy at the time of inclusion, and reporting a high suicidal risk or ideation (item 9 of the PHQ-9). After checking all selection criteria and obtaining written informed consent, the general practitioner referred participants to the internet-based cognitive behavioral therapy service, provided a comprehensive explanation about the intervention, and enrolled participants in the platform, which automatically provided a username and a password to the participant.

Intervention

The Super@ program (Multimedia Appendix 1) consisted of 9 modules (8 regular and 1 extra) composed of videos, text content, and questionnaires to monitor the progression of symptoms and adherence to the intervention. Therapists provided guidance and project management within the BSA team to ensure patient follow-up and activation of the appropriate resources upon an increase of depressive symptoms. A project management team facilitated the project and its implementation process. Table S1 (Multimedia Appendix 1) summarizes the main activities performed in the project and the different professional profiles and teams involved in each. Intervention completion (ie, minimal adequate dose) was defined as engaging in a minimum of 3 modules of internet-based cognitive behavioral therapy.

Cost-Effectiveness Assessment

Model Structure, Transition Probabilities, and Utility Estimates

The cost-effectiveness of the Super@ program was assessed using the MAFEIP tool, which computes costs and utilities using a Markov model of health states and corresponding transition probabilities [40]. Based on previous economic evaluations of treatments for major depressive disorder, we defined a 3-state Markov model, with remission (PHQ-9 score <10), depression (PHQ-9 score r10), and death [41] (Figure 1). Transitions between the 3 states of the Markov model included recovery (ie, the probability of going from depression to remission) and relapse (ie, the probability of going from remission to depression); death was used as an absorbing state. The transition probabilities for the intervention group were calculated based on the changes between the health states at baseline and after the intervention. Given the lack of a control group, the corresponding probabilities for treatment as usual were obtained from a recent meta-analysis [41] assessing the usual care effects on major depressive disorder, which included 38 studies with pooled a remission rate (adjusted for publication bias) of 33% (95% CI 26%-40%). As suggested elsewhere [42], the risk of all-cause mortality was derived from life tables—in this case, the Human Mortality Database [43], which is stratified by gender and provides mortality rates at concrete years of age—and adjusted for depression [44].

In accordance with standard guidelines for estimating quality-adjusted life-years in economic evaluations, the MAFEIP tool recommends computing utilities based on measures of health-related quality of life, preferably the EuroQoL 5-dimension (EQ-5D) questionnaire [45]. However, no estimates of health-related quality of life were collected during the assessment of the Super@ program. Alternatively, based on the relationship between utility scores derived from

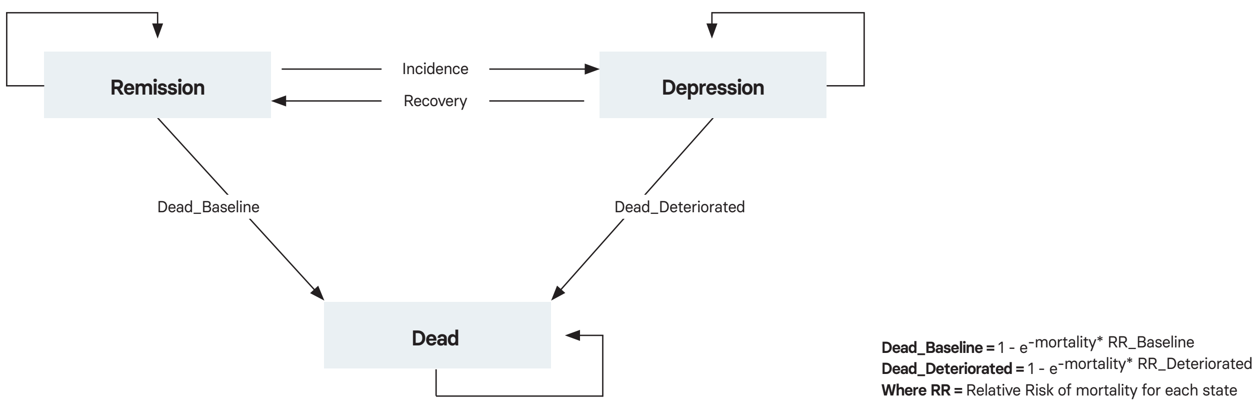

Figure 1. Diagram of the 3-state Markov model of health states and transition probabilities designed for the Super@ intervention.

(including the EQ-5D score) and depression health states reported by Kolovos et al [46], we estimated the remission utility from the results of the PHQ-9 measure: the values proposed for 4 clinical categories of major depressive disorder severity were adapted to the 3-state model by estimating the weighted average of utilities of patients in the remission state (ie, PHQ-9 score <10) and those in the depression state (PHQ-9 score r10) (Multimedia Appendix 1).

Cost Estimate

The MAFEIP tool considers 3 types of costs: one-off costs, which represent the total cost incurred only once at the implementation point (ie, implementation support, training provision of professional staff, and cost of devices), health care costs (ie, health care resources consumption such as costs associated with the time spent by health care professionals on service provision, hospitalizations, pharmacy, etc), and societal costs (ie, related to the time spent by either patients or informal caregivers such as the time spent using the technology or traveling to the hospital).

One-off costs were the main costs of implementing the Super@ services and included the support given to therapists to implement the intervention in their daily routine, the training of professional users, and the costs of development and adaptation of Super@ to the existing information and communication technology platform. Based on the annual gross salary of technical staff in Spain and the number of hours devoted to the project (ie, part-time 50%), we estimated €158 per patient (approximately US $190; an exchange rate of approximately €1 to US $1.20 is applicable at the time of publication). The costs of development and adaptation of Super@ to the existing information and communication technology platform were €237 per patient (US $285). Recurring costs, which included direct costs of each internet-based cognitive behavioral therapy session, amounted to €2439 (US $2927) per patient. For the control group, the typical situation is setting the one-off and recurrent costs at 0, because in most cases, the intervention would mean an additional investment.

Health care and societal costs were not collected in the MasterMind project. These costs were gathered from a previous study [39] that described the costs associated with major depressive disorder in the same area. Based on this study [39], we established the health care costs for patients in remission and depression as €451 and €826, respectively (US $542 and US $993). Correspondingly, the costs due to loss of labor productivity were €991 and €1842 for patients in remission and depression, respectively (US $1191 and US $2214). Health care and societal costs were assumed to be the same for the intervention and control groups.

In accordance with recommendations from local health technology assessment authorities in Spain, we applied a discount factor of 3% for both health care outcomes and costs [47]. The willingness-to-pay threshold was established at €30,000 per quality-adjusted life-year, the threshold most frequently used in Spain (equivalent to approximately $36,060).

The cycle length of the Markov model was set at 1 year (ie, the maximum allowed in the MAFEIP tool). Given the chronic nature of major depressive disorder [48], we established the number of cycles necessary to cover the time lapse between the average age of study participants (ie, 46 years) and a theoretical lifespan time of 100 years.

Analysis

The cost-effectiveness analysis was performed on the intention-to-treat sample, which included all participants who started at least 1 module of the treatment. The clinical and demographic characteristics of study participants were described with R software (version 3.5.3; The R Project) using the frequency percentage and the mean and standard deviation for categorical and quantitative variables, respectively. Variables of time were described as the median and interquartile range. The cost-effectiveness analysis was conducted using the MAFEIP tool including health states, transition probabilities, utility scores, and costs. All participants started on the state depression in the 3-state Markov model.

In addition to the base-case analysis, we conducted deterministic sensitivity analyses for 2 scenarios: reduction in session cost (up to 25%) associated with a lower professional-to-patient ratio expected for a scaling up of the intervention, and 0% to 5% discount in utilities, as recommended by local guidelines for economic evaluations [49]. Sensitivity analyses were nondiscounted.

Transition probabilities were computed using R software, whereas costs and utilities were calculated using a spreadsheet (Excel, version 2013; Microsoft Inc).

Results

Study Population and Intervention Conduct

Of the 253 patients recruited for the study, 229 participants (90.5%) started at least one module of the treatment (intention-to-treat sample), of whom 1 participant (0.4%) did not provide data on posttreatment status, and 81 participants (35.4%) did not complete treatment; therefore, 147 participants completed the treatment (Multimedia Appendix 1). All participants had been recruited during a clinical interview after referral by their general practitioner, and all completed the PHQ-9 questionnaire. Table 1 summarizes demographic and clinical characteristics of the intention-to-treat sample at baseline. Participants in the intention-to-treat sample remained under the Super@ program a median of 96 days (IQR 70-321); 147 participants (64.2%) were considered to have completed the study. At the end of the intervention, 98 participants (66.7%) had achieved the remission state. No adverse events related to the intervention or the major depressive disorder were reported.

Table 1. Clinical and demographic baseline characteristics of the participants who started the treatment.

Characteristic	Intention-to-treat sample (n=229)
Age (years), mean (SD)	46.40 (12.51)
Gender, n (%)	
Male	73 (31.9)
Female	156 (68.1)
Education, n (%)	
Primary	42 (18.3)
Secondary	100 (43.7)
Higher	78 (34.1)
Other	8 (3.5)
Not answered	1 (0.4)
Employment, n (%)	
Yes	169 (73.8)
No	58 (25.3)
Unknown	1 (0.4)
Not answered	1 (0.4)
Depressive episodes, n (%)	
Less than 4 weeks	10 (4.4)
Between 4 and 8 weeks	40 (17.5)
Between 8 and 12 weeks	65 (28.4)
Between 3 and 6 months	51 (22.3)
Between 6 months and 1 year	36 (15.7)
Between 1 year and 3 years	23 (10.0)
Between 3 and 5 years	2 (0.9)
Between 5 and 10 years	2 (0.9)
Antidepressant medication, n (%)	
Yes, for less than 1 month	7 (3.1)
Yes, for less than 2 months	44 (19.2)
Yes, for more than 2 months	74 (32.3)
No	104 (45.4)
Satisfaction with life[a], n (%)	
Preintervention	3.50 (1.16)
Postintervention	4.03 (1.28)
Satisfaction with mental health[a], n (%)	
Preintervention	3.23 (1.03)
Postintervention	3.98 (1.32)

[a]Assessed using a single-item question (How satisfied are you with your life as a whole today? or How satisfied are you with your mental health?) and rated on a 6-point scale (1=couldn't be worse, 2=displeased, 3=mostly dissatisfied, 4=mixed, 5=mostly satisfied, 6=pleased, 7=couldn't be better).

Study Parameters and Base Case Analysis

Table 2 summarizes the inputs of the cost-effectiveness analysis, including transition probabilities, costs, and utilities.

The Super@ program cost more than usual care from both health care and societal perspectives (Table 3).

Table 2. Inputs of the MAFEIP tool for computing the cost-effectiveness analysis.

Input	Control group	Intervention group (n=229)
Transition probabilities (%)		
Remission	14	0
Depression	29	48.53
Costs (€[a] per patient and year) One-off cost per patient	N/A[b]	395.26
Recurring cost per patient per year	N/A	2439
Health care cost		
Remission	451	451
Depression	826	826
Societal cost		
Remission	991	991
Depression	1842	1842
Utilities		
Remission	0.62	0.665
Depression	0.532	0.529
Relative risk of mortality		
Remission	1	1
Depression	1.68	1.68

[a]An exchange rate of approximately €1 to US $1.20 is applicable at the time of publication.
[b]N/A: not applicable.

Table 3. Incremental costs, effects, and cost-effectiveness ratio from health care and societal perspectives.

Perspective	Incremental cost (€[a])	(QALY[b])	Incremental cost-effectiveness ratio (€/QALY)
Health care perspective			
Discounted (3% for both costs and effects)	50,924.53	1.734	29,366.92
Nondiscounted	87,807.06	3.315	26,484.27
Societal perspective			
Discounted (3% for both costs and effects)	48,178.53	1.734	27,783.38
Nondiscounted	83,181.81	3.315	25,089.21

[a]An exchange rate of approximately €1 to US $1.20 is applicable at the time of publication.
[b]QALY: quality-adjusted life-year.

The nondiscounted incremental cost-effectiveness ratios were below the willingness-to-pay threshold of €30,000 (Figure 2): €26,484 and €25,089 for health care and societal perspectives, respectively (US $31,833 and $30,162). The discounted incremental costs and effects were higher, although the incremental cost-effectiveness ratios remained below the willingness-to-pay threshold of €30,000.

In addition, we conducted a deterministic sensitivity analysis assuming that a greater number of participants to the program would results in a reduction of cost per session. A 25% reduction in the cost per session would reduce the incremental cost-effectiveness ratio from €26,484 to €19,623 (US $31,833 to $23,591) in the health care perspective analysis and from €25,089 to €18,228 (US $30,162 to $21,914) in the societal perspective analysis (Figure 3A and 3B). From the health care perspective (Figure 3C), the incremental cost-effectiveness ratio at the 5% discount in utility (worst-case scenario of the sensitivity analysis) was €71,041 (US $85,405). The corresponding intersection and lowest incremental cost-effectiveness ratio values for the societal perspective were 2.773 quality-adjusted life-years and €30,000 (Figure 3D).

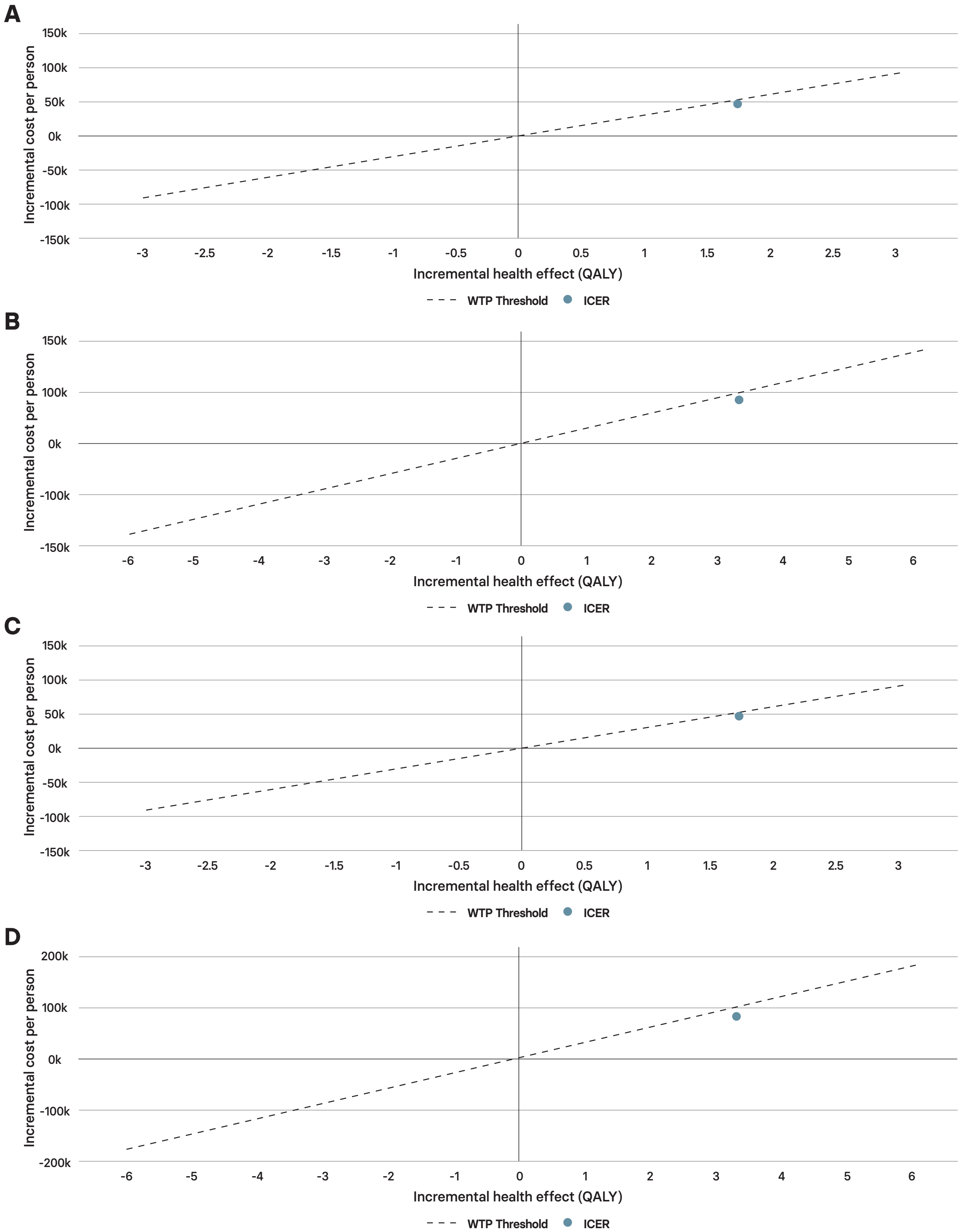

Figure 2. Cost-effectiveness plane of the Super@ intervention Healthcare perspective discounted (3% for both costs and health effects) (A) and non-discounted (B) analyses. Societal perspective discounted (3% for both costs and health effects) (C) and non-discounted (D) analyses. The solid line shows the 30,000 €/QALY willingness-to-pay threshold (equivalent to approximately US $36,060; an exchange rate of approximately €1 to US $1.20 is applicable at the time of publication). QALY: quality-adjusted life-year. WTP: willingness-to-pay.

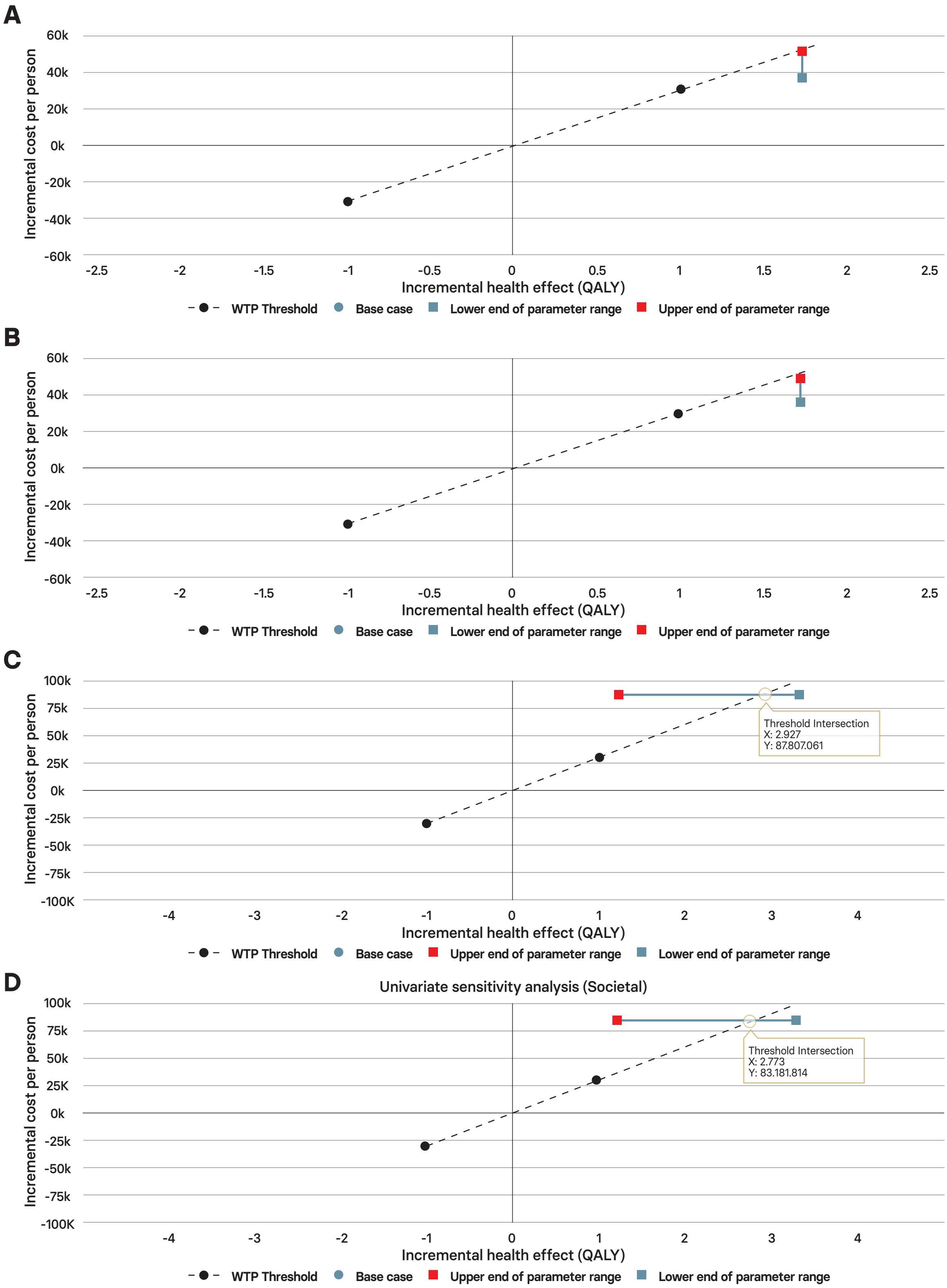

Figure 3. Cost-effectiveness planes of sensitivity analyses. A reduction of up to 25% in cost per session (A and B for healthcare and societal perspectives, respectively), and 0% to 5% discount in effects (C and D for healthcare and societal perspectives, respectively). The dotted black line shows the 30,000 €/QALY willingness-to-pay threshold (equivalent to approximately US $36,060; an exchange rate of approximately €1 to US $1.20 is applicable at the time of publication). The solid green line shows the range of the incremental cost-effectiveness ratio, with the red and green squares indicating the range extremes for the worse (more costly or less effective) and best (less costly or more effective) scenario, respectively. QALY: quality-adjusted life-year. WTP: willingness-to-pay.

Discussion

In this analysis of the cost-effectiveness of an internet-based cognitive behavioral therapy intervention for mild or moderate major depressive disorder, we found that the intervention was more effective than treatment as usual, with incremental costs of €87,807 and €83,181 (nondiscounted from the health care and societal perspectives, respectively; US $105,561 and $99,999), according to costs reported for routine care of patients with mild-to-moderate major depressive disorder in our area (Badalona, Spain). Despite the higher cost of the internet-based cognitive behavioral therapy intervention, it remained below the willingness-to-pay threshold of €30,000 typically used in Spain for making decisions in health care policies. According to the sensitivity analyses, the internet-based cognitive behavioral therapy would remain more expensive and more effective than treatment as usual in the onset of the cost reduction expected when scaling up the intervention (with the consequent decrease of the professional-to-patient ratio), with an incremental cost-effectiveness ratio below the willingness-to-pay threshold. When considering a 5% reduction in utility (ie, as suggested by local guidelines for economic evaluations), the intervention remained more effective than treatment as usual, although with an incremental cost-effectiveness ratio above the willingness-to-pay threshold.

In the last decade, many studies [50-53] have investigated the costs associated with internet-based cognitive behavioral therapy interventions, including therapies for major depressive disorder; however, most are based on descriptive approaches, which preclude drawing conclusions that can be used for making decisions on their implementation. More recently, Paganini et al [22] reviewed economic evaluations of internet-based cognitive behavioral therapy interventions for major depressive disorder that fulfilled preselected quality criteria, including the presence of comparator groups such as treatment as usual, another intervention, or wait-list controls. The case-mix of these interventions and heterogeneity of analyses precludes direct comparisons regarding the cost-effectiveness of each intervention. Nevertheless, they found that guided interventions (such as the Super@ program) tended to be more cost-effective than self-help ones, despite the higher cost associated with professional honoraria [22]. The incremental cost-effectiveness ratio of our intervention for the base-case health care perspective (€26,484 per quality-adjusted life-year) was in the lower zone of the wide range of values reported for guided interventions (ie, €19,616 [54] to €157,900 [55]; approximately US $19,616 and $189,825, respectively) and below that of unguided interventions (ie, €40,412 [56] to €178,700 [57]; approximately US $48,583 and $214,831, respectively).

Additionally, such studies [51,52] can only report on cost-effectiveness measures in controlled settings. Our study focused on the assessment of cost-effectiveness under real-world conditions free from biases possibly being introduced within efficacy studies such as a stricter application of protocolized procedures, eligibility criteria, and randomization [23-25]. Nevertheless, this approach resulted in some disadvantages, and our results should be interpreted with caution due to several limitations.

The lack of a comparator group has been considered among the limitations of economic evaluations of internet-based cognitive behavioral therapy interventions for major depressive disorder [22]. The pragmatic approach of our study, which took advantage of the implementation of the Super@ program by the local health care provider to assess its cost-effectiveness, precluded collecting treatment-as-usual data in parallel with Piera-Jiménez et al those collected for the internet-based cognitive behavioral therapy intervention; however, the MAFEIP tool allowed us to rely upon literature for gathering these data. Of note, the source of cost-estimate data of treatment as usual for major depressive disorder corresponded to the same area in which the Super@ program was deployed [39]. Hence, the costs attributed to treatment as usual are expected to be similar to those we would have observed in a control group.

The MAFEIP tool also allowed us to bypass the unavailability of EQ-5D scores of health-related quality of life, a widely accepted measurement for computing utilities in cost-effectiveness analyses [45,58]. Other measures, such as disease severity scores, have been proposed as a proxy for health-related quality of life [59]. Taking advantage of the analysis by Kolovos et al, who established a relationship between health-related quality of life and PHQ-9 score for major depressive disorder severity [46], we computed the utility of the remission state of our 3-state Markov model using the PHQ-9 scores at the cutoff for minor depressive symptoms in the 5-state scale defined by the American Psychiatric Association [60] and the National Institute for Clinical Excellence [61].

Readers should take into consideration some limitations of the study design. First, the pragmatic approach constrained the number of participants to the implementation capacity, rather than the adequate sample size to achieve precision in our estimates. Second, like many other information and communication technology-based solutions, the success of an internet-based cognitive behavioral therapy intervention requires minimal technological literacy, which in our intervention was measured in an unstructured way at each general practitioners discretion. Technological literacy and keenness for the use of digital gadgets are expected to influence not only adherence but also the benefit that the patient may obtain from the intervention; the unstructured assessment of digital literacy may have introduced heterogeneity in the intervention outcomes. Third, the transferability of the results to other settings should be considered carefully. There are many reasons why cost-effectiveness analysis of health technologies may differ across jurisdictions and researchers and implementers should always refer to national guidelines in order to shed some light on the applicability of the results emerging from other contexts [62].

Our results suggest that the Super@ program provided benefits to patients at a cost that would allow its implementation in Spain, where interventions below €30,000 per quality-adjusted life-year are accepted. Costs associated with the intervention are expected to decrease in a scaling-up scenario; however, the sensitivity analysis of utility indicates that small reductions in effects would place the intervention at a nonacceptable incremental cost-effectiveness ratio based on the €30,000 threshold. Future studies should explore the patient profile that can benefit most from the intervention so that general practitioners have more information to target the therapy adequately.

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Authors' Contributions

JPJ was the principal investigator at the Badalona pilot site for the MasterMind project. JPJ and AE contributed to the study design and data collection. JPJ and AE conducted the statistical analyses. JPJ drafted the manuscript. AE and SK contributed to the different versions of the paper. FLV and FF supervised the study. All authors critically revised and approved the final version of the manuscript.

Conflicts of Interest

Author AE is employed by the Institute for health training online as research coordinator. All other authors declare no competing interests.

Multimedia Appendix 1

Supplementary file 1.

[PDF File (Adobe PDF File), 279 KB-Multimedia Appendix 1]

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Abbreviations

BSA: Badalona Serveis Assistencials.
EQ-5D: EuroQoL 5-dimension questionnaire.
MAFEIP: Monitoring and Assessment Framework for the European Innovation Partnership (on Active and Healthy Ageing).
PHQ-9: Patient Health Questionnaire–9.

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5. CONCLUSIONS

5.1 Summary of main findings

In respect of the three research questions:

Research question #1: In adult patients with cardiovascular disease managed in the outpatient setting, would a mHealth-driven intervention for behavioral life-style change increase the patients' quality of life in a cost-effective manner compared with usual care?

The starting point of this Ph.D. thesis consisted of a study aimed to provide evidence and gain understanding on the financial consequences of implementing a behavioral change mHealth intervention for the prevention and control of CVDs (Chapter 2). For assessing the digital health intervention (DHI), we constructed an evaluation framework using as a basis the Model for Assessment of Telemedicine (MAST) [1]. The study was a proof of concept conducted in a multisite randomized controlled trial (RCT) involving three different countries: Spain, the Netherlands, and Taiwan [2]. The cost-effectiveness analysis was based on a Markov model of five health states and used the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing (MAFEIP) [3] tool to perform the outcome estimates. The health states were established based on the systolic and diastolic blood pressure according to the classification of the American Heart Association and the utilities estimated using the EQ-5D-3L instrument from the EuroQol Group [4] as recommended by Health Technology Assessment bodies in Spain [5].

A total of 75 patients were involved in the Catalan pilot site. Of these, 38 received the new DHI, while 37 received treatment as usual. The intervention showed high adherence rates that we claim are associated to the personalized nature of the intervention (e.g., behavioral nudges, personalized feedback according to performance and remote monitoring devices). Despite the methodological limitations, the intervention was considered cost-effective (less costly: incremental costs -2,514.90€, less effective: incremental effects -0.134).

Answer to research question #1:
The intervention delivered within the Do CHANGE project proved to be cost-effective (less costly and less effective) and helped us to showcase the capabilities of digital health technologies to tackle with the most prevalent group of chronic conditions (CVDs) throughout a secondary prevention intervention. Furthermore, our results demonstrate the high heterogeneity that digital health interventions might show depending on the country where they are implemented and recommend assessing them in each setting before scaling up.

Research question #2: In complex chronic patients managed in an integrated care domiciliary setting, would a telehealth and telecare intervention be cost-effective when compared to usual care?

In Chapter 3, the focus of the cost-effectiveness assessment was shifted towards a DHI aimed to support domiciliary care of complex chronic patients. The main characteristics of the intervention provided in the BeyondSilos project were the following: a) involvement of a multidisciplinary team of professionals from various healthcare levels, b) involvement of social care professionals and providers (including the volunteer organizations from the third sector), c) continuous remote monitoring through a telehealth and telecare platform, and d) access to shared information for all involved parties (including formal and informal caregivers). The DHI was analyzed throughout a quasi-experimental study compared to basic health and social care coordination in a group of 198 patients (98 in intervention and 100 in control group). The evaluation framework was also defined according to the MAST model. After the analysis period, the Instrumental Activities of Daily Living significantly decreased in both groups, the Geriatric Depression Scale remained unchanged and a significant change in the Barthel index was found in the comparator group possibly associated to the differences among study groups at inclusion.

The cost-effectiveness analysis was modeled using a 3-state Markov model and was calculated with the MAFEIP tool. Utilities were computed using the change in the Barthel index as a proxy of the health-related quality of life [6]. The intervention proposed in the BeyondSilos project was deemed cost-effective and accepted for all willingness-to-pay (WTP) thresholds above 6,500€, far below the traditional thresholds considered in Spain.

Answer to research question #2:
The ICT-enhanced integrated health and social care intervention provided by the BeyondSilos project effectively covered patients' needs and was considered cost-effective (more costly and more effective) compared to a basic integrated care service. The quasi-experimental design followed by the project allowed us to identify the challenges for implementation in real-world scenarios, which in our case related to the commitment of professional staff with the model and the difficulties to quantify the different contribution of each element to costs.

Research question #3: In adult patients with Major Depressive Disorder managed in the primary care setting, would an Internet-based Cognitive Behavioral Therapy intervention be cost-effective when compared to usual care?

Finally, Chapter 4 describes the implementation and cost-effectiveness analysis of an Internet-based Cognitive Behavioral Therapy to support patients with major depression syndrome in Badalona. This project did not aim to test a new intervention but to implement already existing evidence-based iCBT solutions [7]. In our case, the intervention "Super@ tu Depresión" was offered to 253 recruited patients. Following the same pathway as in the previous DHI, the evaluation framework was designed according to the MAST model and the cost-effectiveness was calculated with the MAFEIP tool.

In MasterMind, the cost-effectiveness was performed on the intention-to-treat sample (participants who started at least one module of the online treatment). The pragmatic approach of our study did not allow to collect data from treatment as usual, thus data for this group had to be inferred from the scientific literature (i.e., costs, utilities and transition probabilities). Our results suggest that the "Super@ tu Depresión" program was more costly (incremental costs 87,807.06€) and more effective (incremental effects 3.315 QALY) but provided an incremental cost-effectiveness ratio (26,484.27 €/QALY), below the WTP threshold of 30,000€ commonly used in Spain.

> **Answer to research question #3:**
> The Internet-based Cognitive Behavioral Therapy intervention implemented in the context of the MasterMind project was considered cost-effective (it delivered better health outcomes at higher costs) when compared to standard care. Economies of scale would likely help reduce the costs when upscaling the intervention, however the sensitivity analysis showed that small reductions in health outcomes would position the intervention above the WTP-threshold, thus nonacceptable.

In respect to the main objective:

The main aim of this thesis was to assess the cost-effectiveness of digital health solutions designed to support the management of major chronic conditions that can be implemented within the Catalan health system an ultimately help inform health systems for future deployments.

The implementation of digital health solutions aimed to support the management of major chronic conditions within the Catalan health system can provide cost-effective results.

Barriers towards the implementation are nontechnological and relate to other aspects such as the organizational structure, governance and professionals' culture.

5.2 Reflections on the main findings

The pathway to disseminating results in the scientific sphere is driven by well-established quality guidelines that guide the reader towards the main point of the research results [8]. The internal structure of high-quality scientific manuscripts allows discriminating between aseptic conclusions arose from results and personal opinions of researchers. Given the vast amount of research published every year, this style is a mainstay for scientific advance. However, it loses sight of personal experiences and subjective appraisals that may help other researchers continue along the path towards the ultimate research goal.

In a dissertation by compendium of articles, it is therefore necessary to reserve a place to express these opinions that in the framework of scientific research have not been able to be demonstrated in an unequivocal way but on the other hand are valuable and can bring knowledge, and ultimately advance science. Thus, this section aims to be a compilation of learning and experiences during the long period of execution of this thesis and with a very personal vision that aims to advance the implementation of digital health in the Catalan health system environment.

Reflections on digital health assessment frameworks
Systems and entities providing health services are currently absolutely inundated with a large volume of studies that incorporate digital health technologies. Regardless of whether they have been promoted by a health professional, a pharmaceutical laboratory, a technology start-up, an initiative of the national health system or the pressure of the consumer market, all have in common the need to evaluate these solutions before being introduced into routine care. We are talking about a wide range of professionals who, in many cases, do not have sufficient knowledge about the scientific method and the particularities of healthcare to carry out these processes. The most common is that all these projects begin with the definition of a study protocol aimed to assess the possible benefits of the proposed intervention.

The first reflection is on the need to standardize these evaluation processes to have research results that are as homogeneous as possible and that facilitate comparison and interpretation by the competent authorities [9]. In this sense, it is important considering the perspectives of all stakeholders in the value chain and taking into account the different dimensions associated with the deployment of the new intervention (and not only the ones related to the health and economic outcomes) [10]. Having standard evaluation frameworks would save effort at the start of every project.

In the framework of the three studies that make up this dissertation, the evaluation framework that was used is the MAST. This is a model that originated in a European project (MethoTelemed) [11], precisely with the idea of solving the aforementioned problems. The MAST method has gained relevance in recent years, especially in the field of European projects, and in some regions such as Denmark it has become a standard adopted at country-level for the evaluation of digital health solutions. MAST is based on the EUnetHTA Core Model [12], but instead of having 9 domains of interest like the original, it has 7 that merge the content of the others. This model provides researchers with a three-dimensional evaluation framework (stakeholders involved in the intervention, domains of interest, and use cases of technology) that allows systematization of the design of evaluation processes so as not to forget any important aspect in the evaluation process. It is worth noting the versatility that MAST has demonstrated in many projects and supporting different study designs. Finally, it is also worth mentioning the theoretical adoption of the MAST methodology for the Catalan health system throughout the LATITUD project [13], led by the TICSalut i Social Foundation and participated by the Health Quality and Evaluation Agency and the Catalan Health Service. *The model is there, it is time to move from design to action and start pushing its usage throughout the Catalan health system.*

Reflections on study designs in digital health assessment

Randomized controlled trials (RCTs) are considered the most rigorous type of study design to investigate health interventions. These studies are very strict in the processes of incorporating individuals into the trial and in the methods of intervention [14]. The RCT design, originally suited for investigating the efficacy of active molecules under ideal conditions, can yield results which are far from those expected in the real world, particularly when assessing DHI, whose adequate implementation strongly depends on attitudes of the stakeholders. For this reason, more and more voices are calling for an approach that is closer to what the intervention would be like in the usual clinical practice and not in an environment as controlled as that of the RCTs [15].

This dissertation presents three different types of studies (RCT, cohort study, and implementation study) that somehow illustrate the benefits of some models over others. Therefore, it should not be common to find systematic differences between study groups in an RCT if the inclusion and exclusion criteria, randomization criteria, and sample size have been well defined from the beginning. On the other hand, it is more common for this to happen in quasi-experimental study designs, but their results will surely be more applicable in real clinical practice settings.

Pragmatic trials are much more flexible than RCTs with respect to routine treatment. In fact, they are so flexible that the variation that may exist in the control group can cause differences in effectiveness outcomes between different sites of intervention. This, which could be identified as a drawback of such trials, should be seen as an opportunity to observe how the new treatment would be implemented in a real environment including the whole gradation of possibilities [16].

Another aspect that should not be overlooked is the costs associated with conducting an RCT. These types of studies involve a great clinical and administrative burden which, in most cases, is translated into a duplication with respect to treatment as usual and, therefore, an associated effort that translates into more professional time [17]. It is common that in RCTs the pressure to reach the number of patients to be included may create a tendency among recruiters to relax inclusion criteria and may translate into differences between study groups.

A growing group of scientists are advocating towards providing study results that focus on the external validity of results (those being generalizable in real-world scenarios) rather than in the internal validity (those preventing bias). Pragmatic RCTs could provide a solution to such situations by removing possible biases due to the lack of randomization and still deliver some evidence related to the implementation in real-world settings [15,16]. *Catalonia should explore the usage of this type of study designs when implementing DHIs.*

Reflections on the economic evaluation of digital health

One of the promises of digital health has been cost containment for all stakeholders in the value chain. Avoiding unnecessary travel for both patients and relatives, increasing the reach of interventions to larger populations, improving the effectiveness of treatments due to more personalized and appropriate care, or the deployment of public health policies through digital channels are just some examples [18]. In this context, the need to unequivocally measure the effects of these digital health interventions from an economic perspective is clear.

For a long time, the world of digital health has been mirrored to the world of pharmacoeconomics to develop economic studies on the impacts of interventions. Among the different methods used in drug research are for: cost-effectiveness studies, cost-benefit studies, cost minimization, cost-utility studies, among others [19]. Traditionally, Health Technology Assessment (HTA) agencies have encouraged the reimbursement of those new technologies that report a quantification of the additional cost of using the technology in relation to health effects [20]. Solutions are introduced in routine care as long as they are within a threshold that the health system or the user are willing to pay. In these models, the gold standard for measuring health effects has historically been the quality-adjusted life-years (QALY) used in cost-effectiveness or cost-utility analysis. QALYs relate the effects of a specific technology to the effects on health outcomes through improvements in quality of life and mortality [21].

For the three studies presented in the framework of this thesis, the Model Assessment Framework for the European Innovation Partnership on Active and Healthy Aging (MAFEIP) has been used. This tool allows modelling cost-effectiveness studies in a very simple way through a web platform that is fed from the inputs provided by the user. MAFEIP has proven to be a very versatile and relatively easy-to-use tool as it provides guidance for all those people who are not experts in health economics. Proceeding in such a way, *this tool could help carrying out the processes of economic evaluation of digital health solutions for all those public and private institutions that do not have the expert resources in this specific matter.*

Reflections on what is needed to implement digital health

Chapter 1 of this dissertation gives a series of arguments to justify the reasons for digital health not being deployed at-scale. Among the different barriers for the adoption, we can find issues related to scientific evidence, organizational issues, resistance to change by both professionals and patients, ethical questions, and also issues related to legal frameworks. While it is true that the non-implementation of digital health is associated with barriers that are multidimensional, there are some aspects that have a greater impact compared to the rest.

Digital health interventions have little or nothing to do with the introduction of new pharmacological treatments where, in a very simplified way, a new drug is introduced for a particular health problem with the idea of getting better health outcomes. In contrast, the nature of such interventions is closer to new clinical pathways or healthcare delivery models, where implementation goals may go beyond the pursuit of improved health outcomes [10]. In such scenarios, other aspects can be considered as for example the accessibility or equity. The introduction of a new DHI usually requires changes in organizational workflows, changes that by nature professionals and patients will resist, changes to which must be added the difficulty of using the technologies that not everyone has to feel comfortable with, in short, changes that disrupt the usual activities of healthcare organizations [22]. In this sense, the deployment of digital health technologies in routine care is much more complex than it might seem and requires several multidisciplinary capabilities that are not always available in the organizations where deployments are to be made [23]. *Catalonia needs to advance in the field of implementation science and in the incorporation of professionals specialized in this area in order to improve adoption.*

Many times, professionals who work in technology tend to take for granted a series of concepts that do not have to be understood by healthcare workers and patients. We arrive at healthcare organizations with great technological developments, with the idea of saving the world, but we leave aside the question of whether the professionals who have to interact with these technologies are clear about what we are talking about. The way health professionals, especially physicians and nurses, are being taught has changed very little in recent years, while technology has been advancing by leaps and bounds [24]. If we want health professionals to embrace these deployments and identify opportunities for digital transformation, we must equip them with the knowledge to make this possible. Some regions have long been aware of this need and have implemented strategies such as the NHS Digital Academy in the UK [25] or the GCC Taskforce on Workforce Development in Digital Healthcare in the UAE are good examples. *Catalonia should advance in this line too and provide its workforce with the appropriate digital health knowledge.*

When the research period for this thesis began, the evidence for the benefits of digital health solutions was relatively small. Now, there is growing evidence of the virtues of some of these solutions. A relevant fact in this process has been the great deployment that digital health technologies have experienced due to the pandemic caused by COVID-19 [26]. With the objectives of protecting health professionals and citizens from possible infections and with the idea of guaranteeing continuity of care, there has been a great adoption of these solutions around the world, also in Catalonia [27].

However, digital health solutions do not usually escalate and tend to disappear after the piloting phases [28]. If we use as an example the three solutions that were tested in the framework of this thesis, only one of the solutions is still in operation. Why are solutions that have proven their benefits in health outcomes and in economic terms not routinely deployed? The answer is simple and is related to the financing or reimbursement model. A digital health solution which is good in terms of health outcomes, saves costs for the system and has a better acceptance by users and professionals does not necessarily mean is going to be deployed in routine care.

So, what's the problem? In Catalonia we have a reimbursement system that mostly recognizes activity-based actions. This model, which is more than 30 years old, does not consider the contribution on value for DHIs that save costs to the system (for example hospital admissions) since the provider institutions precisely invoice activities such as hospital stays [29]. This immobility and lack of update of the funding model results in many solutions that are beneficial to the individual, formal and informal caregivers, and globally to the health system not being deployed by healthcare providers because it goes against their funding. I call this process, the perversion of the financing system. This situation poses an ethical challenge for many professionals working in the field who see solutions that could be beneficial to the public are not being deployed. The saddest thing is that this situation has nothing to do with the cost-effectiveness of these solutions but with a lack of willingness to update the healthcare delivery model and associated reimbursement schemes. *Decisive action by the competent authorities is therefore needed to provide incentives to healthcare providers implementing DHIs.*

5.3 Suggestions for future research

Even though the focus of this thesis was the Catalan health system, the suggestions for future research can help inform other health systems about the main problems related to the implementation of DHIs.

Research on the cost-effectiveness of DHIs is an area of outmost interest given the sustained increase of costs for healthcare systems worldwide. The provision of good quality research in the field can help inform policy makers and ultimately advance in the implementation of innovative interventions to ensure the sustainability of healthcare systems. The previous section on final reflections and recommendations identified a series of pressing issues for the Catalan health system that can help put forward some suggestions for future research:

1. Decision makers struggle to understand evaluation outcomes for DHIs. Advancing in the standardization of evaluation frameworks is an option that should be explored. Future research should aim to identify candidate assessment tools and validate its benefits when providing homogeneous easy-to-understand results for policy makers. In the specific case of Catalonia, extending and validating the model proposed by the LATITUD project should be a priority.
2. RCTs provide strong evidence but require a lot of effort by all professionals involved. Solutions at early stages of development may benefit from less strict study designs. At the same time, there is a growing need to gain knowledge about the implementation results of such solutions in real-world settings. An interesting course of research action should be fostering pragmatic studies in the field of digital health.
3. The QALY approach used in cost-effectiveness and cost-utility analysis only considers the gains in terms of health outcomes (improved quality of life and mortality) related to the implementation of a new technology. If the implementation of DHIs is multidimensional so are the possible benefits. A growing amount of academics suggest that only considering the health outcomes in relation to the implementation of technologies leaves aside other types of benefits. Because of this, future research should focus on other approaches to measure the implementation benefits such as Multicriteria Decision Analysis [30].
4. The implementation of DHIs in routine care is a complex matter that should not be underestimated. Classic change management approaches may not suffice when trying to introduce new technological means in healthcare settings. Globally, implementation science is advancing and may provide useful information for those wishing to implement DHIs. Further research is needed on the application of implementation science approaches in the Catalonian healthcare system.
5. Reimbursement models remain static and not provide incentives for healthcare providers to implement DHIs. Changes in the financing model are complex and should be considered carefully because they may have a strong impact in healthcare organizations. An interesting research line emerging from this issue relates to the investigation of new financing schemes for healthcare organizations considering the implementation of DHIs and the impacts on service provider budgets.

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APPENDIX I

This appendix includes all the research-related activities conducted during the development of this Ph.D. project.

6.1 Publications included in this thesis

This section contains the main compendium of publications included in this Ph.D. thesis.

Table 7.1 Set of articles included in this thesis.

	Title	Journal	Impact Factor *	Quartile	Authorship position
1	Changing the Health Behavior of Patients With Cardiovascular Disease Through an Electronic Health Intervention in Three Different Countries: Cost-Effectiveness Study in the Do Cardiac Health: Advanced New Generation Ecosystem (Do CHANGE) 2 Randomized Controlled Trial	Journal of Medical Internet Research	5,034	Q1: Medical Informatics Q1: Health Care Sciences & Services	1
2	BeyondSilos, a Telehealth-Enhanced Integrated Care Model in the Domiciliary Setting for Older Patients: Observational Prospective Cohort Study for Effectiveness and Cost-Effectiveness Assessments	JMIR Medical Informatics	2,577	Q2: Medical Informatics	1
3	Guided Internet-Based Cognitive Behavioral Therapy for Depression: Implementation Cost-Effectiveness Study	Journal of Medical Internet Research	5,034	Q1: Medical Informatics Q1: Health Care Sciences & Services	1

(*) Impact factor according to InCites Journal Citation Reports for year 2019.

6.2 Publications not included in this thesis

This section includes all the other scientific publications (published, submitted and peer-reviewed) for the same research period of this thesis that are not part of the main compendium.

6.3 Published articles

Table 7.2 Set of articles not included in this thesis.

	Title	Journal	Impact Factor *	Authorship position
1	Protocol for regional implementation of community-based collaborative management of complex chronic patients	npj Primary Care Respiratory Medicine	3,231	14
2	Enhancing Lifestyle Change in Cardiac Patients Through the Do CHANGE System ("Do Cardiac Health: Advanced New Generation Ecosystem"): Randomized Controlled Trial Protocol	JMIR Research Protocols	-	3
3	The Reference Site Collaborative Network of the European Innovation Partnership on Active and Healthy Ageing	Translational Medicine @ Unisa	-	132

4	Evaluation of integrated care services in Catalonia: population-based and service- based real-life deployment protocols	BMC Health Services Research	1,987	20
5	Usefulness of a Lifestyle Intervention in Patients With Cardiovascular Disease	American Journal of Cardiology	2,570	6
6	Personalized eHealth Program for Life-style Change: Results From the "Do Cardiac Health Advanced New Generated Ecosystem (Do CHANGE 2)" Randomized Controlled Trial	Psychosomatic Medicine	3,702	8
7	Turning the Crisis Into an Opportunity: Digital Health Strategies Deployed During the COVID-19 Outbreak	JMIR Public Health and Surveillance	-	Last
8	Type D personality and global positioning system tracked social behavior in patients with cardiovascular disease	Health Psychology	3,052	7
9	Dimensionality of the system usability scale among professionals using internet-based interventions for depression: a confirmatory factor analysis	BMC Psychiatry	2,704	14
10	A Personalized eHealth Intervention for Lifestyle Changes in Patients With Cardiovascular Disease: Randomized Controlled Trial	Journal of Medical Internet Research	5,034	7
11	Patient Identification Techniques – Approaches, Implications, and Findings	Yearbook of Medical Informatics	-	2
12	The emergent potential of mundane media: Playing Pokémon GO in Badalona, Spain	New Media & Society	4,577	Last
13	Tailored implementation of internet-based cognitive behavioural therapy in the multinational context of the ImpleMentAll project: a study protocol for a stepped wedge cluster randomized trial	Trials	1,883	6
14	Characteristics of citizens and their use of teleconsultation in Primary Care in the Catalan public health system before and during COVID: Retrospective Descriptive Cross-Sectional Study	Journal of Medical Internet Research	5,034	10

(*) Impact factor according to InCites Journal Citation Reports for year 2019.

6.4 Book chapters

Table 7.3 Book chapters.

	Book title	Chapter title	Editor	Authorship position
1	Hybrid Play: Crossing Boundaries in Game Design, Players Identities and Play Spaces	Chapter 9: Haptic Play	Routledge	3

6.5 Submitted articles

Table 7.4 Set of submitted articles.

	Title	Journal	Impact Factor *	Authorship position	Status
1	A systematic analysis of the multi-annual journey of Badalona towards integrated care	International Journal of Integrated Care	2,753	Last	Under peer-review
2	Web App for Emotional Management During the COVID-19 Pandemic: Platform Development and Retrospective Analysis of Its Use Throughout Two Waves of the Outbreak in Spain	JMIR mHealth and uHealth	4,313	6	Under peer-review
3	Determinants of Catalan public primary care professionals' intention to use digital clinical consultations (eConsulta) in the post-COVID-19 context: optical illusion or permanent transformation?	Journal of Medical Internet Research	5,034	10	Under peer-review
4	Performance of Quantitative Measures of Multimorbidity: A Population-Based Retrospective Analysis	BMC Public Health	2,521	7	Under peer-review
5	Development and performance of a population-based risk stratification model for COVID-19	European Journal of Epidemiology	7,135	10	Submitted

(*) Impact factor according to InCites Journal Citation Reports for year 2019.

6.6 Articles as peer-reviewer

Table 7.5 Peer-reviewed articles.

	Title	Journal	Impact Factor *	Status
1	Health outcomes from home hospitalization: Multisource predictive modeling	Journal of Medical Internet Research	5,034	Published
2	Harnessing digital health technologies during and after the COVID-19 Pandemic: Context matters	Journal of Medical Internet Research	5,034	Published
3	Adoption of digital technologies in health care during the COVID-19 pandemic: Systematic review of early scientific literature	Journal of Medical Internet Research	5,034	Published
4	Feasibility of a voice-enabled medical diary app (SpeakHealth) with caregivers of children with special healthcare needs and healthcare providers: A mixed methods study	JMIR Formative Research	-	Published

(*) Impact factor according to InCites Journal Citation Reports for year 2019.

6.7 Editorial roles

Table 7.6 Editorial roles.

	Issue title	Journal	Publisher	Role
1	Advancing Integrated Care with Digital Health Innovation	Journal of Integrated Care	Emerald	Guest Editor

6.8 Scientific and non-scientific conferences

This section aims to include all the scientific and non-scientific conferences where the author has been part with different roles during the research period of this Ph.D. thesis.

Table 7.7 Scientific and non-scientific conferences.

	Conference	Date	Activity	Location	Session
1	XXXVIII Congreso Nacional de la Sociedad Española de Medicina Interna (SEMI)	24/01/17	Poster presentation	Madrid (Spain)	BeyondSilos: Resultados de la asistencia integral con telemonitorización tras evento agudo
2	HIMSS17	20/02/17	Presentation	Orlando (United States of America)	Coordinating care through the Continuity of Care Maturity Model
3	BeyondSilos and CareWell Final Conference	28/02/17	Presentation	Barcelona (Spain)	Lessons learned from CareWell and BeyondSilos
4	HIMSS Liège	29/03/17	Presentation	Liège (Belgium)	Soins intégrés en Europe
5	International Conference of Integrated care 2017	09/05/17	Poster presentation	Dublin (Ireland)	The Badalona Story: integrating the integration initiatives
6	URBACT City Festival	04/10/17	Presentation	Tallinn (Estonia)	Spotlight on good practices: Building an age-friendly city
7	Week of Health and Innovation 2017	10/10/17	Presentation	Odense (Denmark)	Badalona moving towards an innovative urban age-friendly city
8	9th ISRII Scientific Meeting	11/10/17	Poster presentation	Berlin (Germany)	Evidence-based Tailored Implementaton Strategies for eMental Health - The ImpleMentAll Project *
9	Master on Integrated Care – Faculty of Medicine (Università degli Studi di Udine)	12/10/17	Opening keynote	Udine (Italy)	Una realtà innovativa di integrazione sociosanitaria: l'esperenzia della BSA
10	Cuidados Integrados	20/10/17	Presentation	Amadora (Portugal)	Building an age-friendly city
11	Jornada PRL i noves tecnologies en l'àmbut sanitari	06/02/18	Presentation	Barcelona (Spain)	Disseny i implantació de les app TeledermatoBSA i super@ tu depression

12	European Innovation Partnership on Active and Healthy Ageing Conference of Partners 2018	28/02/18	Presentation	Brussels (Belgium)	MAFEIP 2.0: Decision to invest, Decision to buy
13	South by Sount West (SXSW)	11/03/18	Presentation	Austin (United States of America)	SXSW eHealth Program
14	23rd Congress: Coordinated and Personalized Healthcare	24/04/18	Opening keynote	Katowice (Poland)	The story of Badalona after 18 years integrating health and social care
15	HIMSS18 Europe	29/05/18	Presentation, moderator, and jury	Sitges (Spain)	Young innovators competition
16	Unitss: jornades tècniques	13/06/18	Presentation	L'Hospitalet de Llobregat (Spain)	Model d'innovació de Badalona Serveis Assistencials
17	Symposium: Rethinking healthcare for the future	05/07/18	Presentation	Barcelona (Spain)	Building an age-friendly city
18	Connected Health Cluster	23/08/18	Presentation	Tallinn (Estonia)	Taking innovative solutions beyond pilots: what does it take?
19	Do CHANGE Final Conference	25/09/18	Presentation	Eindhoven (The Netherlands)	Cost-effectiveness analysis via the MAFEIP tool
20	27th EAHM Congress	27/09/18	Presentation	Estoril (Portugal)	Going for Integrated Care: What does it take?
21	Week of Health and Innovation 2018	10/10/18	Presentation	Odense (Denmark)	Did you know this about eHealth implementation? Taking innovations beyond pilots
22	Incontro HIMSS Italian Community	12/12/18	Presentation	Rome (Italy)	La gestione digitale della continuità di cura nel sistema sanitario italiano ed in alcune realtà europee
23	HIMSS19	10/02/19	Presentation	Orlando (United States of America)	Coordinating care through the Continuity of Care Maturity Model
24	Reinventar Comunidade	29/03/19	Presentation	Lisboa (Portugal)	Interagindo com o Envelhecimento: A experiência da Cidade de Badalona
25	International Conference for Integrated Care 2019	04/04/19	Presentation	Donosti (Spain)	A systematic analysis of the multi-annual journey of Badalona towards integrated care
26	Towards evidence-based tailored implementation strategies for eHealth	07/05/19	Presentation	Torino (Italy)	Data quality / collection process
27	HIMSS19 Europe	12/06/19	Presentation	Helsinki (Finland)	Getting implementation right
28	Foro de transformación sanitaria. Ciencia de datos y Big Data en Salud	27/06/19	Presentation	Bilbo (Spain)	¿Cómo montar unidades de análisis de datos masivos?

29	European Innovation Partnership on Active and Healthy Ageing Conference of Partners 2019	25/09/19	Presentation	Aarhus (Denmark)	MAFEIP - What does it take to go for cost-effectiveness evaluation?
30	9th AHIMA World Congress - Helathcare Information Summit	03/10/19	Presentation	Abu Dhabi (United Arab Emirates)	Implementation of Electronic Medical Records and relationship with social services
31	Health Outcomes Observatories	09/10/19	Presentation	Utrecht (The Netherlands)	Developing a health outcomes observatory
32	GCC eHealth Workforce Development Conference	02/11/19	Presentation	Dubai (United Arab Emirates)	Population Health & AI Executive Meeting
33	3rd NATIONAL CONFERENCE ON PRIMARY CARE - Telemedicine for home health care	15/11/19	Presentation	Rome (Italy)	An eHealth Strategy for Catalonia
34	Digital Health and Care Conference	20/11/19	Presentation	Glasgow (United Kingdomm)	Augmented Reality Games and Quotidian Digital Health: Intergenerational Pokémon Go Play in Badalona
35	Join the dots conference	28/11/19	Presentation	Brussels (Belgium)	The MAFEIP tool utilisation in Badalona
36	Las unidades de lípidos y la pandemia SARS-COV2	10/06/20	Presentation	Webinar	El despliegue de la telemedicina en tiempos de la SARS-COV2
37	Care during and beyond the COVID-19 Crisis: Building integrated care as the cornerstone of our new reality	18/06/20	Presentation	Webinar	The experience of Catalonia
38	Digital Health Rewired	19/02/21	Presentation	Webinar	Information Systems in the Catalan health system – A paradigm shift towards an open future
39	European Health-Tech Innovation Week	21/05/21	Presentation	Webinar	Information Systems in the Catalan health system – A paradigm shift towards an open future

(*) Best conference poster award.

6.9 Teaching

This section includes all the teaching activities linked to different universities and official studies performed during the research period of this Ph.D. thesis.

Table 7.8 Teaching activities.

	Course	University	Faculty	Subject	Role
1	2017-2018: MSc in Integrated Care	Università degli Studi di Udine	Faculty of Medicine	Information and Communication Technologies for Integrated Care	Visiting lecturer
2	2018-2019: MSc in Integrated Care	Università degli Studi di Udine	Faculty of Medicine	Information and Communication Technologies for Integrated Care	Visiting lecturer
3	2018-2019: BSc in Informatics	Universitat Oberta de Catalunya	Faculty of Informatics, Multimedia and Telecommunications	Information Systems Strategic Planning	Professor collaborator
4	2019-2020: MSc in Telecommunications	Universitat Oberta de Catalunya	Faculty of Informatics, Multimedia and Telecommunications	Information Systems Management	Professor collaborator
5	2020-2021: Executive MSc in Digital Healthcare	Universitat de Barcelona and Barcelona Technology School	Faculty of Medicine	Various subjects	Content Coordinator and Lecturer

6.10 Grants

This section includes all the project grants obtained as principal investigator.

Table 7.9 Project grants.

	Funding program	Name of the project	Project acronym	Funding obtained (€)	Role
1	CIP - Competitiveness and innovation framework programme (CIP) (2007-2013)	Learning from integrated eCare practice and promoting deployment in European regions	BeyondSilos	270,006	Project partner
2	CIP - Competitiveness and innovation framework programme (CIP) (2007-2013)	MAnagement of mental health diSorders Through advancEd technology and seRvices – telehealth for the MIND	MasterMind	494,450	Project partner
3	H2020-EU.3.1.4. - Active ageing and self-management of health	Do Cardiac Health: Advanced New Generation Ecosystem	Do CHANGE	389,125	Project partner
4	H2020-EU.3.1.6. - Health care provision and integrated care	Towards evidence-based tailored implementation strategies for eHealth	ImpleMentAll	347,966.64	Project partner
5	URBACT III Transfer Network	Building an age-friendly city	SilverCities	800,000	Project coordinator
6	Support to a Digital Health and Care Innovation initiative in the context of Digital Single Market strategy (SC1-HCC-05-2018)	Datta Matters	Data Matters	15,800	Project coordinator