UNIVERSITAT DE BARCELONA

Evaluation and digital transformation of integrated care services

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EVALUATION AND DIGITAL TRANSFORMATION OF INTEGRATED CARE SERVICES

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אף חולה אינו דומה במחלתו למשנה

One should never say: “This disease is similar to that [other] one.”
... Nor should one say: “I have seen how my elders have treated [this disease] in such or such way.”
[As a matter of fact] a physician does not treat a disease, he rather treats a sick person.

The Book on Asthma

רבי משה בן מימון)רמב״ם(
Maimonides (1138 – 1204)

Memoria de la tesis doctoral presentada por

Erik Baltaxe

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לאורית, אלון וניר שתמכו בי בסבלנות, אהבה והרבה הבנה בכל הזמנים ובעיקר בשעות הקטנות של הלילה או כשהייתי בנסיעות. גם ברגעים הקשים בהתחלת הדרך וגם ברגעים המאושרים. נהנינו בכל רגע בטיולים, ומהחברים החדשים שהכרנו. ללא ספק והייתה לנו הרפתקה גדולה.

לאריה וחיה שתמיד עזרו לנו, גם בברצלונה, ובעיקר בארץ. תמיד היה לנו מקום טוב להגיע לחגים ולחופשים כדי להיות עם המשפחה.

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LIST OF ACRONYMS

CFIR: consolidated framework for implementation research
EMRs: electronic medical records
GDPR: general data protection regulation
ICTs: information and communication technologies
KPI: key performance indicator
MAST: model for assessment of telemedicine
MCDA: multicriteria decision analysis
PDSA: plan-do-study-act
PREMs: patient reported experience measures
PROMs: patient reported outcomes measures
RCT: randomized controlled trial
SWOT: strengths, weaknesses, opportunities and threats

LIST OF ARTICLES IN THE THESIS

Thesis in compendium of publications format.

The thesis consists of two objectives and five articles:

1.**Baltaxe E**, Cano I, Herranz C, Barberan-Garcia A, Hernandez C, Alonso A, Arguis MJ, Bes cos C, Burgos F, Cleries M, Contel JC, de Batlle J, Islam K, Kaye R, Lahr M, Martinez- Palli G, Miralles F, Moharra M, Monterde D, Piera J, Ríos J, Rodriguez N, Ron R, Rutten- van Mölken M, Salas T, Santaeugenia S, Schonenberg H, Solans O, Torres G, Vargiu E, Vela E, Roca J. Evaluation of integrated care services in Catalonia: population-based andservice- based r eal- life deployment protocols. *BMC Health Services Research*. 2019; 19:370. http s://doi.org/10.1186/s12913-019-4174-2
Impact factor: 2.91; Quartile: 1st

2. **Baltaxe E**, Czypionka T, Kraus M, Reiss M, Askildsen JE, Grenovic R, Lindén TS, Pitter JG, Ru tten-van Molken M, Solans O, Stokes J, Struckmann V, Roca J, Cano I. Digital health transformation of integrated care in Europe: an overarching content analysis of 17 integrat ed care programmes. *J Med Internet Res*. 2019; 21(9):e14959.
https://doi.org/10.2196/14956
Impact factor: 7.08; Quartile: 1st

3. **Baltaxe E**, Embid C, Aumatell E, et al. Integrated Care Intervention Supported by a Mobil e Health Tool for Patients Using Noninvasive Ventilation at Home: Randomized Controll ed Trial. *JMIR Mhealth Uhealth*. 2020;8(4):e16395.
https://www.doi.org/10.2196/16395
Impact factor: 4.95; Quartile: 1st

4. **Baltaxe E**, Cano I, Risco R, Sebio R, Dana F, Laxe S, Martinez R, Ozores F, Roca J, Martinez- Palli J. Role of co-creation for large-scale sustainable adoption of digitally sup ported integrated care: prehabilitation as use case. *Int Journal Integrated Care*. 2022. 22(4): 1, 1–12. https://doi.org/10.5334/ijic.6503
Impact factor: 2.91; Quartile: 1 (sociology and political science), 2 (health policy)

5. **Baltaxe E**, Hsieh M, Roca J, Cano I. Assessment of digital tools supporting healthcares ervices for chronic patients: experience from a dual hospital. J Med Internet Res. 2022. https://www.doi.org/10.2196/40976
Impact factor: 7.08; Quartile: 1st

ABSTRACT

Integrated Care is acknowledged as an effective and efficient (value-based) approach to cover health and social care needs of patients with chronic disorders. However, its large-scale adoption requires solving unmet needs in two main fields: evaluation of service implementation in real-world settings, and achievement of mature digital support for integration among the different complexity levels of healthcare assistance, in addition to the stakeholders involved in the process.

The current research was performed in the context of the Catalan original Good Practice of the European **Joint Action on implementation of digitally enabled integrated person-centered care** (www.jadecare.eu), an initiative launched to address core aspects of health system transformation in the European Union. The PhD thesis involves five studies that encompass the two main blocks of unmet needs for health system transformation.

The rationale behind the first block is that clinical medicine relies on evidence of efficacy produced by randomized clinical trials. However, proven efficacy-effectiveness gaps seen in complex interventions, such as integrated care, are limiting adoption, as well as comparability among sites. The first manuscript (*BMC Health Services Research. 2019; 19:370. 10.1186/s12913-019-4174-2*) hypothesized that a comprehensive, highly applicable, evaluation framework should foster adoption and transferability of integrated care services in different contexts, as shown for prehabilitation and hospital at home services in Catalonia. Moreover, the identification of key performance indicators, encompassing different service dimensions, should lead to creation of user-profiled dashboards to facilitate service monitoring after adoption. Likewise, the co-creation process conducted to shape the prehabilitation service (*IJIC*, 2022; 22(4): 1, 1–12. 10.5334/ijic.6503), combining design thinking techniques and quality improvement methodologies (PDSA cycles, SWOT analysis and assessment of maturity of the landscape) with contributions of the relevant stakeholders, showed its crucial role to efficiently shape and implement innovative care pathways, as well as to create usable and acceptable digital tools to support value-based integrated care services. The approach proposed was useful for solving maturity gaps facilitating sustainable adoption of novel services. A lesson learnt during the research lifespan was that future co-creation processes could be optimized by adopting a building-blocks strategy wherein each block addresses a specific target.

The second objective of the thesis was to explore the pre-pandemic technological ecosystem supporting integrated care in terms of maturity and integration with the aim to generate actionable recommendations for the different stakeholders. The rationale behind the

technological block was that digital transformation in healthcare is already a reality in every day clinical practice. Nonetheless its implementation has been uneven and is still immature. Therefore, the second block of the thesis addresses three core aspects: i) Performs a structured descriptive approach of the status of digital transformation in Europe (*J Med Internet Res 2019;21(8):e14956. 10.2196/14956*); ii) Explores the potential and the limitations of mHealth in a specific use case – Home-based non-invasive ventilation (*JMIR Mhealth Uhealth.2020;8(4):e16395. 10.2196/16395*); and iii) Generates recommendations for evaluation of digital health tools (*J Med Internet Res. 2023 Jan 4;25:e40976. 10.2196/40976*). The three studies confirmed the key role mHealth tools to support collaborative adaptive case management and identified major pending challenges of digital transformation, namely: change management, interoperability, integration into clinical workflows, and health risk assessment for service selection. The experience acquired with the development of digital solutions supporting different integrated care services, and the analysis of existing regulatory frames, allowed the formulation of recommendations for pre- and post-marked evaluation of digital health tools.

While acknowledging that relevant challenges still need to be faced, it is concluded that the evaluation framework and the co-design strategy proposed in the thesis demonstrated their usefulness to facilitate scalability and transferability of the integrated care services, whereas the second block of the thesis constitute a valuable contribution towards digital health transformation.

INTRODUCTION

The modern practice of medicine has seen a change in the paradigm towards the care of a more elderly and multimorbid populations. Around fifty million people in Europe suffer from multiple chronic diseases, and it is estimated that 60% of this multimorbid population is over 65 years. Moreover, it has been shown that this multimorbid population constitutes the costliest patients in the healthcare system accounting for around 75% of its total costs [1–7].

These elderly patients often require medical and social care from different disciplines. For example, specialized physicians in the hospital setting, alongside physiotherapists' evaluation and physical rehabilitation in a completely different geographic location outside the hospital. Not to mention social services given at public offices. The harmonization of all the required attention given to a single patient (and the caregiver) can become a daunting challenge for the patient itself, the family and the different stakeholders trying to cooperate and coordinate care [8–12].

Within this clinical and economic scenario, the emergence of Integrated Care services has been proved a cost-effective approach to overcome these health and social care needs and challenges [13], making healthcare systems more efficient by containing costs and thus ensuring sustainability in the long term, as well as providing evidence-based patient-centered care.

This new paradigm does not only apply to multimorbid elderly patients but can be seen as a step pointing towards a more personalized medicine, where preventive services, citizen empowerment, services optimization and patient-centered research all interact in a coordinated and harmonized way, creating cost-effectiveness and adding value to already existing care pathways and services (**Figure 1**).

So far, one of the main problems in such healthcare transformation has revolved around the way to deploy and transform health systems into digitally enabled Integrated Care services at wide scale.

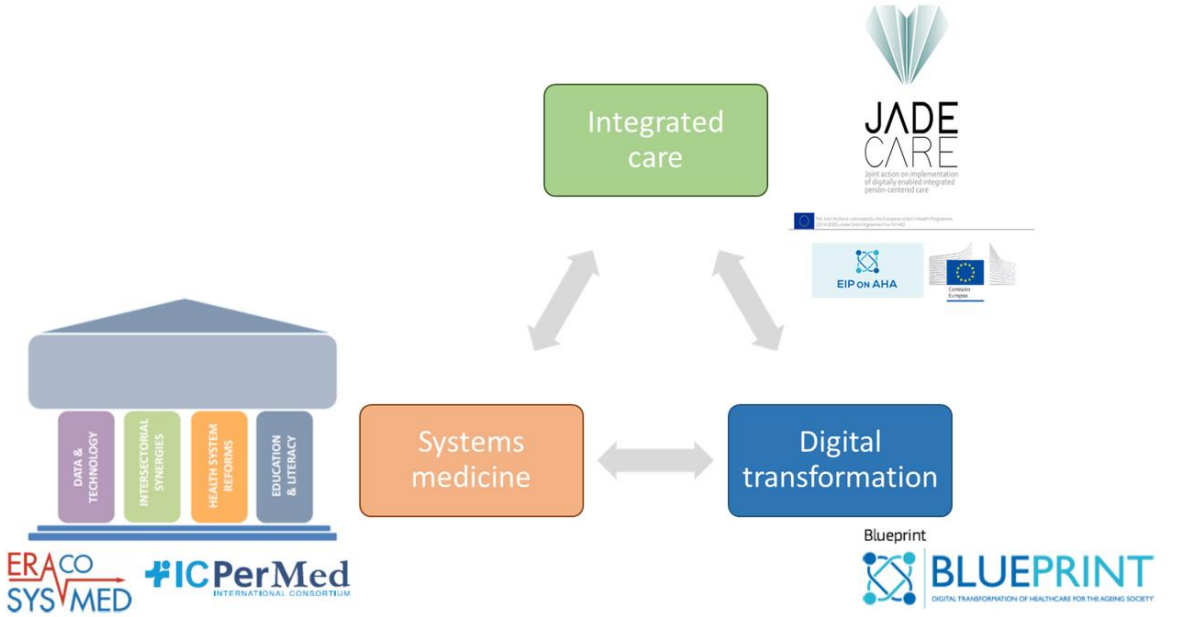

Figure 1. Next Generation Medicine: A new paradigm in medicine.
Multidirectional interactions between digitally enabled Integrated Care and a systems medicine approach can help create new personalized care pathways within well characterized and mature clinical services. The figure displays different European initiatives and programs converging to pave the way toward adoption of integrated care and personalized medicine for chronic patients, namely: ERACoSysMed: Collaboration on systems medicine funding to promote the implementation of systems biology approaches in clinical research and medical practice (https://www.eracosysmed.eu); ICPerMed: International Consortium for Personalized Medicine (https://www.icpermed.eu); JadeCare: The Joint Action (JA) on implementation of digitally enabled integrated person-centered care (https://jadecare.eu); EIP on AHA: European Innovation Partnership on Active and Healthy Ageing (https://ec.europa.eu/eip/ageing/home_en.html); Blueprint on Digital Transformation of Health and Care for the Ageing Society (https://ec.europa.eu/eip/ageing/blueprint_en.html)

The World Health Organization defines Integrated Care as "an approach to strengthen people-centered health systems through the promotion of the comprehensive delivery of quality services across the life-course, designed according to the multidimensional needs of the population and the individual, and delivered by a coordinated multidisciplinary team of providers working across settings and levels of care. It should be effectively managed to ensure optimal outcomes and the appropriate use of resources based on the best available evidence, with feedback loops to continuously improve performance and to tackle upstream causes of ill health and to promote well-being through intersectoral and multisectoral actions" [14].

Although integrated care services aim to be well-defined interventions, main recognized problems are: i) deployment and adoption at large scale, and, ii) the way to evaluate this large-scale deployment, where technological tools are also part of the intervention [15].

In order to understand and tackle these two main problems, Integrated Care should be understood as a complex interplay between different actors and stakeholders across the health and social care systems. **Table 1** summarizes the different points of view in Integrated Care. Such complex interplay may constitute a limiting factor for effective deployment which, in part, can be solved by change management and enhanced interactions between the different players with support of technological tools, alongside standardized evaluation methodologies to assess its large-scale deployment and adoption over time.

Table 1. Integrated Care Definitions and Points of View

Health system-based perspective	Services that are managed and delivered so that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease-management, rehabilitation and palliative care services, coordinated across the different levels and sites of care within and beyond the health sector, and according to their needs throughout the life course [16]
Manager's point of view	The process that involves creating and maintaining, over time, a common structure between independent stakeholders … for the purpose of coordinating their interdependence in order to enable them to work together on a collective project [17]
Social science-based definition	Integration is a coherent set of methods and models on the funding, administrative, organizational, service delivery and clinical levels designed to create connectivity, alignment and collaboration within and between the cure and care sectors. The goal of these methods and models is to enhance quality of care and quality of life, consumer satisfaction and system efficiency for people by cutting across multiple services, providers and settings. Where the result of such multi-pronged efforts to promote integration leads to benefits for people the outcome can be called 'integrated care' [17]
The patients' perspective	I can plan my care with people who work together to understand me and my career(s), allow me control, and bring together services to achieve the outcomes important to me [18]

Large scale deployment and different evaluation models have been well studied and described since the European Innovation Partnership on Active and Healthy Aging (EIP on AHA) was created in 2012. Its objectives were i) Improving the health and quality of life of Europeans with

focus on elderly people; ii) Supporting the long-term sustainability and efficiency of health and social care systems and iii) Enhancing the competitiveness of EU industry through business and expansion in new markets.

This European initiative has generated evidence in two complementary areas that can help to clarify how the general transformation of healthcare systems into Integrated Care services, while adopting and adapting technological tools, can add value to existing services and at the same time deliver high-quality medicine.

Firstly, the need to implement the principles of Integrated Care to the care of chronic patients, as part of the transformation of health systems in general, to ensure healthcare value generation, and their long-term sustainability, with the objective of promoting digitization and convergence with the principles of systems medicine in terms of caring for the patients' needs as a whole and not in a fragmented manner (**Figure 1**).

Second, the identification of main modulating factors, in terms of facilitators and barriers, for transformation of the healthcare systems. In this regard, the Expert Group on Health System Performance Assessment [19], under the umbrella of DG Sante within the European Commission, has identified nine key modulating factors which can be summed as: i) Change management and re-organization of the existing care models; ii) Embedding digital technologies and tools in care services; iii) Re-organization of patient pathways; iv) Health workforce roles and skills with digital technologies and data management; v) Building capacity of individuals and communities to participate in the care process; vi) Citizen empowerment; vii) Use of patient reported data; viii) New payment methods; and; ix) Performance assessment of new care models**.**

However, this same document acknowledges that there is still uncertainty on how to best design, implement, transfer and evaluate digitally enabled Integrated Care. The inherent complexity of Integrated Care (**Table 1**) can be seen as a barrier to widescale implementation and evaluation. But, as seen in **Figure 1,** a rational, multidirectional approach can help create a framework for the adoption and evaluation of digitally enabled Integrated Care services.

In the current PhD thesis, we will specifically focus on the assessment and large-scale deployment of Integrated care in which digital technologies are embedded to promote and facilitate the change in the paradigm of care (i.e., digitally enabled Integrated Care). As stated by the EU Blueprint on Digital Transformation on Health and Care for the Ageing Society: "The

ability to spread and accelerate transformation of health and social care delivery is enriched by the care recipient's experience – that must be seen as part of the evaluation process – and also supported by a robust evidence-base that expresses in terms of measurable outcomes the return on investments dedicated to implementing innovative digital solutions and the associated changes to care delivery. We must allow technology-enabled solutions to support the disruptive health and care innovation, and not measure their impact solely within the constraints of the existing health and care processes." [20].

Implementation and evaluation strategies

Clinical interventions have been traditionally evaluated by randomized controlled trials (RCT), which are considered the gold standard to assess efficacy. In other words, for simple interventions (i.e., a single, well-defined intervention such as pharmacotherapy for a single disease) the RCT is the most powerful way to answer the question "does the intervention works independently of its context, and all known variables are controlled for?". And, as such, it is an invaluable tool to generate evidence on efficacy in the modern clinical practice upon which professional practice guidelines are built.

But, for complex clinical interventions, the RCT have many inherent flaws that may limit generalization of the results in real-life settings [21,22]. It must be said that the simple clinical interventions within an Integrated Care scenario are usually deemed efficacious on previous RCTs (for example, the use of lipid lowering drugs in patients after myocardial infarction which are enrolled in an Integrated Care program for frail elderly people). **Figure 2** summarizes the spectrum of evidence generation and implementation of any proposed clinical intervention.

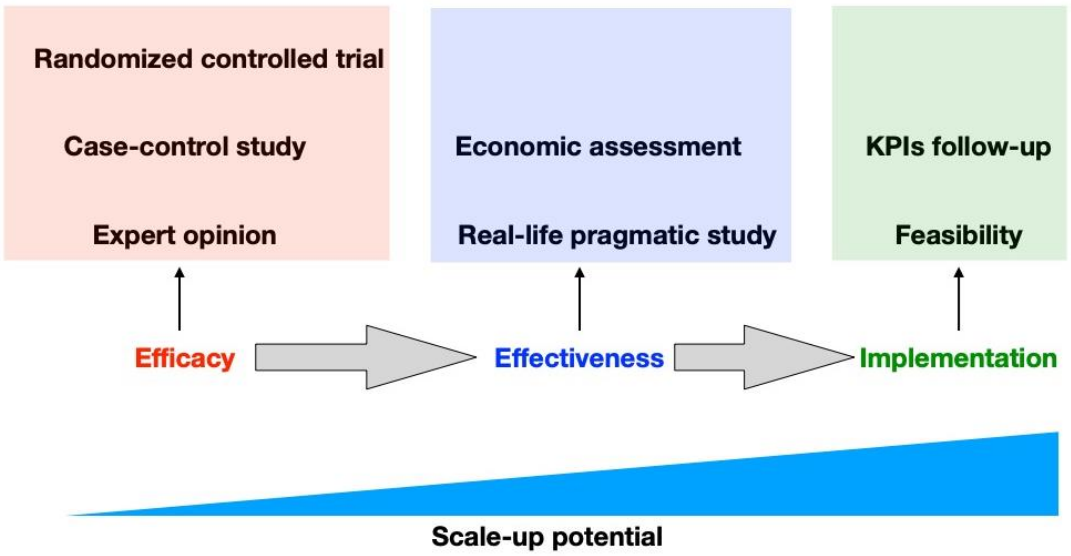

Figure 2. Scaling up a medical service or clinical intervention
Efficacy is usually proven in clinical studies, being the randomized controlled trail the gold standard (due to ethical or logistical constraints sometimes case control or similar types of evidence is used for to prove efficacy). Generalizability of results is enhanced by real word studies and cost-effectiveness (or similar economic analysis). Finally, an intervention achieves full scalability potential upon proving its successful implementation and long-term sustainability (using key performance indicators [KPIs]).

Complex interventions, such as digitally enabled Integrated Care can be seen as difficult to evaluate. In order to make the evaluation more rational, its goal should not only be if the intervention works (efficacy), but how it works, on whom it works, what are the variables modulating (positively and negatively) the intervention and what are the necessary adaptations of an original intervention to be adapted in differing contexts. We see that the focus of the evaluation shifts from efficacy to effectiveness.

Real-world studies can help provide effectiveness data derived from different sources, namely: i) Electronic health records, ii) Claims' data, iii) Registry data, as well as iv) Data derived from wearables and mobile applications [21,22].

Using these different sources to evaluate the effectiveness for a complex intervention the following aspects should be considered:

1) *Outcomes*, in the form of the Triple/Quadruple aim [23–26], which takes into account not only classical clinical outcomes such as mortality or emergency admissions, but also patients' and professionals' needs and preferences, alongside costs.
2) The *maturity of the ecosystem for implementing the intervention*. The SCIROCCO model [27] (which will be expanded later in this Section) is one of the most widely used models

in this regard. Also, SWOT (strengths, weaknesses, opportunities and threats) analysis complement any maturity assessment of an intervention.

3) The characteristics of the *implementation process* which should strive to describe the intervention characteristics, the overall context of the intervention (external and internal), the individuals taking part in the implementation process as well as those taking part in the intervention per se. A good use case to understand the complexity of the process is the implementation of interventions using multidisciplinary teams across horizontal health care sectors (e.g., primary care and social care) or vertical health care sectors (e.g., specialist service in a tertiary hospital and primary care). The Consolidated Framework for Implementation Research (CFIR) [28,29] is a good example of an evaluation framework for implementation process.

Also, the evaluation of a complex intervention does not end immediately after its implementation. As a matter of fact, the failure to provide continued evaluation may miss many important outcomes for the different stakeholders due to the nature of the intervention (ceiling effect against a very well treated control group for example). Therefore, appropriate *key performance indicators* (KPIs) should be set and monitored via quality control systems over the lifetime of the Integrated Care intervention.

While this scheme can be useful, the real-life examples of evaluation have been proven to be more challenging. Literature has shown that evaluation of these aspects is limited [30–32] and in most cases, reports are of pilot and circumscribed experiences.

A comprehensive document published by The King's Fund report on Providing integrated care for older people with complex needs described seven programs from the United States, New Zealand, United Kingdom, Canada, the Netherlands and Sweden. It showed high heterogenicity in program design and delivery alongside differences in the concept of integration and stakeholder involvement. Moreover, a recent systematic review on measuring Integrated Care [33] studied the data derived from 300 articles, yielding 209 evaluation instruments. They grouped the instruments in the following domains: patient-centered care (49%), care integration (33%), continuity of care (15%) and care coordination/case management (3%). It is of note that most of the studies focused on the evaluation of clinical integration (84%), while just a few evaluated professional (3.7%), organizational (3.4%) and functional (0.5%) integration. Moreover, the quality of the measurement properties of the overall assessment instruments was deemed to be of good or excellent quality in less than 50% of the studies.

One of the main barriers for a comprehensive evaluation is the atomization of the assessment in aspects such as continuity of care [34,35] chronic disease management [36] patient-centered care [37,38] experience with care, quality of care delivery [39] collaborative care [40] and care coordination [41–43].

Recently, a Nuffield Trust seminar [44] in which 50 Integrated Care experts shared their ideas, identified three hypotheses on why the evaluation of Integrated Care do not produce expected results. Firstly, they identified flaws in Integrated Care service models, such as context identification and failure to address patients' preferences and needs (e.g., continuity of care). Secondly, implementation issues arising from context misinterpretation, or target population misidentification can hinder adoption in real-world settings. And, thirdly, a very limited use of outcomes, short evaluation timelines, data reliability and availability can impair sound scientific conclusions from the evaluation. They conclude that using a co-design process involving all stakeholders can help overcome flaws in service design and evaluation.

Following the previous rationale and lessons learned from the literature, evaluation of any Integrated Care service should encompass the following domains: i) Outcomes; ii) Ecosystem maturity; iii) Implementation processes and iv) Long term follow-up using key performance indicators.

Outcomes: The most widely adopted and studied model to evaluate outcomes in Integrated Care is the Quadruple Aim, initially developed as the Triple Aim by Berwick and colleagues in 2008 [24]. Fully attaining its postulates can potentially benefit not only the population as a whole; also, patients can foresee more coordinated and less complex care delivery, thus dampening the burden of illness. Moreover, with cost containment at population level, business opportunities and competition can be expected, positively impacting the much-needed innovation in healthcare. In Berwikck's first publication, the main components of the model were proposed: improved population health, enhanced patient experience with healthcare and low system costs. To this end, they proposed that the first step was to delineate a well determined population in which to apply the model. Since the model was conceived initially for the US healthcare system, different populations could be defined, such as for example, all the people being served by a determinate physician group. In countries where there is a single payer, the population is determined by geographical regions. The second step is to nominate an integrator, which serves as the entity responsible for managing and achieving the model's aims. In the US, one of the best examples is the Kaiser Permanente. In countries with a single-payer system, is the country

itself which hires a provider to integrate care on a caped budget.

Building on these principles, Whittington and colleagues [45] evaluated the adoption of the Triple Aim approach in 141 sites across North America, Europe, Australia and South-East Asia. The report clearly shows how adoption of well-defined clinical outcomes at population level such as mortality, emergency visits, health-related quality of life, health-style factors (smoking, diet, etc.) and specific disease outcomes (blood pressure, blood sugar control) can be tackled alongside costs reductions while enhancing patient experience in the form of patient satisfaction, continuity of care, patient safety and empowerment among others.

A later addendum to the model was proposed by Bodenheimer et al and Sikka et al [25,26] where they propose also to assess healthcare professional joy and meaning at work. The proposed domains to be measured are professional engagement and burn-out alongside workforce safety. In a recent case-use of Quadruple Aim evaluation, a regional implementation of an eConsult intervention in Canada was assessed among patients and primary care providers. While the intervention showed positive impact on reducing costs, patients and professionals' satisfaction, it was difficult to demonstrate impact on population health. This reflects the challenges facing the interaction of digital tools and a comprehensive evaluation of Integrated Care.

It is important to note that the Quadruple Aim has been widely adopted and endorsed by leading clinical colleges [46].

Ecosystem maturity: This evaluation domain refers specifically to the capacity of a healthcare system to deliver a technologically supported Integrated Care scenario to accomplish a progressively organized methodology for scaling-up and transferability.

To accomplish these aims, all through Europe, the B3 Action Group on Integrated Care of the European Innovation Partnership on Active and Healthy Aging built up the B3 Maturity Model. The model comprises 12 measurement domains. This in turn led to EU funded SCIROCCO Project, which aimed to develop, test, and validate the maturity model.

Every one of the measurements has a specific 6-point ordinal scale (0 to 5). A maturity map is built on a radar graph by assigning a score to each one of the evaluation domains. This graph gives a straightforward outline of a regions' strengths and shortcomings on the implementation of Integrated Care. Therefore, allowing comparison among regions a way to transfer lessons

learned from one region to another.

An initial validation of the tools was done within the scope of the SIROCCO project [47]. The 12 dimensions were compared to reported measurements in the literature which showed good agreement between the new tool and the literature. Afterwards, three Delphi study rounds helped to refine the content of the SCIROCCO maturity tool. A more recent study [48] showed good structural validity and internal consistency.

Figure 3 shows the graphical representation of the maturity tool (taken from https://www.scirocco-project.eu/maturitymodel/).

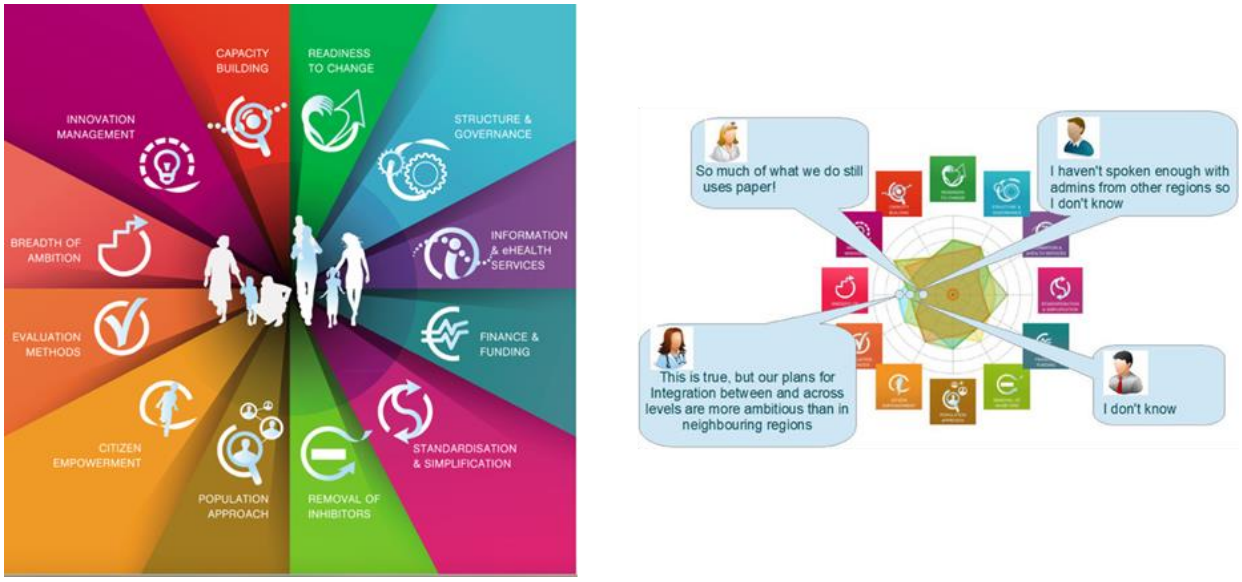

Figure 3. SCIROCCO tool for maturity evaluation of Integrated Care.

Another tool for maturity analysis of an ecosystem is the SWOT analysis (strengths, weaknesses, opportunities and threats). A recent proposed application of this tool will be done in the JADECARE project (Joint Action on Implementation of Digitally Enabled Integrated Person-Centred Care) [49]. As part of a comprehensive scheme to transfer and implement mature Integrated Care practices in new geographical regions, the SWOT analysis is seen a central component to create an initial "snap-shot" of the internal and external factors modulating the Integrated Care service to be implemented. This analysis can be used later to define action plans during implementation and as such is not and static analysis tool.

As seen from the use case of SWOT analysis, the evaluation process may occur before, during and after the implementation of an Integrated Care service. In the JADECARE project the

SWOT analysis plays a major role in the pre-implementation phase to define the implementation strategies at site level. Implementation being the act of carrying an intention into effect, which in health research can be policies, programs, or individual practices (collectively called interventions).

The interest of evaluating the implementation process is reflected by the fact that even though Integrated Care is a well stablished and accepted model, the real-world experience has yielded sometimes contradictory results in terms of effectiveness [50–56]. The practical impact of evaluating the implementation a service allows for a thorough understanding of the context (clinical social, etc.), target population and stakeholders' perception (including patient experience) which in turns help define clear evaluation objectives to guide a co-design process for a successful intervention [44].

Implementation processes: In 2009 Damschroder and colleagues published the Consolidated Framework for Implementation Research (CFIR) [28]. It was developed in the context of the Veterans Affairs managed care organization in the US. The overall aim of the framework is to assess formative outcomes directly related to the implementation process evaluating its effectiveness, sustainability, and transferability to other settings. It is composed of five major domains: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process of implementation. Within each domain constructs are identified. See **Table 2** (taken form cfirguide.org).

Table 2. CFIR Constructs and its' elements

Construct	Elements
Intervention Characteristics	Intervention source; evidence strength & quality; relative advantage; adaptability; trialability; complexity; design quality & packaging; cost.
Outer Setting	Patient needs & resources; cosmopolitanism; peer pressure; external policy and incentives.
Inner Setting	Structural characteristics; networks & communications; culture; implementation climate; tension for change; compatibility; relative priority; organizational incentives & rewards; goals & feedback; learning climate; readiness for implementation; leadership engagement; available resources; access to knowledge & information.
Characteristics of Individuals	Knowledge & beliefs about the intervention; self-efficacy; individual stage of change; individual identification with organization; other personal attributes.

Process	Planning; engaging; opinion leaders; formally appointed internal implementation leaders; champions; external change agents.

A recent systematic review [29] on the use of CFIR to assess implementation processes showed that although the framework has been used in a wide array of study types and designs (n= 26 papers), the primary use done was mainly on identifying barriers and facilitators for implementation. Only two studies used the CFIR before the implementation of the intervention to guide future policies, therefore, hindering, in a majority of cases, the opportunity to create co-design processes during implementation to fine-tune the intervention and overcome barriers. Interestingly, two more recent papers not included in the systematic review [57,58] explore the CFIR use specifically in the setting of digital tools implementation. Lambert-Kerzner et al used the CFIR to guide a Surgical Risk Preoperative Assessment System from design adaptation phases up to the successful implementation of the digital tool, concluding that its use from the beginning facilitates future large-scale adoption of the intervention. Warner et al used a CFIR-inspired interview that allowed them to elucidate aspects of implementation to be accounted for at multiple levels of the implementation process.

In the current PhD thesis, we will try to integrate and adapt the CFIR into a comprehensive framework to evaluate real-world scenarios.

Key performance indicators: Care providers are continually looking for ways to improve the safety and quality of the care they offer, and patients are largely concerned about the quality of services provided by multiple professionals and organizations. A landmark report published by the United States (US) Institute of Medicine, To Err is Human [59] recognized shortcomings in the safety and quality of healthcare services in the United States, contributing to the global recognition that there was an immediate need to improve the safety and quality of services provided and to expand attempts to improve it.

There have been 3 separate forces which can encourage organizations to improve the performance as well as quality of the healthcare they provide: professionalism, policy and market forces [60].

With respect to professionalism, practitioners of the different professional societies may establish and uphold quality criteria via a governance structure. At policy level, the

administration, and autonomous regulatory agencies, set guidelines that everyone should conform, resulting in a total gain in the service quality. Lastly, via market forces, customers have an effect on maintaining safety and quality by choosing certain companies that have attractive quality and safety records.

The assessment of the safety and quality of treatment has now become extremely important since, only if we accurately measure the safety and quality of care, we will not decide if progress has been made. While it is a major factor, quality assessment by itself does not result in better performance. Nonetheless, performance assessment enhances quality in several forms [61].

Initially, it promotes innovation through motivating people to make choices based on quality indicators, and this in turn generates an opportunity for providers to increase performance to retain additional users. Additionally, professionals have an inherent willingness to improve quality once they are informed, via performance assessment, that there's still room for change. Ultimately, performance assessment contributes to change by measuring the performance of professionals and organizations culminating in a commitment to improving and sustaining performance in comparison to others, and the safety and quality of the programs they offer.

The principle of measuring the quality of healthcare has been in operation for many years, but it is only in recent years that it has gained a great deal of attention from the published literature. One of the most important contributions in the field came from Avedis Donabedian scheme on process, structure, and outcomes for the purpose of defining and measuring quality [62,63].

It is important to decide what factors need to be assessed to track the performance of the healthcare system. Monitoring success relies on good accurate information, that can only be accomplished through a structured process to make sure the data is being collected regularly, within and throughout participating entities. Key performance indicators (KPIs) are the instrument that is most commonly used to aid with performance monitoring and can ultimately lead to performance improvement. KPIs have become an essential tool which significantly adds to the performance monitoring phase [64]. Nevertheless, in order to KPIs to be successful, these should have to be clearly delineated to guarantee that the information collected is of excellent quality (i.e., accurate and dependable within accepted standards). Effective KPIs assess what they are designed to measure and accurate KPIs can reliably achieve the same result irrespective of who conducts the evaluation.

The performance of the system is thus monitored at long-term, ensuing quality, sustainability,

transparency, and accountability.

At European level, projects stemming from the EIP on AHA have tried to tackle the practicalities of Integrated Care delivery and evaluation. The CareWell project [65] explored the delivery of ICT-enabled integrated care to frail, multimorbid elderly patients using newly developed care pathways to foster care co-ordination, patient empowerment and home support. Outcomes were evaluated using the MAST framework. Key lessons learned from the project revolve around the involvement of care recipient and family carer into the care pathway as well as active stakeholders' involvement in the planning of a new ICT-enabled care pathway. The importance of the challenges created by a change of management paradigm was highlighted by this project. Another EU milestone during the implementation of Integrated Care was the ICare project [66], which showed the benefits of using an internet-based intervention on mental health care. Finally, ACT and ACT@Scale [67] generated a framework to identify, transfer and scale-up existing and operational care co-ordination and telehealth good practices in multiple European regions. One of the most important lessons learned from the project was that the successful involvement of all stakeholders, creating a sense of belonging, through use of robust technology, can be a facilitator for implementing Integrated Care at large scale.

Also, the MAFEIP tool (a web-based application) [68,69] was created to estimate the health and economic outcomes of social and technological innovation introduced in any Integrated Care service. But it is mostly intended for use in EIP on AHA interventions. Recently, a soundly academic project, SELFIE, developed a multi-criteria decision analysis (MCDA) tool [70] to evaluate in a holistic manner the impact of integrated care interventions in varying contexts (from population-based, to frail elderly and people with problems in multiple life domains).

Key Points
• While randomized controlled trials are the gold standard to prove clinical efficacy, real-life pragmatic studies are best suited to prove effectiveness and healthcare value generation. • Evaluation of effectiveness and scalability can be achieved by using a multidimensional approach based on objective outcomes, ecosystem maturity assessment and qualitative descriptions of the implementation process on such an ecosystem. • The Quadruple Aim approach is a well-defined tool used to assess effectiveness of a health intervention at population level in terms of clinical outcomes, patient experience, costs, and health provider experience. It has proven useful in many scenarios, and it is endorsed by clinical colleges.

- Ecosystem maturity tools rely on qualitative "snap-shot" descriptions to shed light on a wide array of characteristics to help define facilitators and barriers before and during the implementation, scaling-up and/or transfer between health systems of a complex clinical intervention.
- The assessment of the implementation process complements the qualitative nature of the ecosystem maturity evaluation by providing a more dynamic "motion-picture" of the interactions between the intervention, the setting and the individuals within it.
- Implementation studies using well-defined and clinically meaningful KPIs are the foundation to scale-up and transfer complex clinical interventions such as digitally enabled Integrated Care. The success depends mainly on the quality of the indicators and the systematic process to collect them.

Digital Transformation

Healthcare systems have used information and communication technologies since the 1920s, mainly reporting sporadic and anecdotical use cases [71,72]. With the advent of the internet era and the informatics revolution, the field saw exponential growth during the 1990s [73]. Since then, the introduction of different and differing digital tools has been permeating all aspects of the modern practice of medicine [74], with the latest example been the massive digital transformation fueled by the COVID-19 pandemic [75,76].

Although ICTs are well accepted tools to support healthcare interventions and processes, the digital potential has always grown ahead of its application in real-world practice. Such gap has hindered two main aspects, namely: i) wide scale applicability and full exploitation of its whole transformative potential and, ii) its evaluation as components of cost-efficient interventions and its potential to generate added value within the health system. Current limitations for digital transformation are partly explained by the fact that ICT have often been seen as standalone tools instead of looking at them as enablers of efficient health services. Moreover, a more holistic vision of the potential of digital tools would foster convergence of integrated care with systems medicine, as depicted in **Figure 1**, paving the way toward personalized medicine.

This gap between the full potential and the real-world application of digital tools in Integrated Care requires a multifactorial analysis to identify barriers for its wide-scale implementation as part of digitally enabled Integrated Care services. The following factors will be explored in this section: i) what are the different areas encompassing the broad definition of eHealth and how

they have evolved; ii) how the introduction of immature or poorly designed technologies generates opposition to adoption by the intended end-users (patients, health care professional, etc.); iii) how non-linear health care processes (such as Integrated Care) can adopt adaptative case management for collaborative work between the medical and social team members; iv) what is the necessity to use digital tools to support sanitary tasks and services and; v) how can the digital tools be successfully implemented inside the medical workforce.

From telemedicine to eHealth: it has been recognized by some studies [77–79] that the use of telemedicine may decrease the number of hospitalizations and mortality, improve blood pressure and glycemic control in patients with chronic health failure, hypertension, COPD and diabetes. But there are cases of less beneficial or even more mixed outcomes for digital healthcare services [80] and systematic reviews of the literature have showed a lack of cost-effectiveness of telemedicine interventions [81–83], precluding the inclusion these tools in clinical practice guidelines [84,85]. The lack of reliable cost-effectiveness evidence is due in part to the lack of data availability gathered throughout extended periods of time alongside the lack of use of mature implementation research tools for scaling up the pilot interventions.

This disease-oriented medicine approach in which the remote transfer of data (i.e., telemedicine) was thought to be a driver of change for the practice of modern medicine has been since disproven by the Whole System Demonstrator study [83].

A more recent and comprehensive approach to eHealth has evolved in the form of the "Digital Health Roadmap to Support Integrated Care" [86] which was developed as a contribution to the Blueprint on Digital Transformation of Health and Care document from the European Commission [20]. The proposed new approach seeks to engage all the different stakeholders (patients, professionals, providers, payers, etc.) along a six-phase journey to the digital transformation.

Beyond telemedicine, the roadmap begins by patient-centric data collection, based on the use of the electronic medical records (EMRs), with a humanistic design thinking approach in order not to alienate the different users of the EMRs [87]. Other sources of data are wearable devices. Probably one of the most important aspects of wearable technology is on generating and supporting behavioral changes towards diseases prevention and management. A recent systematic review and metanalysis on the impact of wearables on behavioral changes towards physical activity [88] showed a statically significant increase in the number of steps per day (N

= 4528 participants). Controversy still exists in reference to the benefit of wearables in specific pathologies, as shown by a systematic review done by Jo et al [89]. Finally, social media, -omics and patient reported outcomes are all non-traditional data sources, but nonetheless useful for the digital transformation.

In order to make sense of this (vast) amount of data, it should be aggregated and shared, being the next step in the roadmap. For this, semantic interoperability alongside technical standards for sharing should be put in place. Natural language processing can help all stakeholders to retrieve and use data in a more fluid manner. Using data sharing mechanisms in an efficient and coordinated manner between existing multidisciplinary teams and other stakeholders involved in the care process can help them to interact in a more harmonized way. ICT support and bidirectional instantaneous communication are required elements for this step in the roadmap. The main barrier in this phase is the proper establishment of mechanisms allowing the ease for patient consent while safeguarding privacy and proper data usage.

Having in place quality data collection, secure data aggregation and sharing alongside strong ICT support and communication between medical teams, patients, caregivers and others, the roadmap proposes the use of advanced technologies to adapt care needs to a complex, changing environment as is the case of Integrated Care. The digital tools encompass the use of machine learning and artificial intelligence to support adaptive case management, gamification, and telehealth. Deep learning methods applied to electronic patient record data have been shown to be capable of accurately predicting multiple medical events from multiple centers [90,91]. Artificial intelligence can also identify unexpected physiological deterioration and predict subsequent outcomes for in-hospital patients and help to predict individual response to treatment [90,91].

The final stage on the roadmap builds on all the previous experience to generate a population-based approach, based on big data analytics, predictive modelling and decision support rules leading to a more personalized medicine based on risk stratification and service selection [90–93].

Throughout the evolution of digital technologies, a potential barrier to their implementation has been long recognized: the professionals involved in the care process can become alienated and even outright reject the new technologies. One of the main concerns is the erosion of the patient-clinician relationship [94]. Historically, medical technologies such as the EMR have been

developed with an emphasis on administrative, financial, and regulatory processes, usually without the input form "field" clinicians. Therefore, it is of no surprise that the everyday users feel an imposed technology that do not help them navigate established and demanding clinical care pathways. Lately, the explosion of new apps [95] to help manage clinical conditions, empower patients or enhance their wellness, has suffered from a lack or rigorous assessment in terms of clinical and technical effectivity (does the app works as is intended to? Does the app improve clinical outcomes? Is it safe?). This situation is fueled by the fast production process of these new technologies, as opposed to well stablished industrial and clinical processes as in the case of classical medical devices (e.g., pacemakers) or drugs. Ultimately the clinicians, payers, caregivers and patients find themselves in front of a myriad new and immature technologies (most of them apps and wearables) of unproven efficacy or effectiveness, frustrating well-intentioned efforts to implement new technologies for everyday clinical care [96]. **Figure 4** summarizes the relationship between the technological complexity and the maturity of the clinical service needed for its implementation.

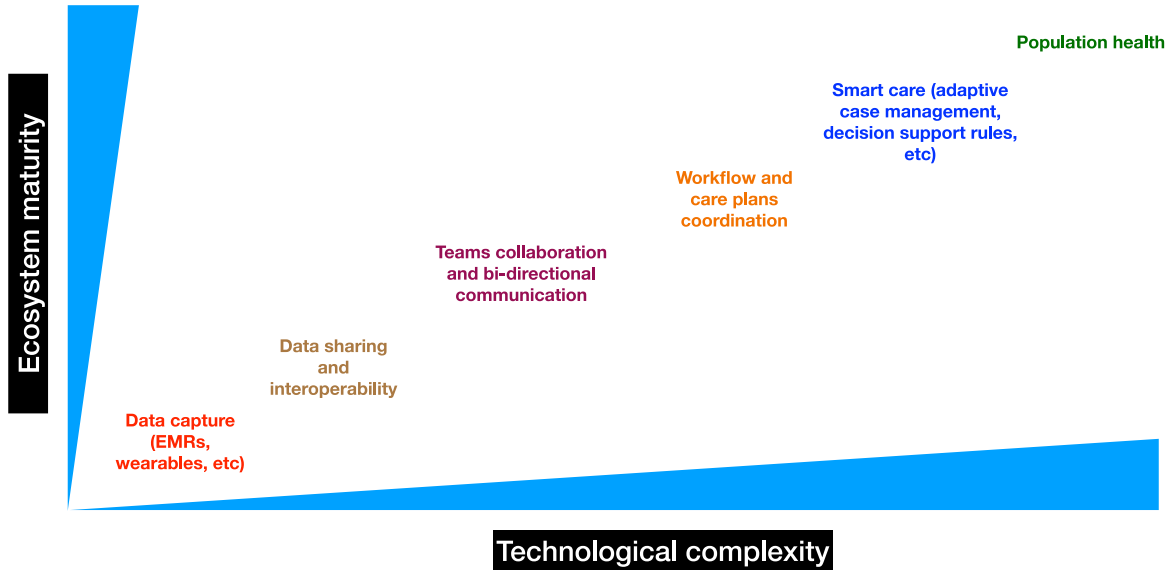

Figure 4. **The technological-implementation gap**.
The figure shows the relationship between the level of technological complexity and the ecosystem maturity in terms of clinical and technical requirements. Technological complexity usually evolves independently of the clinical ecosystem where it can be applied, creating an important gap (and stakeholders' rejection) between its transformative potential and its real-world application, thus hindering wide-scale adoption. Different colors group similar categories of technological tools as described in [86]. EMRs: electronic medical records.

Notwithstanding, there have been some instances in which digital tools have proven to be effective and well regarded by clinicians. Specifically, the fields of pathology, radiology, dermatology and ophthalmology have seen an increase in applied research in terms of deep

learning applied to medical images. Several examples are discussed by Topol [90]. Most of these use cases are applied for automated image interpretation and predictive analytics. But when it comes to more complex and fluid clinical scenarios, such as Integrated Care, there is a lack of practical solutions. In this case, the most useful approach may be the implementation of digital tools capable of supporting adaptive case management [97,98]. The approach should lend flexibility to the workflow, allowing clinicians, patients, caregivers, and other stakeholders to interact in a more fluid and predictable manner, avoiding "reactive" medicine (i.e., last minute changes and decisions during the course of chronic disease management).

It follows from the previous reasoning the need of i) robust implementation tools and methodologies, especially among healthcare professional an ii) rational assessment frameworks in the real-world setting. To this end, the Model for Assessment of Telemedicine (MAST) was created as a result of the interest of the European Commission to assess telemedicine applications [99]. This multidisciplinary framework seeks to evaluate medical, social, economic, and ethical aspects of a digital tool application. Recently, a scoping review of empirical studies applying the MAST was done [100]. The review included 22 studies, of which 11 were RCTs, precluding the effectiveness evaluation of the intervention. Moreover, most of the studies focused on only one of the MAST domains, even though the recommendation is to apply it as a whole framework. As such, it has the unlocked potential to allow effective comparison between geographical regions allowing for knowledge transfer, adoption and scalability. Moreover, the MAST can be used to evaluate mature technology, but is less useful during the development and production phases.

In this respect, some other dimensions during the development and production phases may help generate mature and robust products. It is of note that, ideally, development and production should benefit from the input of all the stakeholders involved, including end-users (i.e., co-design process) benefiting also from well-known production processes such as a plan-do-study-act (PDSA) approach [101–103]. Iterative production cycles should evaluate aspects such as usability, acceptability, compatibility, and capacity of integration to existing ICT systems (e.g., hospital EMR). Also, patient-reported outcomes such as person-centered care and/or continuity of care may add important dimensions for the final product deployment in real life.

It is of note that there are other theoretical evaluation frameworks, such as the one reported by Jasehn (which builds on MAST) and the one proposed by the World Health Organization [15,104]. While they may serve as important guidelines, so far none of these frameworks has been used extensively [100].

In summary, the digital transformation within the healthcare systems has evolved at a fast pace within a complex environment, differing from one geographical region to the other. In many cases its efficacy has been proven, but its (cost) effectiveness has been more difficult to assess, alongside it potential to generate value. While multifaceted evaluation models exist, they still are imperfectly applied. A maturity analysis that includes the digital health tools, interoperability standards, national (or regional) policies, alongside evaluation frameworks, modeling tools for clinical risk assessment and innovation strategies at transnational level should facilitate transferability and wide scale adoption of sustainable, digitally enabled Integrated Care services.

Key Points
• The full transformative potential of digital tools applied to clinical care pathways has yet been fully exploited due to their evolution ahead of the capacity of the health care systems to evaluate their (cost) effectiveness, and value generation, in real-world, complex care scenarios. • Most of the time digital health tools are used as stand-alone applications leading to providers' and patients' negative perceptions and rejection. • Digital health tools that are not mature enough, adaptable, collaborative, integrated within care pathways, and do not meet regulatory frames, usually fail during implementation and scale-up. • The Blueprint on Digital Transformation of Health and Care EU document lays the basis for the integration of digital tools by defining phases and application fields for ICTs beyond telemedicine. • Digital tools can become more complex as a function of the level of maturity of the ecosystem in which they are integrated. • Some digital health evaluation tools have been developed but most lack the capacity to assess digital tools during their development and implementation in complex clinical interventions.

Towards maturity of implementation of digitally supported Integrated Care services

The present thesis was conceived and developed within the Catalan Open Innovation Hub for ICT-supported Integrated Care Services for Chronic Patients. Briefly, this digitally enabled Integrated Care initiative seeks to integrate vertical (tertiary and primary healthcare) and horizontal (healthcare and social care) services from a population health-care point of view. Five areas are covered by the initiative, namely: i) health risk assessment and enhanced clinical decision making at population level; ii) promotion of healthy lifestyles; iii) vertical and

horizontal integration; iv) innovative assessment and regulatory aspects, and v) digital support of integrated care services [84,105–114].

While similar regional initiatives have evolved within the European Union, the level of maturity in terms of clinical integration and digital support varies widely from program to program. As a result, societal and political motivation at regional and continental level led to the creation of the Joint Action on Implementation of Digitally Enabled Integrated Person-Centered Care (JADECARE). This Joint Action project was conceived to face the challenges of the (digital) transformation of healthcare. Specifically, it will address the process of knowledge transfer from well-established good clinical practices to other member states of the EU. One of the original good practices in JADECARE is the Catalan experience described above. The other three being the Basque health strategy on ageing and chronicity (Spain), the Optimedis model (Germany) and the Digital roadmap to an integrated health care sector (Denmark).

The evidence derived from other European projects on integrated care and digital health [27,65,67,115–122] will be used to build upon and create the proposed framework within JADECARE for knowledge transfer from the early adopters of original good clinical practices to the next adopters.

To achieve the project objectives, it will cover general dimensions such as the evaluation of stakeholders' participation, the overall implementation experience and the capacity of the next adopters' clinical practice(s) to achieve sustainability over time. Also, specific objectives regarding the digital transformation, based on the SMART principles (specific, measurable, appropriate, realistic and time-bound) will be addressed. Those principles will be applied in areas such as digital infrastructure, risk stratification, data analytics, use of EMRs, citizen empowerment, use of patient-reported data and care pathways adaptation (including new or modified workforce roles)

The transfer of knowledge and adoption of digitally enabled integrated cares services to the next adopters will be based upon a pre-implementation phase (including action plans and future visions), an implementation phase based on PDSA cycles and SWOT analysis, and a final post-implementation phase were KPIs will be defined to achieve sustainability. Evaluation of the implementation process as well as the digital tools enabling it will be done using tools such as the SCIROCCO maturity model, and the CFIR, among other. As such, this thesis if fully aligned with these novel developments at European level.

Summary

The aging of the general population in Europe has led to an "epidemic" of multimorbid, complex patients. This new reality has strained healthcare systems, impacting on its capacity to deliver care in terms of quality, equity, safety, patient-centeredness and (cost) efficiency. Integrated care has become a well-accepted intervention in which the different stakeholders caring for an individual patient as well as the supporting management system can "row" in the same direction, therefore generating value in healthcare.

Notwithstanding, the widescale implementation and evaluation of digitally enabled integrated care in Europe has been hindered by its inherent complexities and the different contexts to which it can be applied. Some EU initiatives have sought to address these questions, and as result some valuable evaluation frameworks and tools have been developed. But the heterogeneity of such tools hinders a unified evaluation in different contexts. Building on this, the JADECARE project will seek to develop tools and policies to transfer and evaluate integrated care experiences initially developed and tested in specific contexts and later adopted in different settings and regions within Europe.

In line with these current developments, this thesis will seek to develop a timely framework, based on implementation methodologies and the proper management of digital technologies embedded in the integrated care system, to facilitate cost-effective healthcare for the aging, multimorbid and/or complex patients. The attainment of this goal will lead to better care, patient (and caregiver) compliance and satisfaction.

HYPOTHESIS

A timely evaluation framework based on implementation science, combined with mature and usable digital health tools, should facilitate large scale implementation and adoption of value-based integrated care services for chronic patients.

MAIN OBJECTIVES

The general objective of this PhD thesis is twofold. Firstly, to propose articulated and broad evaluation tools for the use during real-life implementation of integrated care services. The flexible use of such tools aims for standardization during transferability and scaling-up in different contexts.

The second objective is to explore the technological ecosystem supporting Integrated Care in terms of maturity and integration across Europe with the aim to generate actionable recommendations for the different stakeholders.

More specifically, the objectives of the research are:

OBJECTIVE 1 – TO ELABORATE A COMPREHENSIVE EVALUATION FRAME FOR INTEGRATED CARE SERVICES APPLICABLE IN REAL-WORLD SCENARIOS, AIMING AT FACILITATING ADOPTION AND TRANSFERABILITY ACROSS DEPLOYMENT SITES.

Rationale: Clinical medicine relies on evidence of efficacy produced by randomized clinical trials. However, proven efficacy-effectiveness gaps seen in complex interventions, such as Integrated Care, are limiting implementation and adoption. A comprehensive, highly applicable, evaluation framework should foster adoption and transferability of integrated care services in different contexts.

Manuscript 1

Baltaxe E, Cano I, Herranz C, Barberan-Garcia A, Hernandez C, Alonso A, Arguis MJ, Bescos C, Burgos F, Cleries M, Contel JC, de Batlle J, Islam K, Kaye R, Lahr M, Martinez-Palli G, Miralles F, Moharra M, Monterde D, Piera J, Ríos J, Rodriguez N, Ron R, Rutten-van Mölken M, Salas T, Santaeugenia S, Schonenberg H, Solans O, Torres G, Vargiu E, Vela E, Roca J.

Evaluation of integrated care services in Catalonia: population-based and service- based real-life deployment protocols. *BMC Health Services Research.* 2019; 19:370. https://doi.org/10.1186/s12913-019-4174-2

Manuscript 4

Baltaxe E, Cano I, Risco R, Sebio R, Dana F, Laxe S, Martinez R, Ozores F, Roca J, Martinez-Palli J. Role of co-creation for large-scale sustainable adoption of digitally supported integrated care: prehabilitation as use case. *Int Journal Integrated Care.* 2022; 22(4): 1, 1–12. https://doi.org/10.5334/ijic.6503.

OBJECTIVE 2 – TO EXPLORE THE MATURITY OF DIGITAL SUPPORT TO VALUE-BASED INTEGRATED CARE SERVICES IN EUROPE TOWARDS THE FORMULATION OF RECOMMENDATIONS FOR ASSESSMENT OF DIGITAL HEALTH TOOLS.

Rationale: Digital transformation in healthcare is already a reality in every day clinical practice. Nonetheless its implementation has been uneven and is still immature. Objective 2 of the current thesis addresses three aspects: i) Performs a structured descriptive approach of the status of digital transformation in Europe; ii) Explores potential and limitations of mHealth in a specific use case – Home-based non-invasive ventilation; and iii) Generates recommendations for evaluation of digital health tools. The final aim of the research is to generate contributions toward a mature digital health transformation of integrated care.

Manuscript 2

Baltaxe E, Czypionka T, Kraus M, Reiss M, Askildsen JE, Grenovic R, Lindén TS, Pitter JG, Rutten-van Molken M, Solans O, Stokes J, Struckmann V, Roca J, Cano I. Digital health transformation of integrated care in Europe: an overarching content analysis of 17 integrated care programmes. *J Med Internet Res.* 2019; 21(9):e14959. https://doi.org/10.2196/14956

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Manuscript 5

Baltaxe E, Hsieh M, Roca J, Cano I. Assessment of digital tools supporting healthcare services for chronic patients: experience from a dual hospital. J Med Internet Res. 2022. https://www.doi.org/10.2196/40976

RESULTS

MANUSCRIPT 1

Baltaxe E, Cano I, Herranz C, Barberan-Garcia A, Hernandez C, Alonso A, Arguis MJ, Bescos C, Burgos F, Cleries M, Contel JC, de Batlle J, Islam K, Kaye R, Lahr M, Martinez-Palli G, Miralles F, Moharra M, Monterde D, Piera J, Ríos J, Rodriguez N, Ron R, Rutten-van Mölken M, Salas T, Santaeugenia S, Schonenberg H, Solans O, Torres G, Vargiu E, Vela E, Roca J. Evaluation of integrated care services in Catalonia: population-based and service- based real-life deployment protocols. *BMC Health Services Research.* 2019; 19:370. https://doi.org/10.1186/s12913-019-4174-2

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Evaluation of integrated care services in Catalonia: population-based and service-based real-life deployment protocols

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Abstract

Background: Comprehensive assessment of integrated care deployment constitutes a major challenge to ensure quality, sustainability and transferability of both healthcare policies and services in the transition toward a coordinated service delivery scenario. To this end, the manuscript articulates four different protocols aiming at assessing large-scale implementation of integrated care, which are being developed within the umbrella of the regional project Nextcare (2016–2019), undertaken to foster innovation in technologically-supported services for chronic multimorbid patients in Catalonia (ES) (7.5 M inhabitants).
Whereas one of the assessment protocols is designed to evaluate population-based deployment of care coordination at regional level during the period 2011–2017, the other three are service-based protocols addressing: i) Home hospitalization; ii) Prehabilitation for major surgery; and, iii) Community-based interventions for frail elderly chronic patients. All three services have demonstrated efficacy and potential for health value generation. They reflect different implementation maturity levels. While full coverage of the entire urban health district of *Barcelona-Esquerra* (520 k inhabitants) is the main aim of home hospitalization, demonstration of sustainability at Hospital Clinic of Barcelona constitutes the core goal of the prehabilitation service. Likewise, full coverage of integrated care services addressed to frail chronic patients is aimed at the city of Badalona (216 k inhabitants).

Methods: The population-based analysis, as well as the three service-based protocols, follow observational and experimental study designs using a non-randomized intervention group *(integrated care)* compared with a control group *(usual care)* with a propensity score matching method. Evaluation of cost-effectiveness of the interventions using a Quadruple aim approach is a central outcome in all protocols. Moreover, multi-criteria decision analysis is explored as an innovative method for health delivery assessment. The following additional dimensions will also be addressed: i) Determinants of sustainability and scalability of the services; ii) Assessment of the technological support; iii) Enhanced health risk assessment; and, iv) Factors modulating service transferability.

(Continued on next page)

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(Continued from previous page)
Discussion: The current study offers a unique opportunity to undertake a comprehensive assessment of integrated care fostering deployment of services at regional level. The study outcomes will contribute refining service workflows, improving health risk assessment and generating recommendations for service selection.

Trials registration: NCT03130283 (date released 04/06/2018), NCT03768050 (date released 12/05/2018), NCT03767387 (date released 12/05/2018).

Keywords: Chronic patients, Integrated care services, Multimorbidity, Service transferability, Home hospitalization, Prehabilitation, Digital tools, Implementation science, Risk assessment, Multi-criteria decision analysis

Background

Core elements of integrated care (IC) are connectivity, alignment and collaboration within and between the cure and care sectors. The goal is to enhance quality of care and quality of life, consumer satisfaction and system efficiency for patients suffering from chronic disorders, that need multiple services, providers and settings in different levels of care [1–3]. Useful approaches [4] have identified two main systemic levels (i.e. horizontal and vertical) at which integration of health and social care sectors can occur. Horizontal integration links community-based services while vertical integration brings together specialized and primary care under one functional (or structural) management umbrella through shared care agreements framed into well-defined service workflows.

Since early 2000's, large scale implementation of IC is being strongly promoted by relevant international agencies and governments [5, 6] because of its high potential to effectively address the healthcare and societal challenges generated by population ageing and unhealthy lifestyles. However, several aspects implicit in the transition towards real care coordination scenarios, must be taken into account and properly solved to ensure adoption. First, since IC services are applied to complex patients and in evolving settings, the need for flexible standardization of the interventions, as well as changes in the roles of patients and health professionals is a must. Second, the coordination between several stakeholders and/or healthcare tiers often requires profound organizational adaptations which, in turn, involve the need for novel business models and reimbursement incentives to drive management change. Last but not least, quickly evolving digital technologies are facilitating coordination and personalization of care, as well as complex data management, but extensive adoption of digital health supporting IC needs to be accelerated.

All of the above factors contribute to explain the difficulties encountered in the process of standardization of IC assessment. Over the past several years, evaluation of well-established IC programs, alongside pilot experiences, has been undertaken in several countries with mixed results [7–9]. Overall, these experiences have contributed to the generation of a series of general recommendations on evaluation of IC with focus on service transferability across geographical sites aimed at fostering regional scalability [4, 10]. It is of note, however, that application of these recommendations for a comprehensive assessment of deployment of IC services in real-life scenarios is clearly an unmet need.

The current manuscript aims to describe a structured evaluation framework (Fig. 1) that articulates four comprehensive assessment protocols covering both vertical and horizontal levels of integration. One assessment protocol reports a population-based assessment of outcomes from past and current Catalan Health Plans, 2011–2015 [11] and 2016–2020 [12], respectively, whereas the other three assessment protocols address the deployment of specific IC services during the period 2017–2018, namely: i) Home hospitalization [13]; ii) Prehabilitation of candidates for major surgery [14]; and, iii) Community-based advanced care service for frail elderly [15, 16]. The ultimate aim of the research is to explore the application of innovative evaluation strategies [4] for IC services deployed in real-life settings. To this end, a comprehensive evaluation of outcomes following a Quadruple Aim approach [17, 18], deployment strategies and maturity of implementation will be performed within each of the four assessment protocols of the study.

The Catalan Health Care System dispenses services for 7.5 inhabitants, providing universal coverage through a tax-based system. Administratively, it is composed by a single public payer and multiple service providers publicly or privately owned. Since 2006, the implementation of IC services in one of the four healthcare sectors in the city of Barcelona (520 k inhabitants) was instituted by the Hospital Clinic of Barcelona (HCB), a tertiary university hospital [19], adopting the Chronic Care Model as the conceptual reference [20, 21]. Moreover, the subsequent Health Plans for Catalonia after 2011, have addressed the deployment challenges by giving priority to new modalities of healthcare delivery for chronic patient care including empowerment of patients and carers. To date, clear examples of clinical effectiveness have been produced for the three IC services presented

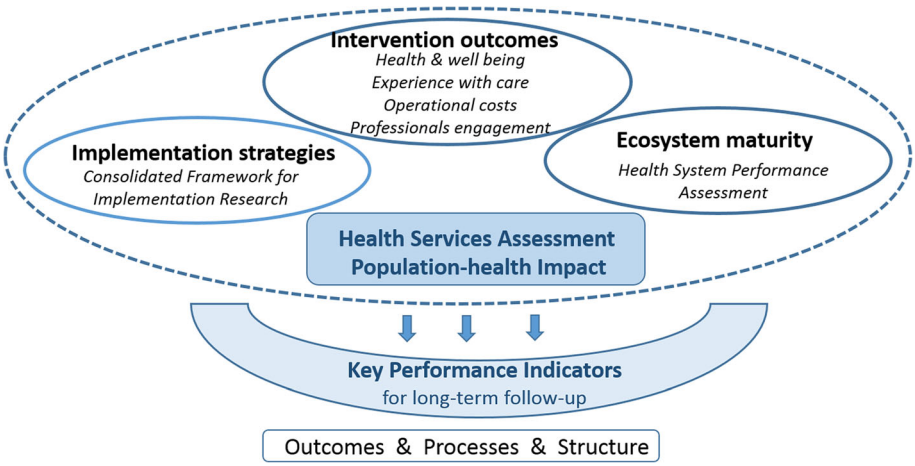

Fig. 1 The figure depicts the main elements of the structured evaluation framework that articulates the four assessment protocols described in the current report. The proposed comprehensive assessment of integrated care services includes their impact at population level. A core component of the assessment protocols includes the identification of Key Performance Indicators (KPI) useful for long-term follow-up of health services after adoption encompassing three dimensions: health outcomes, processes and structure

in this report: Home hospitalization [13, 22, 23], prehabilitation [14] and community-based services for frail patients [9]. It is expected that lessons learned from the implementation of the four protocols reported in the current manuscript will foster regional scalability and sustainability of IC services in Catalonia. Moreover, it is also expected that the recommendations generated by these deployments in real-life settings will significantly contribute to facilitate transferability and comparability of IC services at international level. The context in which these four assessment protocols will take place is described in [11] and [19].

Methods

The four protocols (Table 1) follow observational and experimental non-randomized study designs. In all cases, comparability between the intervention group and the control group will be achieved using a propensity score matching (PSM) [24, 25] method, as described in detail below. The common methodology for assessing health-value generation of the interventions in each protocol will follow a Quadruple Aim approach [17, 18] considering pre-defined variables for: i) Health and well-being; ii) Experience with care; iii) Operational costs; and, iv) Health professionals' engagement, as summarized in the second column of Table 2. It is of note that the outcomes of the three first dimensions (Triple Aim approach) [26, 27, 30] will be assessed both separately and jointly. The later will consist of a multi-criteria decision analysis (MCDA) recently developed [31, 32] and currently applied in 17 selected IC programs from 8 European countries [33]. The MCDA approach broadens the scope of the evaluation taking into account patient health reported outcomes and stakeholders' views on those same outcomes allowing standardized comparisons between seemingly dissimilar IC programmes. Moreover, engagement of health professionals, the fourth pillar of the Quadruple Aim approach, will be assessed using the questionnaires currently applied in [34], aiming at assessing main drivers of large-scale deployment of IC services in 5 European regions.

The current assessment protocols also aim to separately establish key factors that modulate the success of IC service deployments in order to identify their potential for transferability to other sites. To this end, we will use standard implementation science tools [28, 29, 35, 36] to answer the questions delineated in the third column of Table 2, as well as to report the results of the implementation process following standards for reporting implementation studies (StaRI) [28]. This will allow us to identify facilitators, barriers, solutions and critical success factors during the course of the implementation process with relevant implications for analysis of service transferability. It must be highlighted that collaborative tools and methodologies were applied for the implementation of the three service-oriented studies. The process incorporates co-design elements, with participation of different stakeholders, including patients, following a Plan-Do-Study-Act (PDSA) iterative cycles approach [37] adapted to the characteristics of each assessment protocol, as summarized below. Last, but not least, the maturity of the ecosystem in which the service is being deployed will be assessed following the twelve-dimension measurement protocol described in [4] and summarized in the fourth column of Table 2.

It is assumed that the three assessment categories depicted in Fig. 1 and in Table 2: i) Outcomes, ii) Deployment strategies, and, iii) Maturity level, will provide

Table 1 Main characteristics of the four assessment protocols

Protocol	Aims	Study design & Measurements	Intervention group	Comparator group	Expected outputs
(1) Population-based study	(1.1) Impact of integrated care on cost-effectiveness	(1.1) Case control study matching registry data using PSM methods (2011–2017) (Additional file 1: Table S1)	(1.1 and 1.2) Residents living in the healthcare district of Barcelona-Esquerra (n = 516 K inhabitants)	(1.1 and 1.2) Residents living in the other 3 healthcare districts of Barcelona (~ 400 k inhabitants each), as well as the entire region of Catalonia (n = 7.5 M inhabitants)	(1.1a) Health value generation of integrated care
	(1.2) Enhanced health risk assessment and service selection	(1.2) Fixed cohort study			(1.1b) Enhanced Key Performance Indicators (KPI) for long-term assessment of integrated care
					(1.2) Proposal for health risk assessment for service selection
(2) Home hospitalization	(2.1) Assessment of hospital avoidance and early hospital discharge at district level	(2.1) Prospective controlled cohort study using PSM methods (2017–2018) (Additional file 2: Table S2)	(2.1) All patients admitted to the home hospitalization directly from the emergency room (n = 800 patients). Study of a deeply characterized subset (triple aim approach) of 200 patients. This subset will be used to generate (2.2).	(2.1) Patients admitted to conventional hospitalization directly from the emergency department of the same hospital (n = 800 patients). Study of a deeply characterized subset (triple aim approach) of 200 patients. This subset will be used to generate (2.2).	(2.1a) Health value generation of the service; expanded HDA using MCDA (n = 200). Factors modulating success of the implementation strategy.
	(2.2) Recommendations for shared-care agree ments between specialized and community-based care	(2.2) Observational mixed-methods study combining network and cluster analyses with qualitative methodologies			(2.1b) KPI for service assessment
					(2.2) Strategies for enhanced interactions between specialized-community-based care.
(3) Prehabilitation	(3.1) Sustainability (cost-effectiveness of prehabilitation at HCB	(3.1) Prospective controlled cohort study using PSM methods (2016–2018) (Additional file 3: Table S3)	(3.1) All candidates for major surgery at HCB receiving prehabilitation (n = 500)	(3.1) Candidates for major surgery at HCB receiving usual care in the same hospital (n = 250)	(3.1a) Health value generation of prehabilitation at HCB
	(3.2) Recommendations for transition toward a regional peri-operative care program	(3.2) Randomized controlled trial to assess peri-operative care	(3.2) Candidates for major surgery at HCB receiving peri-operative care (n = 60)		(3.1b) KPI for service assessment
	(3.3) Enhanced pre-operative risk assessment	(3.3) Fixed cohort study	(3.3) All surgical patients in the last 5 years at HCB	(3.2) Candidates for major surgery at HCB receiving usual care (n = 60)	(3.2) Cost-effectiveness of peri-operative care and strategies for regional deployment.
					(3.3) Risk assessment tool for personalized prehabilitation
(4) Frail elderly patients	(4.1) Assessment of community-based integrated care services for frail patients at BSA	(4.1) Prospective controlled cohort study using PSM methods (2018) (Additional file 4: Table S4)	(4.1) Individuals enrolled in BSA integrated care programs for frail elderly that includes: i) Early Discharge support (n = 144); ii) Long-term home-based support services (n = 566) and iii) Geriatric residences care (n = 920)	(4.1) Individuals living in Badalona receiving usual care: i) After hospital discharge (n = 144), ii) At home (n = 566); and, iii) Living at geriatric residences (n = 920)	(4.1a) Cost-effectiveness of the service; and, expanded HDA using MCDA (n = 250). Factors modulating success of the implementation strategy.
					(4.1b) KPI for service assessment

Abbreviations: *HDA* Health Delivery Assessment, *MCDA* Multi-Criteria Decision Analysis, *HCB* Hospital Clinic de Barcelona, *PSM* Propensity Score Matching, *KPI* Key Performance Indicators for service long-term assessment after the deployment phase, *BSA* Badalona Serveis Asssistencials

Table 2 Three main assessment dimensions: effects of the intervention, determinants of success of implementation and maturity of integration

Study Protocol	Outcomes of the intervention [26, 27]		Deployment strategies [28, 29]	Maturity level [4]
(1) Population-based	Mortality, general practitioner visits, community-nurse visits, cumulative days per year admitted in hospital, emergency department visits, all hospital admissions, potentially avoidable hospitalizations, multiple drug prescription, needs for social support, costs per patient per year (Additional file 1: Table S1)		A. What are the possible factors and agents responsible for good implementation of a health intervention? B. What are the possible factors for enhancing or expanding a given health intervention? C. What describes the context in which implementation occurs? D. What describes the main factors influencing implementation in a given context? To be assessed using a mixed methods approach: combining qualitative and quantitative methods	Assessment of the twelve dimensions of the Maturity Model for Integrated Care, both at health system and health services levels, promoted by the European Innovation Partnership for Active and Healthy Ageing, following the instructions reported in reference (4). These twelve dimensions are: 1. Readiness to Change 2. Structure & Governance 3. Information & eHealth Services 4.Standardization& Simplification 5. Finance & Funding 6. Removal of Inhibitors 7. Population Approach 8. Citizen Empowerment 9. Evaluation Methods 10. Breadth of Ambition 11. Innovation Management 12. Capacity Building
(2) Home hospitalization	Health and well-being	Mortality rate 30/90 days after discharge, place of death, avoidable hospital admissions, total bed days, 12 months before admission (hospital and community resources); 30-day after discharge (hospital and community resources), transitional care strategies (palliative care, primary care or hospital care)		
	Patient experience	Person centeredness, continuity of care (Additional file 2: Table S2)		
	Costs	Operational costs		
(3) Prehabilitation	Health and well-being	Cumulative hospital days of stay, intensive care unit length of stay, number of complications per patient, costs from the perspective of the hospital including inpatient services, diagnostic procedures, pharmaceutical consumption and blood products consumption, aerobic capacity, physical activity, psychological status, health status (Additional file 3: Table S3)		
	Costs	Operational costs		
(4) Frail elderly	Health and well-being	Mortality rate, avoidable hospital admissions, total bed days, 30-day readmissions, number of ER visits in the month, physical functioning, psychological well-being, social relationships & participation, enjoyment of life, resilience, autonomy		
	Patient experience	Person centeredness, continuity of care, burden of medication, burden of informal caregiving (Additional file 4: Table S4)		
	Costs	Operational costs		

the basis for identification of general, and service-specific, key performance indicators (KPI) useful for long-term follow-up of IC services after the initial deployment period, taking into account outcomes, processes and structure [38].

The assessment protocols will combine three different data sources. First, registry data obtained from the Catalan Health Surveillance System (CHSS) [16, 39, 40], as briefly described below. Second, individual data extracted from the electronic healthcare records from primary care and specialized care. Third, data derived from prospectively applied standardized questionnaires to patients, health professionals and managers (Additional file 1: Table S1, Additional file 2: Table S2, Additional file 3: Table S3 and Additional file 4: Table S4). The challenges involved in the combination of different datasets used in these four assessment protocols have been overcome within the framework of the recent EU General Data Protection Regulation (GDPR) [41].

The CHSS includes updated registries from primary care, hospital-related events (e.g. hospitalization, emergency room and specialized outpatient visits), pharmacy, mental health, socio-sanitary services, respiratory therapies, dialysis, outpatient rehabilitation and non-urgent transport of all citizens living in Catalonia (7.5 M) since 2011. The information is updated every 6 months. It provides a basis for cost analyses of the use of healthcare resources, pharmacy consumption, and prevalence of key health problems. The CHSS feeds the regional population-based risk stratification tool named Adjusted Morbidity Groups (GMA) that complies with the following characteristics: i) A population health approach; ii) No licensing constraints; iii) Open source computational algorithms; and, iv) The adjusted morbidity grouper relies mostly on statistical criteria, as opposed to other tools that include expert-based coefficients, thus facilitating quick transferability to other territories [39, 42].

Assessment protocols

Assessment protocol 1: population-based analysis

This protocol will take into consideration the entire population of healthcare users in Catalonia. The health system in Catalonia (7.5 M inhabitants) has three organisational levels, with the seven health regions at the top level (Fig. 2). Each region includes several geographical areas called health districts, second level, covering both specialised and primary care needs of the population. The third level corresponds to clusters of primary care centres within each healthcare district. The region has a

Fig. 2 The figure displays the seven health regions of Catalonia. The urban area of Barcelona (1.8 million citizens) has four health districts. The South-Eastern healthcare sector of the Barcelona city, which encompasses 520 k inhabitants, is Barcelona-Esquerra (AISBE). Taken from the Catalan Health Service (CatSalut) website. https://catsalut.gencat.cat/ca/coneix-catsalut/transparencia/territori/informacio-cartografica/mapes/ This is a public access image.

total of 369 primary care units covering approximately 20 k citizens, on average, each of them.

Integration of health and social services in the entire Catalonia is being promoted under the umbrella of the five-year regional health plans. Key goals in terms of deployment of the integrated model were established during the 2011–2015 Plan [11] and consolidation of the program is expected during the 2016–2020 period [12].

The Integrated Health District in Barcelona-Esquerra (AISBE) (n = 520 k inhabitants) [19] is the intervention district and includes HCB as reference centre, two general hospitals and 19 primary care centres run by different healthcare providers. Since mid-2000s, AISBE has deployed, and continuously developed, IC services for chronic patients across healthcare tiers [9, 19]. Deployment of IC services in AISBE is based on the hypothesis that an appropriate transfer of selected care complexities from hospital-based to community-based care, within an IC scenario, can increase healthcare value generation both at provider and at health system levels. The main characteristics and achievements of technologically-supported IC services evaluated and adopted in AISBE have been reported elsewhere [8, 9, 14, 16, 19, 43].

The main objective of this assessment protocol is the analysis of health-value generation of IC in Catalonia (Table 1). An ancillary aim is to enhance health risk assessment for clinical purposes and service selection, taking into account the population-based risk assessment tool, (i.e. GMA), as reported in [39]. For the principal objective, health-related outcomes in AISBE will be compared using a case-control design with three other healthcare districts of the city of Barcelona (approximately 400 k inhabitants each), and the entire region (7.5 M inhabitants), considered as control areas. A PSM method will used for comparability purposes using age, sex, health-risk grading based on GMA [39, 42], and socioeconomic status as matching variables. Comparisons between intervention and controls will be done on a yearly basis for the period 2011–2017. Key specific aspects of the assessment protocol are summarized in Additional file 1: Table S1.

Health risk assessment and service selection will address enrichment of the predictive role of standard clinical information using population-based health risk assessment (GMA grading) and patient self-tracked information obtained through the regional personal health folder in Catalonia (La Meva Salut). Evaluation of resulting clinical predictive modelling (Table 1) will be based on fixed cohort study designs with 1 year follow-up, as already reported in [40].

Assessment protocol 2: home hospitalization (HH)

The intervention group to be analysed will include all the patients admitted to HH and early discharge service from HCB during a one-year period (October 2017–October 2018) (n = 1146), approximately 70% of the patients were admitted to HH directly from the emergency room. A subset of the patients admitted to HH directly from the emergency room throughout the study period will be assessed separately (n = 200).

The characteristics of the intervention have recently been described by Hernandez et al. [13] in terms of implementation strategy, outcomes and costs during the deployment of the service in a real-life setting during the years 2006–2015. During the period 2017–2018, the programme was expanded to 48 beds per day to cover the entire AISBE health district.

The principal objective of this protocol is to assess hospital avoidance and early hospital discharge at health district level. Moreover, the approach aims to generate recommendations for shared-care agreements between specialized and community-based care after discharge to ensure safe transitional care strategies.

The assessment protocol will consist of a prospective controlled cohort study wherein patients admitted to HH directly from the emergency room (intervention) (n = 800) will be compared with conventional hospitalisation (control) (n = 800). The control group will include patients admitted to conventional hospitalization directly from the emergency room of the same hospital (HCB). PSM will be used for comparability purposes using age, sex, GMA, socioeconomic status, number of hospitalisations during the previous year and polypharmacy as matching variables. As described above, a sub-group of 200 consecutive patients recruited on a voluntary basis, admitted through the emergency department during the study period, from each arm (HH and conventional hospitalization) will be also thoroughly characterized using a set of standardized questionnaires [26, 27, 30], as depicted in Tables 2 and Additional file 2: Table S2. It is of note that these two well defined sub-groups of 200 patients each (n = 400) will also constitute a single fixed cohort for later analysis on the interactions between specialized and community-based care using network and cluster analyses alongside qualitative methodologies.

Assessment protocol 3: Prehabilitation service

This is a preventive intervention targeted at high risk candidates for major surgical procedures carried out preoperatively aiming at reducing complications and enhancing postoperative recovery. It combines: i) Motivational interviewing; ii) High-intensity endurance exercise training; iii) Promotion of physical activity; iv) Nutritional supplementation; and; v) Psychological support.

The intervention is currently deployed as a mainstream service at HCB in several types of major surgeries. During fall 2017, three multidisciplinary workshops

using a design-thinking approach were carried out to refine the service workflow and to explore the potential for service scalability. The outcomes of the co-design process provided a robust background for the design of a future personalized perioperative care service at regional level covering three phases: prehabilitation, inpatient care, and post-discharge rehabilitation.

The current assessment protocol aims to assess cost-effectiveness of prehabilitation as a mainstream service in the ongoing deployment at HCB, as well as to generate a roadmap for regional scalability of the service. It is planned as a prospective controlled cohort study including 500 consecutive patients undertaking prehabilitation, as the intervention group, and patients following standard care before surgery, in the same hospital (i.e. HCB), as the control group (2:1 intervention to control ratio). The patients will be included from the following type of surgeries: major digestive surgery ($n = 525$), lung volume reduction ($n = 30$), radical cystectomy ($n = 30$), major cardiovascular surgery ($n = 165$). Study groups will be made comparable using PSM with the following matching variables: type of surgery, age, sex, American Society of Anaesthesiologists index and GMA grading. Patients' clinical outcomes will be assessed at baseline, pre-surgery and 30 days after surgery. The primary outcome will be cost-effectiveness, meaning reduced hospital stay and early re-admissions. Secondary outcome variables will include number of complications per patient, healthcare use, aerobic capacity, physical activity and psychological and health status. The specificities of the assessment protocol are summarized in Additional file 3: Table S3.

Assessment protocol 4: community-based care for the frail elderly

The assessment protocol will evaluate three types of specific interventions during the period from 1st January to 31th December 2018: i) Early discharge service ($n = 144$) which includes acute patients admitted to the medical and/or surgical hospital wards and promptly discharged to receive home-based post-acute care and/or rehabilitation; ii) Home-based Case Management service ($n = 566$) which includes complex chronic patients or patients receiving long-term care by a case management nurse; and, iii) Geriatric residences service ($n = 920$) will include patients receiving acute support, post-acute or continued care for elderly people living in geriatric residences. It will be conducted by Badalona Serveis Assistencials (BSA), an IC service provider located in the city of Badalona (216 K inhabitants) in the North-Eastern part of the Barcelona Metropolitan Area.

The current assessment protocol, summarized in Additional file 4: Table S4, aims to assess cost-effectiveness of these three interventions for frail patients, as well as to generate a roadmap for regional scalability of the service. The study protocol will consist of a prospective controlled cohort study wherein each intervention group will be compared with the corresponding usual care group (controls, 1:1 ratio) ($n = 1630$ in each arm), using propensity score matching. Age, sex, GMA, socioeconomic status, number of hospitalisations during the previous year and polypharmacy will be used as matching variables. The patients from the usual care group will be recruited during the study period in the same area. A subset of 250 patients from each control and intervention groups will be thoroughly characterized using a set of standardized questionnaires [26, 27, 30], as depicted in Additional file 4; Table S4.

Additional elements toward enhancement of IC services

All four assessment protocols will also integrate the following dimensions described below.

Enhanced risk assessment & service selection

The 2011–2015 Catalan Health Plan extensively implemented a case finding system classifying high risk chronic patients into two different categories based on defined criteria and primary care physician judgement: i) Complex chronic patients (CCP, approximately 3% of the population); and, ii) Patients with less than 12 months expected life survival (Advanced Care Disease, ACD, approximately 1% of the population). The latter category of patients consists of citizens with advanced chronic diseases and/or with oncological problems being potential candidates for palliative care.

Since 2015, the population-based risk stratification tool (i.e. GMA) primarily used for health policy purposes, has been extensively implemented in primary care. The clinical workstation currently displays the GMA grading of the patient being attended by the health professionals, without specific connections with the patient's care plan. The current assessment protocols offer an opportunity to explore enhanced clinical risk assessment modalities aiming at facilitating preventive strategies, improving service selection and providing clinical decision support. To this end, the assessment protocols will elaborate and evaluate novel approaches to health risk assessment following the orientations described in [39, 40, 42].

Assessment of technological support

The three service-oriented assessment protocols will assess acceptability, usability and value generation of digital tools supporting the different services with focus on personal health systems, and collaborative adaptive case management (ACM). Since these key supporting technologies are required to be integrated with provider-specific and regional health information systems for a large-scale implementation in the region (i.e., Catalonia), the protocols will be built upon the regional digital

health framework [44] (Additional file 5: Figure S1). Specifically, two personal health systems for patient self-management at community level are being tested: i) MyPathway® (http://mypathway.healthcare); and, ii) CONNECARE Self-Management System (SMS) [45]. The former is a secure digital communications channel connecting patients to clinicians and services. It is a browser and app-based commercial application to use on phones, tablets and PCs. The SMS is a prototype application to use on smartphones that allow patients' self-tracking, monitoring by health care professionals and bi-directional messaging to improve the patients' treatment and encourage them in following it.

The assessment protocols also consider ACM as key supporting technology [46–48] to enhance collaborative work among health professionals and patients themselves (actively participating in his/her healthcare via the above personal health systems). To this end, an ACM process based on the Camunda® open-source platform (https://camunda.org) was selected to support process workflow specification, case management and decision automation. The ACM process engine is aimed at providing the required process engine functionality to current hospital information systems.

Acceptability (by means of 3 Likert scales alongside a net promoter score) [49] and usability (by means of the System Usability Scale - SUS) [50] of MyPathway® and/or SMS will be assessed by patients (at patient discharge from the protocols), and of ACM process engine (i.e. Camunda®) by healthcare professionals. Moreover, assessment of consolidated implementation of the digital health tools supporting each of the four assessment protocols will be done using the mini-MAST tool [51] (Additional file 6: Annex S1).

Co-design activities

Deployment of the Catalan Health Plans involves a highly structured co-design system ensuring follow-up and continuous improvement of the different implementation initiatives. Likewise, the deployment of IC within AISBE has a well-defined structure of committees at different levels ensuring refinement of the implementation processes, as described in detail in [19]. Moreover, two of the EU projects supporting the current assessment protocols [34, 45] have built-in co-design protocols applying collaborative tools and methodologies following a PDSA (Plan, Do, Study, Act) approach [37]. The PDSA cycles are a systematic series of steps for gaining valuable learning and knowledge for the continual improvement of a product or process. All in all, the different levels of co-design activities alluded to above provide information for undertaking a mixed-methods approach combining quantitative and qualitative methodologies to assess implementation of IC services, as indicated Table 2, third column.

Discussion

The current document provides the core information on a framework applicable for the evaluation of large-scale deployment of IC services in Catalonia. The approach relies on the use of assessment of shared interventions, within well-defined service workflows, that have been previously tested in terms of efficacy and potential for value generation. The three assessment categories depicted in Table 2: i) Value generation of IC services following standard and novel approaches, i.e. MCDA; ii) Deployment strategies; and, iii) Maturity level of the ecosystem for implementation will provide the basis for a comprehensive evaluation of IC and should contribute to the identification of KPIs useful for long-term follow-up after IC service adoption (Fig. 1).

Observational and experimental non-randomized controlled cohort study designs using PSM have been adopted, instead of randomized controlled trials, as a pragmatic option to assess events in a real-life setting [52, 53] The assessment protocols also take into account the role of digital health as enabling tools supporting different strategic aspects of care coordination, namely: service scalability, service evaluation and personalization through enhanced service selection, as described in [39].

We believe that the current regional context in Catalonia facilitates full alignment between the Catalan Health Plan 2016–2020 [12] and the ongoing Nextcare program [54] aiming at fostering innovation of digitally-supported healthcare services for chronic patients with multimorbid conditions. It is of note that Nextcare acts as an umbrella program wherein three EU projects with similar timeframes converge covering complementary facets of IC implementation, namely: i) CONNECARE [45], addressing enhanced digital support of IC services; ii) SELFIE [33], exploring novel modalities of health delivery assessment like multi-criteria decision analysis; and, iii) ACT@Scale [34], analysing key factors that modulate large scale deployment of IC services. All in all, the scenario described facilitates the progressive expansion of the results of the assessment protocols to analyses of other IC services (i.e. non-invasive home-based ventilation, cardiopulmonary rehabilitation of chronic patients, etc.) and to distinct healthcare districts toward achievement of effective full regional deployment of care coordination.

Real-life assessment of IC services using the proposed implementation research methodologies will contribute to quantify health value generation of care coordination. The approach should also contribute to generating recommendations for transferability of the services facilitating outcomes comparability across sites.

Additional files

Additional file 1: Table S1. Population-based protocol. (DOCX 26 kb)

Additional file 2: Table S2. Home Hospitalization protocol. (DOCX 35 kb)

Additional file 3: Table S3. Prehabilitation protocol. (DOCX 28 kb)

Additional file 4: Table S4. Three interventions addressed to frail complex chronic patients. (DOCX 35 kb)

Additional file 5: Figure S1- Digital health framework in Catalonia (IS3). (DOCX 75 kb)

Additional file 6: Annex 1 - Method for ASsessment of Telemedicine (mini-MAST). (DOCX 22 kb)

Abbreviations

ACD: Advanced care disease; ACM: Adaptive case management; AISBE: The Integrated Health District in Barcelona-Esquerra; BSA: Badalona Serveis Assistencials; CCP: Complex chronic patients; CHSS: Catalan Health Surveillance System; GDPR: General data protection regulation; GMA: Adjusted morbidity groups; HCB: Hospital Clinic of Barcelona; HDA: Health delivery assesment; IC: integrated care; KPI: Key performance indicator; MCDA: multi-criteria decision analysis; PDSA: Plan-Do-Study-Act; PSM: Propensity score matching; SMS: Self-managemet system; StaRI: Standards for reporting implementation studies

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Authors' contributions

All authors have read and approved the manuscript. EB, JR2, IC, AB-G, CH1, CH2 and FB developed the comprehensive framework for IC evaluation and drafted this paper. AA, M-JA, CB, MC, J-CC, JdB, KI, RK, ML, GM-P, FM, MM, DM, JP, JR1, NR, RR, MRvM, TS, SS, HS, OS, GT, EV1 and EV2 critically reviewed and generated relevant inputs to this paper. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Written informed consent will be obtained from all participants. All the protocols submitted were approved by the Ethics Institutional Board (CEIm) of the Hospital Clinic of Barcelona. Committee reference numbers are: 2016/0883, 2017/0451 and 2017/0453.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Digital Health Transformation of Integrated Care in Europe: Overarching Analysis of 17 Integrated Care Programs

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Abstract

Background: Digital health tools comprise a wide range of technologies to support health processes. The potential of these technologies to effectively support health care transformation is widely accepted. However, wide scale implementation is uneven among countries and regions. Identification of common factors facilitating and hampering the implementation process may be useful for future policy recommendations.

Objective: The aim of this study was to analyze the implementation of digital health tools to support health care and social care services, as well as to facilitate the longitudinal assessment of these services, in 17 selected integrated chronic care (ICC) programs from 8 European countries.

Methods: A program analysis based on thick descriptions—including document examinations and semistructured interviews with relevant stakeholders—of ICC programs in Austria, Croatia, Germany, Hungary, the Netherlands, Norway, Spain, and the United Kingdom was performed. A total of 233 stakeholders (ie, professionals, providers, patients, carers, and policymakers) were interviewed from November 2014 to September 2016. The overarching analysis focused on the use of digital health tools and program assessment strategies.

Results: Supporting digital health tools are implemented in all countries, but different levels of maturity were observed among the programs. Only few ICC programs have well-established strategies for a comprehensive longitudinal assessment. There is a strong relationship between maturity of digital health and proper evaluation strategies of integrated care.

Conclusions: Notwithstanding the heterogeneity of the results across countries, most programs aim to evolve toward a digital transformation of integrated care, including implementation of comprehensive assessment strategies. It is widely accepted that the evolution of digital health tools alongside clear policies toward their adoption will facilitate regional uptake and scale-up of services with embedded digital health tools.

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KEYWORDS

program evaluation; chronic patients; eHealth; elderly; integrated care; social support; telemonitoring; information and communication technology

Introduction

Background

Digital health (eHealth) tools have been proposed to improve access to health care services, enhance care co-ordination and integration, enable self-management, support decision-making, enable monitoring, perform risk analysis, and facilitate proactive interventions [1]. It is within this context that the European Commission has defined eHealth as follows:

> *The use of Information and Communication Technologies in health products, services and processes, combined with organizational change in health care systems and new skills, in order to improve health of citizens, efficiency and productivity in health care delivery, and the economic and social value of health [2]*

The implementation of digital health tools has constituted an area of major research and innovation in the past years [1,4-7]. For example, the impact of electronic health records on health care quality has been explored by Campanella et al who showed improvement in health care quality in terms of guideline adherence and time efficiency while reducing medication errors [8]. In parallel, most countries have recognized the value of patient portals [9-11]. The use of health monitoring devices in the general population is also increasing, with a broad spectrum of sophistication, including examples like integration between artificial intelligence and monitoring in a single device (ie, cardiac rhythm analysis) [12]. Moreover, the use of open-source algorithms for subject-specific as well as population-based risk prediction has been reported [13,14]. Some of these technologies are already in use for the management of chronic multimorbid patients [15-20].

It is currently accepted that eHealth tools can be particularly useful to support Integrated Chronic Care (ICC) programs for patients with multimorbidity, that is, co-occurrence of 2 or more chronic disorders within 1 individual [21]. Insights from the ICARE4EU project [6] concluded that eHealth improves care integration and management processes, but the project identified that inadequate funding mechanisms, poor interoperability, and inadequate technological support represent major barriers for adoption of technologically supported ICC. In fact, it is acknowledged that the takeoff of digital health tools to support ICC is progressing rather slowly. Also, regulatory aspects are still a concern [22-24] to achieve a proper balance between preservation of individual privacy and the need for health data sharing [25], as well as the increasing demand for health data analytics.

The Conceptual Framework

The Sustainable intEgrated care modeLs for multimorbidity: delivery, Financing, and performancE (SELFIE) Horizon 2020 project [26] aims to produce evidence and applicable policy advice on ICC programs for people with multimorbidity. Within the project aims, the SELFIE conceptual framework [27] was developed. It comprises 6 core components of integrated care systems adapted from the World Health Organization, namely: (1) *Service delivery*, (2) *Leadership and governance*, (3) *Workforce*, (4) *Financing*, (5) *Technologies and medical products*, and (6) *Information and research*.

This paper focuses on 2 elements out of the 6 components of the SELFIE conceptual framework [27], which refer to the enabling role of digital health tools (*Technologies and medical products*) and assessment of ICC programs (*Information and research*). For each of these 2 components, the 3 levels of the SELFIE conceptual framework (micro, meso, and macro) were taken into account. The micro level is where the individual with multimorbidity interacts with care professionals and informal caregivers. The meso level relates to the organizational level and the institutional setup of providers. Finally, the macro level includes legislations, governance, policies, and system-wide changes at the national and international level.

For *Technologies and medical products*, the SELFIE framework stresses the need for digital health tools to be widely available and user-friendly to provide robust support to the care processes. At a micro level, the use of technology (eg, electronic medical records [EMR) and patient portals) can be a facilitator of collaborative care if tailored to the needs of the patient with multimorbidity. At a meso level, a shared information system (eg, EMR including shared care plans) among multiple providers and care settings can greatly facilitate communication, person-centeredness, personalized care, and care co-ordination. Finally, at a macro level, nationwide and international policies that foster technological development and innovation most likely would benefit from both implementation and continuous assessment of ICC programs for multimorbidity.

For *Information and research*, the project stresses the successful use of collected data from digital health tools for a 3-fold

objective, namely: (1) Population health management; (2) Enhanced subject-specific health care delivery; and (3) Comprehensive assessment of ICC programs. At a micro level, currently collected individual-level data (eg, patient journey record) can effectively be used in the care process for individual risk prediction. At a meso level, shared information systems may further be used for service selection both at individual and group level (eg, triage systems and clinical predictive modelling) to strengthen the evidence base of complex integrated care interventions, as well as to develop indicators particularly relevant for the care of patients with multimorbidity. Alongside data ownership at a meso level, privacy and data protection legislation is an important consideration at macro level.

Aims

It is well accepted that the existence of an important gap between the way in which the role of digital tools is understood and the effective uptake of digital transformation by the different stakeholders in the health care systems at European level. To enable the real implementation and scale-up of the digital health tools with all their potential, we undertook this overarching analysis. Our study aims to synthesize the experiences, views, and opinions (including barriers and enabling factors) of the stakeholders and their impact on the care process, as well as the role and desirable future developments of digital health tools, to foster transformation of health care systems toward sustainability by enhancing management of patients with multimorbidity. A second aim is to characterize the different programs with respect to maturity of their supporting digital health tools and the level of assessment of the ICC program.

Here, we present the results of an overarching analysis of the Thick Descriptions [28] of 17 promising ICC programs selected by the SELFIE project across 8 European countries: Austria, Croatia, Germany, Hungary, the Netherlands, Norway, Spain, and the United Kingdom. Within the overarching analysis, we focus on the different aspects of implementation of digital health tools supporting services and facilitating assessment strategies. This will lead to future directions defining how digital support can contribute to scale-up and evaluation of integrated care services. These services should focus on patient-centered health care provision with dynamic evaluation of technology-enabled integrated care programs, without compromising patient privacy.

Methods

Study Design

To select the 17 ICC programs, each country participating in the SELFIE project [29] applied a search strategy using the findings from an international scoping review, national publications on previous and on-going programs and projects, and consultation with national experts and networks. Details on the process of selection of the programs, as well as the list of the 17 selected programs per country, are reported in Multimedia Appendix 1. The 17 programs were grouped into 4 categories: (1) population health management programs (n=5); (2) frail elderly programs (n=6); (3) programs for individuals at the end-of-life and oncology patients (n=3); and (4) programs for vulnerable individuals who face problems in multiple life domains, like health, housing, and financial problems (n=3).

Procedure and Data Collection

The Thick Description, a qualitative empirical research method, was used in SELFIE to gain a deep understanding of the ICC programs from the different stakeholders' point of view [28,30]. The method undertaken included two different approaches: (1) Study of a variety of documents about each of the 17 ICC programs (ie, official and contractual documents, documents related to past evaluations, and factsheets from each ICC); and (2) interviews conducted with all relevant stakeholders (ie, program managers, initiators, representative of sponsor or payer organizations, health care professionals, informal caregivers, and patients or patient representatives). As described earlier, we concentrate on the two information technology-related dimensions in this paper.

Each partner-country interviewers underwent specific training on how to conduct and analyze the semistructured interviews to ensure uniform procedures. A total of 233 stakeholders were interviewed from November 2014 to September 2016 (see Multimedia Appendix 2 for more detailed information on stakeholder composition per country). The interviews were audio recorded and transcribed verbatim from the audio file by either the interviewer or an independent research transcriber. The resulting transcripts were analyzed by members of the local SELFIE teams using Mayring qualitative content analysis [31]. The quotations which were used in the thick descriptions were edited into readable forms and translated into English. The transcripts were not returned to participants for correction.

When writing this manuscript, we adhered to the COnsolidated criteria for REporting Qualitative research [32]. All information retrieved from the document analysis (including the stakeholders´ interviews) was processed according to the country-specific ethics statement listed under the subheading: *Ethics Approval and Consent to Participate*. The Thick Descriptions of the 17 ICC programs studied can be found on the SELFIE website [33].

Overarching Analysis

The first author did a thematic analysis [34] on the Thick Descriptions of the 2 components of the SELFIE conceptual framework referring to the enabling role of digital health tools (Technologies and medical products) and assessment strategies of the ICC programs (Information and research). He then discussed findings with all other coauthors. For each of these 2 components, this secondary analysis of the Thick Descriptions considered the 3 levels of the SELFIE conceptual framework: micro, meso, and macro. As detailed in Table 1, a 3-level grading system (+ to +++) was developed and used, under the criteria of the coauthors (JR and IC), to score maturity of the 17 ICC programs for each of the 2 components assessed in this research. Finally, the maturity of each of the 2 components of the SELFIE conceptual framework is summarized as the average of the maturity at micro, meso, and macro level.

Table 1. Summary of the maturity grading criteria at micro, meso, and macro level for technologies and medical products and for information and research.

Component	Grading
Technologies and medical products	
Digital health tools (micro)	
Electronic medical records—EMR	+
Personal health records at program level	++
Personal health records at regional level	+++
Organizational interoperability (meso)	
Health information exchange	+
Shared EMR[a]	++
Shared case management systems[b]	+++
Digital transformation policies (macro)	
Only addressing EMR	+
Several initiatives at program level	++
National and regional strategic plans	+++
Information and research	
Evaluation strategies (micro)	
Planned evaluation	+
Partial assessment	++
Full assessment with published papers	+++
Risk assessment (meso)	
Clinical knowledge or rule-based	+
Clinical predictive modelling tools	++
Multilevel predictive modelling tools[c]	+++
Research and innovation policies (macro)	
Incipient initiatives	+
Consolidated programs	++
Strong co-ordination with EU[d] programs	+++

[a]Shared electronic medical records among health care providers.

[b]Shared case management systems among health care providers to support integrated care pathways.

[c]Predictive modelling tools that combine information from various data sources, for example, clinical, population-based, biological, and patient-reported.

[d]EU: European Union.

Ethics Approval and Consent to Participate

Letters of Medical Ethics Approval of study protocols, questionnaires, and informed consent forms were sent and approved by the European Commission as a Deliverable of the SELFIE project.

Austria: Letter from Institute for Advanced Studies (IHS) declaring that ethical approval is not necessary for the evaluation of the two Austrian Integrated Care programs, October 3, 2017.

Croatia: Statement from the Agency for Quality and Accreditation in Health Care and Social Welfare declaring that the two evaluation studies are not within the scope of work of Croatian Central Ethics Committee, August 28, 2017, with reference to Official Gazette No 121/07 and No 25/15.

Germany, Gesundes Kinzigtal: Letter from the Ethical Committee, Technische Universität Berlin, declaring that the research is ethically acceptable (Ref: ST_02_20170620, August 15, 2017).

Germany, Casaplus: Letter from the Ethical Committee, Technische Universität Berlin, declaring that the research is ethically acceptable (Ref: ST_01_20170428, August 4, 2017).

Hungary, OnkoNetwork: The research plan has been authorized under approval No IG/03092–000/2016 by the Director General of Moritz Kaposi General Hospital, based on the positive opinion of the Institutional Research Committee and the

responsible person of the Hospital for data protection. The Institutional Ethics Committee of the hospital double-checked the research and publication plan and confirmed that no ethical concerns were emerging related to this research and to the publication of findings (October 10, 2018, Ref: IKEB_IG_04125-000_2018).

Hungary, Palliative Care Consult Service: Letter from the Medical Research Council (Tudomanyos es Kutatasetikai Bizottsag, ETT TUKEB) declaring that the research is granted with Professional-Ethical Approval (Ref: 18632–4/2017/EKU, 24–4-2017).

The Netherlands, Proactive Primary Care Approach for Frail Elderly (U-PROFIT): Letter from the Medical Ethical Committee (MEC) Erasmus Medical Center Rotterdam declaring that the research is exempt from the Medical Research Involving Human Subjects Act (Dutch acronym: WMO; Ref: MEC-2017-402, July 25, 2017).

The Netherlands, Care Chain Frail Elderly (CCFE): Letter from the Medical Ethical Committee (MEC) Erasmus Medical Center Rotterdam declaring that the research is exempt from the Medical Research Involving Human Subjects Act (Dutch acronym: WMO; Ref: MEC-2014.558, December 18, 2014).

The Netherlands, Better Together in Amsterdam North (BSiN): Letter from the Medical Ethical Committee (MEC) of the Free University Medical Centre declaring that the research is exempt from the Medical Research Involving Human Subjects Act (Dutch acronym: WMO; Ref: MEC-2017-121, March 10, 2017).

Norway, Learning Network for Whole, Co-ordinated and Safe Pathways: Letter from the Regional Committees for Medical and Health Research Ethics-West (Komité for medisinsk og helsefaglig forskningsetikk -REK vest) declaring that the research is ethically approved (Ref: 2017/632/REK vest, March 28, 2017).

Norway, Medically Assisted Rehabilitation Bergen: Letter from The Regional Committees for Medical and Health Research Ethics-West (Komité formedisinsk og helsefaglig forskningsetikk -REK vest) declaring that the research is ethically approved (2017/944/REK vest, June 21, 2017).

Spain, Barcelona-Esquerra (AISBE): Letter from Clinic Research Ethical Committee (Comitè Ètic d'Investigació Clinica—CEIC) of the Clinic Hospital of Barcelona (Ref: CIF-G-08431173, Reg. HCB 2017/0451, June 14, 2017).

Spain, Badalona Serveis Assistencials (BSA): Letter from Clinic Research Ethical Committee (Comitè Ètic d'Investigació Clinica—CEIC) of the Clinic Hospital of Barcelona (Ref: CIF-G-08431173, Reg. HCB 2017/0453, June 14, 2017).

United Kingdom: Approval was granted by the National Health Service (NHS) Health Research Authority Research Ethics Committee (SELFIE REF: 16/WM/0295; CLASSIC REF: 14/NW/0206, June 23, 2016).

All participants provided written informed consent before participation.

Results

Overview

Multimedia Appendix 3 provides a high-level description of results for the 2 components of the SELFIE conceptual framework considered in this study. In this table, main features of each ICC program (third and fourth columns) are provided per type of ICC program (first column) and country (second column). Extended results for the 17 ICC programs are reported in the text below. As a summary of the results, Table 2 displays an average of the 3-level maturity grading criteria stated in Table 1 for each of the 17 ICC programs, according to the micro, meso, and macro levels of the SELFIE conceptual framework.

Technologies and Medical Products

The overarching analysis provided the following valuable insights on the implementation and exploitation of digital health tools to support ICC.

Digital Health Tools (Micro)

All 17 ICC programs have at least partial implementation of *EMR* and they are planning to enhance implementation of EMR in the future.

However, *specific personal health records* to enhance patient engagement are not considered in programs like Health Network Tennengau (HNT), Casaplus, OnkoNetwork (ON), Palliative Care Consulting Service (PCSS), Better together in Amsterdam North (BSiN), and Medically Assisted Rehabilitation (MAR). In such programs, digital information exchange between care provider and patient are either not considered or telephone is still the dominant tool for communications. Nevertheless, the use of personal health records has been key to support various telemonitoring services for patient self-management in programs like in GeroS (eKarton). Likewise, South Somerset Symphony Program (SSSP) and Salford Integrated Care Program (SICP), both from the United Kingdom, stress the role of digital health tools (ie, Patients Know Best) to support telemonitoring, albeit suffering from some implementation problems:

> *Tele-dermatology and we're piloting it [...] the GP will take a photograph and email it and get a decision, they're not doing suspected cancers obviously, but rashes. Yeah, we've done it* [IP11_1—SICP]

> *We've also got telehealth, that support. So we've got patients who are on telehealth in their homes, and each morning, the intensivists review the telehealth and see if there's any flags, like, if somebody is on [...] I'm trying to think. If somebody is on some sort of medication that they need to, you know, where fluid balance is an issue, if they've lost six pounds in weight that might flag some medication change. So they get them to weigh themselves, do their blood pressure, and so on. So, telehealth has been hugely supportive, actually, at keeping patients at home* [IP08_2—SSSP]

Table 2. Average maturity levels of the 17 Integrated Chronic Care programs.

Country	Program	Technologies and medical products	Information and research
Austria	HNT[a]	++	+
Austria	SMC[b]	+	+
Germany	Casaplus	++	++
Germany	GK[c]	++	++
Spain	AISBE[d]	+++	++
Spain	BSA[e]	++	++
Croatia	GeroS	++	+
Croatia	PCS[f]	+	+
Hungary	ON[g]	+	+
Hungary	PCCS[h]	+	+
The Netherlands	BSiN[i]	++	++
The Netherlands	CCFE[j]	++	++
The Netherlands	U-PROFIT[k]	++	++
Norway	LN[l]	+	+
Norway	MAR[m]	+	++
United Kingdom	SICP[n]	++	++
United Kingdom	SSSP[o]	++	+

[a]HNT: Health Network Tennengau.
[b]SMC: Sociomedical Centre Liebenau.
[c]GK: Gesundes Kinzigtal.
[d]AISBE: Area Integral de Salut Barcelona-Esquerra.
[e]BSA: Badalona Serveis Assistencials.
[f]PCS: Palliative Care System.
[g]ON: OnkoNetwork.
[h]PCCS: Palliative Care Consulting Service.
[i]BSiN: Better together in Amsterdam North.
[j]CCFE: Care Chain Frail Elderly.
[k]U-PROFIT: Proactive Primary Care Approach for Frail Elderly.
[l]LN: learning network.
[m]MAR: Medically Assisted Rehabilitation.
[n]SICP: Salford Integrated Care Program.
[o]SSSP: South Somerset Symphony Program.

It is of note that the availability of *personal health records at regional level*, which is the case with the programs Area Integral de Salut Barcelona-Esquerra (AISBE) and Badalona Serveis Assistencials (BSA) (La Meva Salut) [35], generates additional potential to foster collaborative work at micro level.

Organizational Interoperability (Meso)

Most of the programs use secure networks for *health information exchange* between hospitals and general practitioners, but with a broad spectrum of maturity. For example, the Casaplus program implemented a specific Web-based platform to support regular communication between case managers and nursing professionals only, but not primary care and the hospital. On the other hand, the health information exchange network used in HNT function only 1 way (Hospital to community). A potentially more mature example can be seen in SICP, which has implemented a single patient record accessible to the professionals of the case management multidisciplinary team and the emergency medicine professionals. Their ultimate goal is for the platform to be accessible by primary, secondary, and community care organizations in the Salford area. In a minority of the programs (eg, ON and PCSS), data transfer across various IT platforms of providers are manually performed by program administrators. All in all, most ICC programs indicate the determinant positive role of the existing regional digital health tools for health information exchange across health care tiers,

which facilitates information sharing among heterogeneous providers, as seen in this example from the Proactive Primary Care Approach for Frail Elderly (U-PROFIT) program in the Netherlands:

> *We are working with a vulnerable population, frail in general, and it is important for them to avoid going from one place to another and visiting different service providers and collecting different forms [...] or duplicate papers because you have to present this paper here and this same paper over there [...] I think this is an important progress for the population* [IP04_1—U-PROFIT]

A step forward in terms of organizational interoperability, the computerization of health and social care records via a *shared EMR* among health care tiers, is at the heart of some ICC programs, such as the GeroS program. In line with organizational interoperability, the Care Chain Frail Elderly (CCFE) program focuses on structuring care and stimulating communication between all chain partners in primary care at various access levels with one another, thanks to an additional digital health tool (Care2U) that is used on top of the existing information systems to access the individual care plan and exchange information. However, although there has been much effort by the governments of these countries to have a shared EMR in place, this has not yet been fully successful, mostly due to data privacy issues. Last but not least, the AISBE program aims to consolidate a *shared case management system* [36] on top of the existing regional shared EMR, aiming to support the regional deployment of adaptive case management processes.

Digital Transformation Policies (Macro)

As all 17 ICC programs have at least partial implementation of EMR, all national and regional policies aim to expand the implementation of *EMR* in the future. However, in most program countries, the use and scope of digital health tools depends on *several initiatives at program level*, which serve as pilot sites for the nation and region wide rollout of digital health tools. This is the case, for example, in the Austrian programs (HNT and Sociomedical Centre Liebenau [SMC]), which are part of the *electronic health files*, the most comprehensive eHealth initiative in Austria. Our research has only been able to identify *national and regional strategic plans* for deployment of eHealth in Croatia, Spain, Hungary, the Netherlands, Norway, and the United Kingdom. The largest digital transformation policy being the Whole System Demonstrator pilots in the United Kingdom, which is a strategy proposed by the Department of Health in England to focus on health and social care for people with long-term needs, emphasizing the use of advanced assistive technologies including telehealth and telecare. It has demonstrated a slight reduction in mortality and emergency admission rates but was not demonstrated to be more cost effective than usual care [37,38].

Under the auspices of the Norwegian Directorate of Health, a *Care Journal* has been recently established for all citizens (voluntary); this is an electronic tool comprising selected and important health data that are accessible for the citizen and health personnel for the whole health care sector in Norway (including the 2 programs analyzed in this paper). Another example is the Catalan Health Plan [39], which prioritizes the improvement and transformation of the health system and health care organization through the intensive introduction of emerging digital health technologies.

Information and Research

As summarized in the Multimedia Appendix 3, the overarching analysis provided the following valuable insights on the assessment strategies of the 17 technology-enabled ICC programs.

Evaluation Strategies (Micro)

This research has shown that in some ICC programs, no comprehensive evaluation has been carried out so far (SMC, Palliative Care System, ON, and Learning network), but is *planned* to be performed.

However, most ICC programs have been subject to *partial monitoring and/or preliminary evaluation* (ie, HNT, GeroS, Palliative Care Consulting Service, CCFE, BSiN, MAR, SICP, and SSSP), involving mainly descriptive data analysis over well-defined outcome measures of interest or key performance indicators. Specifically, the SSSP program includes:

> *Number of bed days, average length of stay, 30 day readmission, avoidable emergency admissions, precautionary emergency admissions, patients admitted multiple times, excess bed days, avoidable A&E attendances, confidence to my own health, received enough support to help self-managed long-term conditions, have a written care plan, care plan regularly reviewed, patient access to GP and nurse, online services, GP referrals, mental wellbeing, the Warwick-Edinburgh Mental Wellbeing scale, patient activation measure [PAM], patient satisfaction experience, and number of contacts made.* [IP03_2—SSSP]

Only some programs report *full scientific assessment* (ie, Casaplus [40], Gesundes Kinzigtal [41,42], U-PROFIT [43,44], and AISBE [45-47]). These programs have been evaluated using randomized controlled trials as well as pre-post evaluation with propensity score matching methods, following the Triple Aim outcomes [48,49]:

> *...was the number of hospital admissions reduced? How did they experience the effects of care (the insured person, the environment, the relatives)? Were the per capita costs reduced?* [IP04_1—Casaplus]

Risk Assessment Strategies (Meso)

Patient management purely based on *clinical criteria* (professional training, knowledge, instinct, and experience) *or combined with rules-based clinical management* [50] (thresholds for certain parameters defining pre-established decision criteria) constitutes current health professional practice in most ICC programs.

In contrast, the regular use of *subject-specific predictive modelling* tools for clinical decision support (predictive modelling establishing relationships between sets of variables and outcomes generated using statistical or machine learning

tools) is still in its infancy, despite the fact that it seems a natural step toward customization of care to patient's needs. Clinical predictive modelling tools are only reported to be used in some ICC programs (ie, SICP, SSSP, U-PROFIT, Gesundes Kinzigtal, and Casaplus) *for individual risk assessment* (which can be considered within the micro level). Within the U-PROFIT program, available data in the general practitioner EMR system are used by the U-PRIM software to screen frail patients of 60 years and older in every participating practice [51]. SICP and SSSP programs in the United Kingdom use a well-known patient-level risk predictive tool, PARS [52] and the Combined Predictive Model [53], to identify those patients that require the most care and support and to assess the risk of patients having unplanned hospital admissions within a 12-month period. It is used to some extent, but more trust is placed in clinical judgement in many cases:

> *...so we'd looked at some of the higher risk patients that were identified by the Combined Predictive Model and PARS (Patient at Risk Score) exactly the same, because I've done that before for the unscheduled care, and we looked at that; and what you find is the high risk people that are identified by this risk stratification models that are promoted nationally, is that the only data that's easy to count is the hospital data, is the Hospital Episode Statistics of your hospital episodic statistics and stuff.* [IP02_1—SICP]

Similarly, Casaplus uses a clinical predictive modelling tool to identify patients in high risk for hospital admissions within the next 12 months.

The use of clinical predictive modelling tools for *population-based risk assessment* is only reported in BSA and AISBE (Catalonia, ES). Since 2011, the Catalan Health Surveillance system collects detailed information on health care usage for the entire population of Catalonia [54], the region in which AISBE and BSA operate. It includes information on hospitalization, primary care visits, emergency department visits, skilled nursing facilities, palliative care and the mental health services, information on pharmacy prescription and expenditure, and a registry on the billing record also encompassing outpatient visits to specialists, home hospitalization, medical transportation (urgent and nonurgent), ambulatory rehabilitation, respiratory therapies, and dialysis. This information is used for provider payment purposes. Also, external audits are performed periodically to ensure the quality and reliability of the data. The Catalan Health Surveillance System is used to update, on a 6-month basis, the regional population-based health risk assessment tool, (the Adjusted Morbidity Groups) that generates the health risk strata pyramid of the general population of Catalonia [13,14].

Furthermore, AISBE is adopting a holistic approach that fosters inclusion of covariates from multilevel data sources, namely *Multilevel Predictive Modelling*: (1) clinical, (2) informal care; (3) biological research; and (4) outcomes from population-health risk predictive modelling (eg, the Adjusted Morbidity Groups), resulting in enhanced patient-based stratification and optimization of service selection. This approach aims to pave the way toward personalized medicine, provided that access to the multilevel data sources is granted. However, most legal frameworks on data privacy of the 17 ICC programs depend on the ongoing implementation of the European Union Data Protection Directive 95/46/EC to make the concept of multilevel predictive modelling operational.

Research and Innovation Policies (Macro)

A majority of the 17 ICC programs are part of *incipient research and innovation initiatives* constantly being implemented in practice, both bottom-up and top-down, using several, sometimes consecutive, project-budgets but without sustainable structural funding.

However, Croatian, Dutch, German, Norway, and Spanish programs are aligned with *consolidated research and innovation programs* at state and regional level. For example, the Gesundes Kinzigtal program in Germany has been extensively evaluated in terms of prevalence of multimorbidity, polypharmacy, proportion of generic drugs, prevalence of problematic drug prescriptions, prevalence of fractures among patients diagnosed with osteoporosis, quality of services, and overall health care costs [42]. Another example is the Research Council of Norway, commissioned by the Ministry of Health and Care Services to carry out a research-based evaluation of the Co-ordination Reform. The Research Council has conducted a research program tailored at integrated care from 2012 to 2015.

Furthermore, the *strong co-ordination* of most programs from Norway, the Netherlands, Hungary, Spain, Croatia, and Germany *with different European research and innovation initiatives* under the umbrella of H2020 [55], EIP-AHA [56], EIT Health [57], and/or RIS3 [58], as well as other specific research and innovation actions, should contribute to cross-fertilization among health care, research, and innovation.

Discussion

Principal Findings

The overarching analysis allowed us to assess the use of digital health tools to support the care process in the 17 ICC programs on the 2 specific aspects analyzed: *Technologies & Medical* products and *Information & Research*. As most of the ICC programs are pilot experiences in terms of nation and region wide rollout of digital health tools, this analysis was useful to learn from them regarding requirements for a successful large-scale implementation elsewhere.

Acknowledging that the 17 ICC programs are highly heterogeneous regarding the use and impact of digital health tools, the main findings are summarized below.

Electronic Medical Records

Each program studied shows at least partial implementation of EMR, and all of them have plans in place for a future mature implementation of EMR.

Personal Health Records

The use of personal health records to support telemonitoring services for patient self-management is not in place in most ICC

programs, for which telephone is still the dominant means of communication.

Health Information Exchange Platforms

Most programs reported on the potential of secure health information exchange across providers to facilitate organizational interoperability for deployment of ICC by facilitating information sharing among heterogeneous providers and avoid generating additional burden of double-registration to health professionals. However, the maturity of implementation is currently rather poor. Moreover, the need for technological tools, on top of health information exchange platforms, supporting collaborative work across health care tiers to foster implementation of shared case management [36,59] was stressed by programs like AISBE.

Digital Transformation Policies

The overarching analysis highlighted the lack of well-defined macro-level policies, with effective operational implementation plans, in the health care systems in which most ICC programs operate. Often, the use and scope of digital health tools depends on local or regional initiatives of individual providers involved in the ICC programs.

Health Data Analytics and Evaluation Strategies

Most programs systematically collect well-defined outcome measures to feed program-specific evaluation strategies, ranging from descriptive data analysis, comparison of trial and control groups, as well as pre- and postmeasuring. Still, some ICC programs recognize barriers for assessment such as a lack of financing, poor research capacity, concerns on data security, and misuse of data. This study clearly shows the need for formulation of structured and comprehensive evaluation and monitoring strategies for ICC including formulation of key performance indicators extensively shared across countries. Moreover, the Quadruple Aim approach [60,61] (ie, the Triple Aim approach plus the health care professionals experience) should serve to standardize the evaluation across European Union sites.

Health Risk Assessment

Just a few of the ICC programs report on the use of clinical predictive modelling tools, and even less ICC programs claim the use of population-based health-risk prediction tools.

Research and Innovation Policies

The majority of the 17 ICC programs (either bottom-up or top-down initiatives) are often based on project-specific budgets without well-defined, operational policies and, consequently, without sustainable structural funding. Implementing the above technological innovations frequently requires hardware and software upgrades. The costs of initial rollout and training of staff also need to be considered and weighed against the likely benefits.

We acknowledge some limitation in our study such as the inherent limitations of the methodological approach adopted. Also, as the study conclusions relate only to programs based in Europe, worldwide representativeness of the study results cannot be assumed.

Comparison With Previous Work and Future Directions

A recent report by the European Union on Integrated Care maturity [62], including the evaluation of Information and eHealth tools, concluded that the level of maturity in Germany, Denmark, Belgium, Italy, Spain, Greece, Sweden, and Iceland scored higher in comparison to their peers in Estonia, the Netherlands, Poland, and Bulgaria. The most mature countries are Denmark, followed by Spain, Germany, and Iceland at the same level. Finally, Sweden, Belgium, Italy, and Greece were in intermediate level. This is line with our findings, except for the 3 case studies in the Netherlands, which in our study were more mature than Dates et al [62] suggests. It is of note that differences between the study by Dates et al [62] and this study might be explained by using different tools as well as the selection of 3 promising cases in the Netherlands which actually use eHealth tools. The European Union on Integrated Care maturity report applies an interactive tool developed by SIROCCO (Scaling Integrated Care in Context) to assess the maturity of ICC programs on a global level using different aspects (one of them being eHealth); whereas in our study, we explicitly focus on different aspects of digital health tools and assessment strategies solely. Also, the previous report is based on a review of the literature on integrated care policies and strategies, whereas our study adds the point of view from the different stakeholders directly involved in generation and implementation of these policies and strategies.

Integrated care programs for chronic patients involve complex interventions for heterogeneous populations; therefore, proper articulation of digital health tools and the different components of the evaluation process are still unmet needs that markedly hinder comparability and scale-up. The overarching analysis of the 17 ICC programs conducted in this study allowed us to identify the following potential areas for future developments:

Refinement of assessment methodologies of large-scale deployment and adoption of ICC programs, likely based on implementation research approaches [63-65], are needed. We understand that assessment should adopt the classical three-dimensional approach including outcomes, processes, and structures [66]. Moreover, usual health outcome variables (ie, mortality, hospital readmissions, etc.) should be ideally expanded [67] considering the Quadruple Aim approach [60,61]. The approach requires the collection of patient-reported outcomes and experience data (PROMS and PREMS) on a regular basis.

The concept of adaptive case management explored in AISBE [36,68] should be made operational. Conventional health information systems rely on the management of clinical episodes with a disease-oriented approach and only very rarely incorporate the required process logics to support continuity of care with a patient-centered approach.

Dynamic health-risk assessment taking into consideration both service commissioning (*population-based health-risk predictive modelling*) and subject-specific service selection involving optimal patient allocation in the health system (*individual health-risk predictive modelling supporting decision support*) should be addressed to improve outcomes [69-71]. Ultimately,

the application of holistic strategies for subject-specific risk prediction and stratification that incorporates multilevel determinants of health (eg, socioeconomic, lifestyle, behavioral, clinical, physiological, cellular, and *omics* information) emerges as a high priority goal to properly pave the way toward personalized medicine for complex chronic patients [72]. Enhanced clinical predictive modelling, personalized diagnostic and treatment tools can contribute to the acceleration of transfer of scientific evidence to practice.

Development of pragmatic trials that incorporate real-life evidence from multilevel determinants of health may require implementation strategies, ideally using cloud computing environments, tackling privacy and regulatory constraints [23,72]. Currently, the articulation of the main technical building blocks, that is, multilevel biomedical data integration, tools for clinical predictive modelling in the cloud and High-Performance Computing, as one integrated system is yet a largely unmet potential.

Conclusions

This overarching analysis informs the current implementation status of digital health tools for management of multimorbidity in the 17 promising ICC programs selected in SELFIE. Notwithstanding the heterogeneity of the results, most studied programs are progressively evolving their supporting digital health tools from pilot prototypes to full scale-up at regional and national level. However, the majority of programs have not yet undergone full evaluation and assessment strategies. Future directions which can enable of digital transformation are based on innovation at micro and meso level with full support from the macro level. Some strategic areas that can help toward this end are the following: (1) implementation of research strategies; (2) explore an adaptive case management approach; (3) further developments of health risk assessment; and (4) holistic implementation strategies using future, regulatory compliant, cloud computing environments.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Essential and additional criteria for preliminary selection of Sustainable intEgrated care modeLs for multimorbidity: delivery, Financing, and performancE (SELFIE) programs.
[PDF File (Adobe PDF), 222KB-Multimedia Appendix 1]

Multimedia Appendix 2

Stakeholders interviews per country.
[PDF File (Adobe PDF), 240KB-Multimedia Appendix 2]

Multimedia Appendix 3

Summary of the overarching analysis of the 17 selected integrated chronic care programs.
[PDF File (Adobe PDF), 184KB-Multimedia Appendix 3]

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Abbreviations

AISBE: Area Integral de Salut Barcelona-Esquerra
BSA: Badalona Serveis Assistencials
BSiN: Better together in Amsterdam North
CCFE: Care Chain Frail Elderly
EMR: Electronic Medical Record

HNT: Health Network Tennengau (Gesundheitsnetzwerk Tennengau)
ICC: Integrated Chronic Care
MAR: Medically Assisted Rehabilitation
ON: OnkoNetwork
SELFIE: Sustainable intEgrated care modeLs for multimorbidity: delivery, Financing, and performancE
SICP: Salford Integrated Care Program
SMC: Sociomedical Centre Liebenau (Sozialmedizinisches Zentrum Liebenau)
SSSP: South Somerset Symphony Program
U-PROFIT: Proactive Primary Care Approach for Frail Elderly

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Original Paper

Integrated Care Intervention Supported by a Mobile Health Tool for Patients Using Noninvasive Ventilation at Home: Randomized Controlled Trial

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Abstract

Background: Home-based noninvasive ventilation has proven cost-effective. But, adherence to therapy still constitutes a common clinical problem. We hypothesized that a behavioral intervention supported by a mobile health (mHealth) app could enhance patient self-efficacy. It is widely accepted that mHealth-supported services can enhance productive interactions among the stakeholders involved in home-based respiratory therapies.

Objective: This study aimed to measure changes in self-efficacy in patients with chronic respiratory failure due to diverse etiologies during a 3-month follow-up period after the intervention. Ancillary objectives were assessment of usability and acceptability of the mobile app as well as its potential contribution to collaborative work among stakeholders.

Methods: A single-blind, single-center, randomized controlled trial was conducted between February 2019 and June 2019 with 67 adult patients with chronic respiratory failure undergoing home-based noninvasive ventilation. In the intervention group, a psychologist delivered a face-to-face motivational intervention. Follow-up was supported by a mobile app that allowed patients to report the number of hours of daily noninvasive ventilation use and problems with the therapy. Advice was automatically delivered by the mobile app in case of a reported problem. The control group received usual care. The primary outcome was the change in the Self Efficacy in Sleep Apnea questionnaire score. Secondary outcomes included app usability, app acceptability, continuity of care, person-centered care, and ventilatory parameters.

Results: Self-efficacy was not significantly different in the intervention group after the intervention (before: mean 3.4, SD 0.6; after: mean 3.4, SD 0.5, P=.51). No changes were observed in adherence to therapy nor quality of life. Overall, the mHealth tool had a good usability score (mean 78 points) and high acceptance rate (mean score of 7.5/10 on a Likert scale). It was considered user-friendly (mean score of 8.2/10 on a Likert scale) and easy to use without assistance (mean score of 8.5/10 on a Likert scale). Patients also scored the perception of continuity of care and person-centered care as high.

Conclusions: The integrated care intervention supported by the mobile app did not improve patient self-management. However, the high acceptance of the mobile app might indicate potential for enhanced communication among stakeholders. The study identified key elements required for mHealth tools to provide effective support to collaborative work and personalized care.

Trial Registration: ClinicalTrials.gov NCT03932175; https://clinicaltrials.gov/ct2/show/NCT03932175

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KEYWORDS

behavioral change; eHealth; noninvasive ventilation; mobile health; chronic diseases

Introduction

In the 1950s, the polio epidemic demonstrated the safety and efficacy of noninvasive ventilation (NIV) to decrease mortality [1]. Since then, the use of this therapeutic approach at home has reduced hospital admissions, has favorably impacted health-related quality of life, improved sleep quality, and reduced mortality in patients with chronic respiratory failure due to diverse etiologies [2-8]. These results have driven a steady increase in the prevalence of patients using home-based NIV in Europe, ranging from 4.5 to 20 per 100,000 adults [9-11].

Despite its proven cost-effectiveness [12], patient adherence to home-based NIV could still improve, which should further enhance health care–related efficiencies of the intervention [13]. Monitoring and optimization of physiological settings have enhanced adherence by improving the timely detection of problems such as mask leaks and patient-ventilator asynchronies [14]. Nevertheless, improvement in the behavioral aspects such as patient motivation and empowerment for self-management are important factors to consider when addressing adherence to respiratory therapies.

The current study sought to explore the transfer of previous positive experiences with behavioral interventions in other fields (ie, physical activity) [15-20] to home-based NIV. Specifically, we addressed the concept of self-efficacy, defined as the individual's perceived capability to perform a particular behavior [21]. Self-efficacy expectations can be affected by enablers or barriers such as the perception of physical function or the capacity for self-management. Therefore, a person who does not believe in her or his capacity to perform the desired action will fail to adopt, initiate, and maintain it. Self-efficacy is therefore seen as the most influential motivational factor and the strongest predictor of behavioral intentions [21].

We propose the use of a behavioral mobile health (mHealth) intervention, which can be framed by Bandura's model [22], to support changes in self-efficacy. This model is based on the concepts of health risk perceptions, health outcome expectancies, and the patients' confidence to engage in certain behaviors. The model has been widely applied in studies of the adoption, initiation, and maintenance of health-promoting behaviors [23].

In addition to self-efficacy as a way to influence behavioral change, previous reports by Hernandez et al [24] and Cano et al [25] identified two common hinderances for the effective implementation of complex respiratory therapies (ie, long-term oxygen therapy, continuous positive airway pressure therapy, home NIV, and home-based nebulizer therapy). First, interaction and communication, which could greatly benefit from digital tools supporting collaborative work, are needed among several stakeholders, namely health professionals at different health care tiers (eg, primary care, specialized care), patients and carers, companies undertaking equipment maintenance, and others. Second, improvement in therapeutic adherence is needed, which could be achieved by empowering patients to perform self-management.

Within this context, information and communication technologies (ICT) have been identified as promising tools to enhance the coordination between stakeholders and contribute to improved health outcomes [26,27]. Nonetheless, the implementation remains immature [28] due to a lack of evidence in a real-world context for the capacity of ICT to sustain behavioral changes, including self-efficacy, in patients with chronic, complex conditions. It is widely accepted that, despite current limitations, patients with chronic, complex conditions are an ideal population for which care coordination, patient and medical staff satisfaction, and patient empowerment are of the utmost importance to produce health benefits.

The principal objective of this study was to explore the capacity of a behavioral mHealth intervention to increase patient empowerment for self-management and adherence to therapy. The secondary aim was to learn, based on the experience of professionals and patients, how the mHealth tool should evolve to support collaborative work.

Methods

Study Design and Participants

A single-blind, single-center, randomized controlled trial with two parallel arms (1:1 ratio) was conducted. Patients were randomized to a control group or an intervention arm, which consisted of the behavioral mHealth intervention in addition to usual care. Inclusion criteria were as follows: all adult patients with hypercapnic ventilatory failure due to chest wall, neuromuscular, lung parenchyma, or airway disease already receiving treatment with NIV irrespective of treatment duration and in possession of a mobile phone or tablet that could support the use of the mHealth app (MyPathway). MyPathway [29] is a secure, digital communication channel connecting patients to clinicians and services. It is an app-based tool for both patients and clinicians to use on phones or tablets. See Multimedia Appendix 1 for more details. Patients with severe psychiatric or neurological diseases were excluded, as well as patients hospitalized at the time of assessment.

Intervention

In addition to usual care, the behavioral mHealth intervention included a face-to-face motivational interview by a psychologist (EA) to assess the patient's adherence profile and lifestyle habits, with a follow-up through the MyPathway app. In contrast, the control group received only usual care, which consisted of manual discharge and review of the NIV machine data by the treating pulmonologist and respiratory nurse. Respiratory parameters were changed, if needed, according to clinical data (anamnesis and physical examination) in addition to NIV data.

At the time of enrollment, semi-structured motivational interviews were conducted individually. Participants were asked about their treatment adaptation experience, lifestyle (physical activity and food habits), and use of ICT. In each session, field notes were taken anonymously, and no recordings were made. The intervention consisted of a 10-50–minute face-to-face session at the hospital or participants' home that followed the principles of a collaborative and evocative motivational interview, favoring the participant's autonomy. The techniques used were open questions, active listening, empathy, returning reflected thoughts, exploring a change in goals, summarizing, and giving feedback. Also, during the enrollment visit, patients were given verbal and written explanation on how to use the app. Free access was granted after receiving an invitation via the hospital health information system (SAP), which prompted the participant to register using an email address as the username. The app could also be downloaded to the carers' phone in case the patient did not have a smartphone.

During the follow-up, the MyPathway app was used by study participants for bidirectional interaction with the research team. It consisted of positive feedback or reinforcement messages in response to the number of hours of NIV use reported by the patient daily. Also, general advice on specific NIV clinical problems was automatically provided by the app according to the patients' weekly input. Additional educational material on physical activity, diet, and sleep hygiene could be accessed at any time via a dedicated link. A web-based clinical portal enabled the research team to monitor the patient-reported NIV hours of use and clinical problems. As indicated, a dedicated nurse with clinical and technical knowledge (one of the authors, MM) took the role of case manager to support collaborative work. She used the web-based portal to identify adherence problems and contacted participants via telephone or at home (for those with severe mobility problems) to enquire about and solve potential clinical or technical problems.

Procedures and Study Outcomes

The primary outcome was a change in self-efficacy, as measured using the Self Efficacy in Sleep Apnea (SEMSA) questionnaire. The SEMSA is a US-designed self-report questionnaire comprised of 26 items that are rated from 1 to 4 on a 4-point Likert scale [30]. The arithmetic mean of the Likert rating for each participant is computed for the overall SEMSA score and each of the 3 factors. The total score ranges from 1 to 4. Higher scores indicate greater risk perception, higher benefit expectancy with treatment, and greater perceived self-efficacy [30].

Secondary outcomes included usability of the ICT tool, as measured using the System Usability Scale [31]; patient satisfaction, as measured using the Net Promoter Score [32] in addition to 3 custom general satisfaction questions measured on a Likert scale; continuity of care, as measured using the Nijmegen Continuity Questionnaire [33]; and the Person-Centred Coordinated Care Experience Questionnaire as described by Leijten et al [34]. Moreover, ventilator-specific data such as the mean hours of daily use, unintentional leaks (L/s), minute ventilation (L/min), tidal volume (mL), and backup rate (breaths/min) were downloaded directly from the NIV machine.

Tertiary outcomes included mortality; health-related quality of life, as measured using the EuroQol 5D questionnaire [35,36]; and sleepiness, as measured using the Epworth Sleepiness Score.

The impact of the motivational mHealth tool recommendations on diet and exercise was indirectly measured by body weight changes.

All assessments were completed at baseline and the final visit scheduled 3 months later. The follow-up was conducted in the outpatient clinic for the control group and remotely by the nurse case manager (MM) using the MyPathway app and its clinical portal for the intervention group. When deemed necessary, the nurse case manager visited the patient at home, or a visit was scheduled in the outpatient clinics. There was no active follow-up for the control group.

Randomization and Masking

All eligible patients were contacted by telephone to briefly explain the study and invite them to participate. Those showing interest were invited to the hospital outpatient clinics. Study investigators (EB, EA, and MM) explained the study face-to-face, and, in case of acceptance, signed consent was obtained. Afterward, the patient was randomized. Before patient enrollment, the randomization scheme was generated using the website randomization.com by one of the researchers (EB). Blocks of 4 were used. Only after the participant provided consent, the investigator opened the envelope with the allocated study group.

Due to the nature of the intervention, neither the participants nor the investigators in direct contact with the participants were blinded. Only the investigator in charge of data analysis was blinded.

Sample Size Calculation, Data Management, and Statistical Analysis

Accepting an α risk of 0.05 and a β risk of 0.2 in a two-sided test, 31 subjects in the intervention group and 31 subjects in the control group were required to achieve a statistically significant difference ≥0.35 units in the SEMSA overall score [37]. The common SD was assumed to be 0.46 [38]. A 10% drop-rate was anticipated.

Baseline and end-of-study data (questionnaires) were collected face-to-face at the outpatient clinic by the investigators (EB, EA, and MM). Study data were collected and managed using the REDCap electronic case report form [39,40] hosted at the Hospital Clínic de Barcelona. Data on patient-reported NIV use and clinical problems with NIV were collected online using MyPathway.

Results are presented as mean (SD) or n (%). Comparisons were conducted using Chi-square or Fisher exact tests for categorical variables and Student *t* or Wilcoxon tests, depending on the distribution of the variables, for numerical variables.

Ethics

Study approval was obtained from the Ethics Committee for Clinical Research of Hospital Clínic de Barcelona (HCB/2019/0510). Patients read, understood, and accepted

informed consent, which was signed before enrolment to the study.

Results

Study Population

Between February and March 2019, all patients already being treated with NIV at the noninvasive ventilation clinic at the Hospital Clínic de Barcelona were assessed for eligibility. From an initial sample of 169 eligible patients, 50 (30%) did not meet the inclusion criteria, including 32 who did not have a smartphone or tablet, and 23 (14%) declined participation. Therefore, 67 patients were randomized between February and May 2019 (see the CONSORT flow diagram in Multimedia Appendix 2). One patient from the intervention group withdrew consent during the trial due to the worsening of his clinical condition. Baseline demographic and clinical characteristics are shown in Table 1 and Multimedia Appendix 3.

Patient-Reported Outcomes

For the primary outcome, the mean SEMSA score for self-efficacy was not significantly different in the intervention group after the intervention (before: 3.4, SD 0.6; after: 3.4, SD 0.5, *P*=.51).

The perceived risks, outcome expectancies, Epworth Sleepiness Score, and EuroQol 5Q-5D questionnaire score were also not significantly different in the intervention group after the intervention (see Multimedia Appendix 3). As for the patient experience questionnaires, neither the Nijmegen Continuity Questionnaire nor the Person-Centred Coordinated Care Experience Questionnaire were statistically significantly different between the groups (see Multimedia Appendix 3).

Table 1. Baseline characteristics of the study groups

	Intervention (n=33)	Control (n=34)	*P* value
Age (years), mean (SD)	68 (15.8)	65 (14.7)	.31
Male gender, n (%)	19 (58)	19 (58)	>.99
Weight, mean (SD)	86 (31.6)	78 (22.4)	.15
Educational level (n, %)			.73
No schooling	3 (9)	1 (3)	
School education	12 (36)	13 (38)	
Professional formation	17 (52)	19 (56)	
Doctorate or equivalent	1 (3)	1 (3)	
BMI (kg/m^2), mean (SD)	30.5 (7.1)	28.9 (7.4)	.35
Smoking status, n (%)			<.001
Never	12 (36)	16 (49)	
Former	18 (55)	16 (48)	
Current	2 (6)	1 (3)	
Smoking (packs/year), mean (SD)	55.5 (35.7)	52.5 (33)	.003
Diagnostic group, n (%)			
Neuromuscular	4 (12)	8 (24)	.25
Chest wall	11 (33)	10 (30)	.81
Obesity-hypoventilation	5 (15)	5 15)	>.99
Airway obstructive disease	3 (9)	2 (6)	.66
OSA[a] to CSA[b]	10 (30)	8 (24)	.60
Number of comorbidities per patient, mean (SD)	2 (1.5)	1.8 (1.6)	.68
Comorbidities, %			
Cancer	3	3	>.99
Congestive heart disease	33	27	.60
Ischemic heart disease	24	15	.37
Diabetes	27	36	.47
Stroke	9	9	>.99
Hypertension	67	52	.20
Dementia	3	0	.32
Neurological disorders other than stroke	3	0	.32
Depression/anxiety	18	18	>.99
Dyslipidemia	15	27	.54
Time on noninvasive ventilation (years), mean (SD)	6.75 (6.5)	4.5 (3.5)	.08
AHI[c], mean (SD)	46 (28.8)	35 (31.6)	.37
CT90[d] (%), mean (SD)	47 (37.3)	44 (40.4)	.91
Mean ventilatory parameters, mean (SD)			
IPAP[e] (cm H_2O)	16 (4.7)	14 (4.7)	.06
EPAP[f] (cm H_2O)	7 (2.8)	6 (2.1)	.31
Leak (L/s)	0.05 (0.2)	0.5 (0.09)	.03
Number of hours used per day	7.4 (2)	6.8 (3)	.28

[a]OSA: obstructive sleep apnea.

[b]CSA: central sleep apnea.

[c]AHI: global apnea-hypopnea index for all diagnostic groups.

[d]CT90: cumulative sleep time percentage with oxyhemoglobin saturation <90%.

[e]IPAP: inspiratory positive airway pressure.

[f]EPAP: expiratory positive airway pressure.

Clinical Outcomes

Adherence was measured as the number of hours the NIV was used per day, as recorded by the ventilator. The mean adherence value was not significantly different in the intervention group after the intervention (before: 7.4 hours, SD 2 hours; after: 7.7 hours, SD 2 hours). Mean minute ventilation was the only significantly different ventilatory parameter after the 3-month intervention in the intervention group (before: 7.0 L/min, SD 2 L/min; after: 6.4 L/min, SD 2.1 L/min, *P*=.03). The remaining ventilatory parameters and weight are shown in Multimedia Appendix 3. None of the patients died during the trial.

mHealth Tool Use, Usability, and Acceptability

The Net Promoter Score was –3 (10/33, 31% promoters; 11/33, 34% passives; 11/33, 34% detractors). The 3 Likert-scale questions about the general satisfaction with the app that were rated from 1 (very bad) to 10 (very good) resulted in a mean score of 7.5/10 for the general impression of the app, mean score of 8.2/10 for the user friendliness, and mean score of 8.5/10 for usability of the app without assistance. The mean System Usability Scale score was 78, a reasonably good grading. Up to 42% of the participants used the link to the educational material, and only 18% (6/33) consulted the terms of use. The mean number of hours of NIV use per day, reported using the mHealth tool, was 7.23 hours (SD 2.48 hours). Use of NIV for more than 4 hours per day during two-thirds of the study period was reported by 45% (15/33) of the patients. Likewise, the reported mean number of days during which NIV was used more than 4 hours in the entire intervention group was 35.6 days (SD 23.6 days). At the end of the study period, 3 participants stopped reporting due to app problems, 1 participant stopped using the app due to health problems, another participant stopped using the app for unknown reasons, and 3 participants decided to use the app on an alternative day basis.

Also, 30% (10/33) of the participants used the app through a family member or carer. It is of note that the nurse case manager was able to solve two-thirds of the technical problems that arose during the first 3 weeks of the study.

The qualitative analysis of the motivational interview as well as the detailed description of the requirements for mHealth to support collaborative work among stakeholders will be reported elsewhere. However, Table 2 summarizes a list of features that the research team agreed were key functional requirements of mHealth tools to effectively support collaborative work among stakeholders involved in home-based respiratory therapies.

Table 2. Requirements to support collaborative work within the noninvasive ventilation service.

Feature	Description of the requirement(s)
Adaptive case management	Capacity to enable the case manager to combine predesigned tasks and approach new cases by reusing structured experiences with previous cases. Over time, the case manager, or other authorized health professionals, should be able to adapt the work plan in a timely fashion to specific patient's requirements without any direct technological support
Team collaboration	Cloud-based, General Data Protection Regulation-compliant, enterprise-proven team collaboration tools to allow patients and health care professionals to break down silos and collaborate seamlessly from any device (mobile phone, tablet, or desktop) towards the health continuum care pathway
Multimedia communication	Enterprise-grade, scalable, high-quality, real-time communication among concurrent participants for file sharing, voice, video, and screen-share sessions with industry-standard encryption
Intelligent bots	Capacity to develop and integrate intelligent bots to guide professionals through continuum care pathways and to improve health risk assessment and service selection
Integration with hospital information systems	Use of HL7 Fast Healthcare Interoperability Resource interoperable middleware to integrate with provider-specific hospital information systems

Discussion

Principal Findings for Patient-Reported Outcomes

We report the results of a behavioral mHealth intervention based on a face-to-face interview and the use of an mHealth tool (MyPathway app) during a 3-month follow-up period with patients with hypercapnic chronic respiratory failure under home-based long-term NIV. To the best of our knowledge, this is the first randomized controlled trial using digital tools to support behavioral changes in this population [41-44].

In this study, the mean self-efficacy score was already high at baseline (Table 1), and we did not find a significant effect of the intervention on behavioral changes. Several explanations can be proposed for these results. First, the intervention may need to be more intensive (ie, more than one face-to-face session) [45]. Second, all the participating patients were long-term users without significant sleep symptoms at the time

of enrollment (average use >6 years with an average Epworth Sleepiness Score <10). Therefore, we could hypothesize that behavioral changes had occurred previously, as evidenced by the good average use of NIV (7.4 h/day) and high scores for self-efficacy at baseline. The inclusion of patients who have been newly prescribed NIV in future studies may show a positive impact of the intervention. Third, we may argue that, although NIV use was good among this sample of long-term users, adherence was more a function of necessity or imposition (by family or physicians) than a real feeling of self-management and that most of these chronic patients had not considered initiating behavioral changes [46,47]. Along this line of thought, the population we studied had mobility problems or poor general health, creating barriers for behavioral change [20]. Therefore, any intervention at this stage is likely to be ineffective. This may also be reflected by the lack of interest in consulting the educational material in the app (<50% of the patients did so). Last, we should note that the control group consisted of more patients with neuromuscular pathophysiology. However, the pathophysiology should not affect or have a direct relationship with the measured behavioral outcomes or the capacity and readiness to use the app. Accordingly, educational level is a more important factor [48,49], and both study groups had similar educational levels.

Usability, Acceptability, and Requirements for Supporting Collaborative Work

Notwithstanding the clinical results, it is important to note that the mHealth tool was well received by the patients and their family/caregivers. Despite their complex conditions (2 comorbidities on average) with considerable needs and burdensome treatment, all patients used the app regularly, grading it as generally good, user-friendly, and easy to use without help. Moreover, the System Usability Scale score was good.

As stated in the methods section, we want to highlight the fact that one of the authors (MM) undertook a new professional role during the study period. She became the clinical case manager with additional technical knowledge on the mHealth tool. Patients appreciated this new role very much despite the use of telephone or Whatsapp for bilateral communication. We found that the app lacked this function, and based on our experience, this should become an integral part of any app that includes case management with technical skills. This type of communication functionality should be cloud-based and General Data Protection Regulation-compliant. Moreover, future developments should consider adaptive case management functionality. Also, this communication should be supported by artificial intelligence to help guide professionals though continuum care pathways and improve health risk assessment and service selection. Finally, integration with hospital information systems may facilitate the whole process. This is in line with a recent report on the digital transformation of health care in Europe, which draws upon the experiences of 17 integrated care programs where the importance of communication technologies, new professional roles, and the relevance of clinical workflow evaluation were highlighted [50].

In this respect, we measured 2 process outcomes [51] related to patient experience [52]: continuity of care and person-centered care. Our study population, which included patients as well as their family and carers for one-third of the cases in the intervention group, evaluated both parameters very well. The importance of well-designed clinical workflows with embedded digital health tools may have an impact on not only an NIV service but also other respiratory services. Commonalities include high-complexity patients with clinical and social needs from different stakeholders (eg, physicians, providers, technicians, social workers) and health care tiers (eg, primary care, specialized care). Hernandez et al [24] showed how this complexity can hamper the effectiveness of long-term oxygen therapy. As mentioned, Table 2 shows the proposed elements to overcome the barriers for the successful implementation of digital health tools within clinical workflows relating to respiratory therapies.

Finally, stakeholders play an important role in the design and evaluation of digital health tools [53,54] and, as such, their input should be taken into account when evaluating a service in which there is considerable interplay between patients, different health care tiers, and social and technical services [55]. For an mHealth tool to produce health care value, it should be embedded in the clinical pathways of a well-evaluated clinical service and not as a standalone tool [56].

Strengths and Limitations of the Study

Our study considered the whole population of patients attending the clinic, resulting in a realistic clinical scenario. Another important strength of our study is its potential to demonstrate the positive interaction and collaborative work among the nurse case manager, patients, and family members or caregivers of complex patients using digital health tools. Previous studies [57-59] reported the use of digital tools by family caregivers, emphasizing the importance of including this group of stakeholders, not only as users but also in the co-design process. This stakeholder involvement is also a further step in scaling up digital health tools within clinical workflows [59], which, in our case, were evaluated well. An interesting aspect of our study was the collateral use of qualitative data collected from the motivational interviews and by the nurse case manager during follow-up. The qualitative results presented in Table 2 can be used to support the implementation of mHealth tools in different contexts, keeping in mind the inherent limitations of qualitative research data. We do acknowledge that, by using an existing app, the co-design phase was skipped. Also, we did not measure the technological literacy of our older population (average age 69 years), but, according to Martinez-Alcala et al [60], adults older than 60 years, if highly motivated, are capable of learning and acquiring digital literacy skills. Nonetheless, for some of our older patients (24% were 70-79 years old), especially those with physical limitations (eg, visual impairment), the motivation to learn and exploit all the app functionality was low, although the perceived usefulness was high. This agrees with other reports on the use of technology by older adults [61,62]. Another potential limitation was the heterogeneity of the study population, which directly influenced the mean number of hours of use of the NIV machines and precludes any interpretation. Nonetheless, we observe a strength

in terms of the generalizability of the mHealth tools within the heterogeneous population. Finally, a clear limitation of our study was the exclusion of new NIV patients, where the behavioral intervention may have had more impact. This warrants further study.

Conclusions

The behavioral mHealth intervention explored in this study did not show any effect on self-efficacy, adherence with NIV, or quality of life in our population of experienced NIV users. Nonetheless, we showed the potential of the mHealth app to manage complex patients and foster collaborative work among stakeholders. Regarding a clinical service that was graded well in terms of continuity of care and person-centered care, in which the needs of relevant stakeholders are properly addressed, we see the potential to further study mHealth tools to induce behavioral change in home-based ventilated patients as well as in other respiratory therapies.

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Conflicts of Interest

JK and JE are employed by Advanced Digital Innovation (UK) Ltd, the creator of the MyPathway app. The remaining authors have no conflicts of interest to declare.

Multimedia Appendix 1

Mypathway adaptation for home-based non-invasive ventilation.
[DOCX File , 562 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Consort flow diagram.
[PDF File (Adobe PDF File), 53 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Baseline characteristics and clinical outcomes tables.
[DOCX File , 36 KB-Multimedia Appendix 3]

Multimedia Appendix 4

CONSORT-eHEALTH checklist (V 1.6.2).
[PDF File (Adobe PDF File), 101 KB-Multimedia Appendix 4]

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Abbreviations

ICT: information and communication technologies
mHealth: mobile health
NIV: noninvasive ventilation
SEMSA: Self Efficacy in Sleep Apnea

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Role of Co-creation for Large-Scale Sustainable Adoption of Digitally Supported Integrated Care: Prehabilitation as Use Case

INTEGRATED CARE CASE

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ABSTRACT

Introduction: The efficacy-effectiveness gap constitutes a well-known limitation for adoption of digitally enabled integrated care services. The current report describes the co-creation process undertaken (2016–2021) to deploy a prehabilitation service at Hospital Clínic de Barcelona with the final aim of achieving sustainable adoption and facilitate site transferability.

Methods: An implementation research approach with a population-based orientation, combining experience-based co-design and quality improvement methodologies, was applied. We undertook several design-thinking sessions (Oct-Nov 2017, June 2021 and December 2021) to generate and follow-up a work plan fostering service scalability. The implementation process was assessed using the Comprehensive Framework for Implementation Research, leading to the identification of key performance indicators.

Discussion: Personalization and modularity of the intervention according to patients' surgical risk were identified as core traits to enhance patients' adherence and value generation. A digitally enabled service workflow, with an adaptive and collaborative case management approach, should combine face-to-face and remotely supervised sessions with intelligent systems for patients' and professionals' decision support. The business model envisages operational costs financed by savings generated by the service.

Conclusions: Evidence-based co-creation, combining appropriate methodologies and a structured evaluation framework, was key to address challenges associated with sustainable prehabilitation service adoption, scalability and transferability.

RESUM

Introducció: La bretxa eficàcia-efectivitat limita l'adopció de serveis d'atenció integrada amb suport digital. L'estudi descriu el procés de co-creació efectuat (2016–2021) per desplegar, a l'Hospital Clínic de Barcelona, un servei de prehabilitació de pacients de risc per a procediments quirúrgics, amb l'objectiu d'aconseguir una adopció sostenible del servei i facilitar-ne la transferibilitat.

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KEYWORDS:

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Mètodes: Es van aplicar eines de recerca d'implementació amb una orientació poblacional, combinant metodologies de codisseny basades en l'experiència i de millora de la qualitat. Es van realitzar diverses sessions de design-thinking (Octubre-Novembre de 2017, Juny de 2021 i Desembre de 2021) per generar, i fer el seguiment, d'un pla de treball concebut per assolir escalabilitat del servei. El procés d'implementació es va avaluar utilitzant el Consolidated Framework for Implementation Research (CFIR), que va conduir a la identificació d'indicadors clau de rendiment.

Discussió: La personalització i la modularitat de la intervenció segons el risc quirúrgic dels pacients es van identificar com a trets bàsics per millorar l'adherència i la generació de valor. La organització de la prehabilitació, amb un enfocament adaptatiu i col·laboratiu de gestió de casos, hauria de combinar sessions presencials i supervisades remotament amb sistemes intel·ligents de suport a la decisió per a pacients i professionals. El model de negoci preveu que els costos operatius de la prehabilitació siguin finançats per l'estalvi generat.

Conclusions: El procés de co-creació, combinant metodologies adequades i un marc d'avaluació estructurat, va esser clau per abordar els reptes associats a l'adopció sostenible del servei, així com la seva escalabilitat i transferibilitat.

INTRODUCTION

Evidence-based benefits of a clinical intervention demonstrated in a highly controlled setting (efficacy) very often cannot be generalized to the real-world scenario (effectiveness) within the same site. The phenomenon, known as efficacy-effectiveness gap (EEG) [1, 2], is one of the major obstacles to demonstrate health value generation, and to achieve sustainable adoption, of integrated care services [3–5]. Likewise, overcoming EEG challenges is crucial for successful transferability of the results across heterogeneous sites. One of the proposed implementation mechanisms to optimize large-scale deployment and adoption of integrated care is to undertake an early process of co-creation with input of key stakeholders [4]. Expected outcomes of such process are service workflow co-design leading to healthcare value generation.

The current report summarizes the process of co-creation and adoption of prehabilitation [6, 7] as a mainstream integrated care service at Hospital Clinic de Barcelona (HCB) during the last five-year period, from its initial piloting in mid-2016 [8, 9] throughout its mature implementation until its readiness for transferability in 2021 [10].

Prehabilitation is defined as a patient-tailored preoperative short-term intervention, four weeks on average, encompassing, but not limited to: exercise training, promotion of physical activity, nutritional optimization and psychological support. Enhanced management of multimorbidity and prevention of unhealthy habits are also tackled. The final aim of prehabilitation is to improve functional capacity of patients undergoing elective major surgery as an attempt to minimize postoperative morbidity and accelerate recovery [6]. It is envisaged as a preventive standard clinical practice to be included into Enhanced Recovery After Surgery (ERAS) programs [11–13].

The primary aim of the Prehabilitation Unit at HCB Unit is to cover the needs generated by high-risk candidates to several major surgical procedures. However, the combination of progressive improvements in longevity, coupled with the increasing prevalence of multimorbidity with age, has resulted in a growing number of surgical procedures taking place in elderly patients with co-existing medical conditions. Since postoperative complications, particularly in this population, constitute a major burden on health systems, there is a need for a population-based approach of perioperative care [7]. Accordingly, an additional aim of the Unit is to foster a population-based approach to personalized prehabilitation covering all surgical risk strata in the HCB reference area.

Whereas prehabilitation for high surgical risk patients can benefit from ad-hoc digital support to enhance interdisciplinary coordination among different in-hospital services implicated the intervention (anesthesia, surgery, rehabilitation, nutrition, psychology); a population-health approach requires prehabilitation to be a digitally-enabled integrated care service by-design, with participation of different community-based stakeholders (i.e., primary care professionals and health coachers based in sports clubs). Consequently, there was a clear need for a co-creation process toward refinement of the standard prehabilitation intervention to build capacity, increase healthcare efficiencies and foster transferability to other sites within the frame of the EIT Health innovation action PAPRIKA [10, 14].

The objective of the current manuscript is to describe the co-creation process undertaken during 2017–2021 to pave the way for large-scale adoption of prehabilitation with a population-based approach.

ETHICAL APPROVAL

The Ethics Committee for Clinical Research at HCB approved the study (HCB/2016/0883). The interviews were recorded. Informed consent was understood, accepted and signed by all patients and caregivers. The study was registered at ClinicalTrials.gov [NCT02976064 – Implementation of Collaborative Self-management Services to Promote Physical Activity (NEXTCARE-PA)].

DESCRIPTION OF THE CARE PRACTICE

Prehabilitation at HCB builds on prior evidence of efficacy and its potential for cost-effectiveness in high-risk patients undergoing major digestive surgery generated through a randomized controlled trial (RCT) during the period 2013–2016 [8, 9]. Prehabilitation added costs to the surgical process, but this was offset by reduction of complications, shorter ICU hospital stay and reduced early re-admissions rates after hospital discharge. Following these encouraging results, the prehabilitation service was deemed ready for implementation as mainstream service at HCB, leading to the creation of the Prehabilitation Unit in 2016 and to the initiation of the current implementation research process.

THE ENTIRE CO-CREATION PERIOD

The core objectives of the co-creation process experienced a clear evolution summarized in three consecutive phases depicted in Figure 1. The first year was devoted to the organization of the Prehabilitation Unit and to develop the basis for an appropriate digital support to the service. During the subsequent period, until end-December 2019, main achievements were refinement of the service at HCB, and assessment of the activity of the Prehabilitation Unit following the evaluation framework described in [15]. The activities undertaken during the last eighteen months, starting at January 2020, had a threefold objective: transferability analysis, achievement of digital maturity and to assess financial sustainability.

The co-creation process was initially focused on adoption of the service at the Integrated Health District of Barcelona-Esquerra, 520 k citizens [16], falling within the activities of the Catalan Open Innovation Hub on Digitally-Enabled Integrated Care Services, one of the four original EU Good Practices in [14]. As such, the deployment strategies reported in the current document were fully aligned with the Catalan Health Plans 2011–2015 [17] and 2016–2020 [18], promoting digitally enabled integrated care. It is of note that the tasks reported have been developed under the umbrella of complementary EU projects [10, 19–21] addressing different facets, all of them converging toward optimization of digitally-enabled integrated care.

During the initial forty two months period, from mid-2016 to end-2019 (Figure 1), a systematic quality improvement approach using iterative 6-month Plan-Do-Study-Act (PDSA) cycles [22–24] was implemented with a twofold purpose: i) to generate the service workflow design of the interventions associated to the two case studies addressed in [19, 20], one of them being prehabilitation; and, ii) to guide the digital developments supporting the target integrated care services with an adaptive and collaborative case management approach [25, 26]. This period was followed by a second co-creation phase, with a more informal PDSA approach, focused on refinement and fine-tuning of the digital tools (end-2019

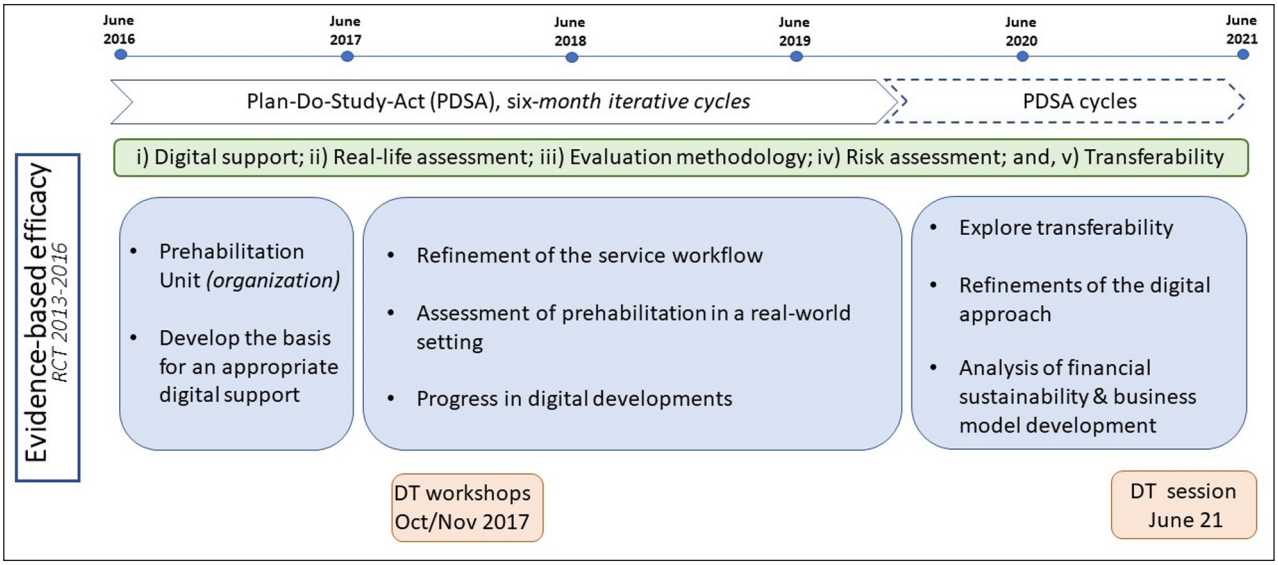

Figure 1 Timeline for co-creation and adoption of prehabilitation at HCB. Distribution of tasks through the experience-based co-design and quality improvement implementation research process; DT: Design-Thinking.

to mid-2021). It should be highlighted that in the analysis of the prehabilitation service, five dimensions were taken into consideration, as reported in [19, 20]: 1) Analysis of deployment in real-life scenarios; 2) Digital support; 3) Health risk assessment and service selection; 4) Evaluation Methodology; and, 5) Transferability and site adoption.

The co-creation process (Figure 1) contributed to consolidate prehabilitation at HCB as a standard service for approximately 150 candidates per year undergoing major surgeries in different specialties, namely: digestive, cardiac, thoracic, urologic and gynaecologic. It is of note that the capacity of the prehabilitation unit covered less than 20% of the estimated demand, mainly due to the limited capacity of the exercise training facilities at HCB. This aspect, together with patient's logistic/accessibility limitations, prompted two types of multimodal prehabilitation programs: i) a physical activity (PA)-based program; and ii) a face-to-face supervised exercise training (ET)-based program, with low and high requirements of human/logistic resources, respectively.

Apart from enhanced management of multimorbidity and prevention of unhealthy habits, the PA-based program included: i) motivational interviewing; ii) a physical activity promotion plan; iii) nutritional optimization; and iv) psychological support.

On the other hand, the ET-based program included all the elements of the PA-based program and, additionally, hospital-based face-to-face supervised exercise training sessions two-three times per week. The ET-based program was prioritized for patients with significant multimorbidity and patients with physical deconditioning undergoing highly aggressive surgeries.

As indicated above, the co-creation process covered five dimensions (i-v) depicted in Figure 1. The analysis of the prehabilitation results in a real-life scenario at HCB was undertaken for a thirty-month period, from mid-2017 to end-2019, as part of the evaluation framework described in [15]. It is of note that PDSA cycles played a major role in the entire quality improvement approach also contributing to feed the Design Thinking sessions. The debates generated during the two initial PDSA cycles consolidated the need for development, adoption/adaptation, of interoperable digital tools providing functional and technological integration with different healthcare providers. The team conceptualized the need for covering three differentiated, though intertwined areas, with specific technological requirements: i) patients' accessibility and empowerment; ii) enhanced management of care paths; and iii) collaborative work between two or more stakeholders (patient/carers and professionals), eventually from different healthcare tiers/providers. The specificities of the technological requirements to be operational on top of existing health information systems were explored, and developed, during the study period. Achievements in the other three dimensions considered in the co-creation process (Figure 1): Health risk assessment and service selection; Practicalities of the implementation of the evaluation framework [15]; and, Analysis of transferability and site adoption are summarized below, as part of the description of the Design Thinking sessions, as well as under the subheading on large scale sustainable adoption.

PDSA CYCLES

Periodical meetings in a monthly basis were held throughout the PDSA cycles. Technologically oriented meetings (the last Thursday of the month) included three professionals with technological profile and seven persons with clinical background. All of them pertaining to the research team. Controversial and strategic aspects were further discussed and decided in the scientific meetings (the last Friday of the month) carried out by a core subset of six professionals with technological and clinical backgrounds. It is of note that patients' inputs were captured with regular interviews and surveys on specific aspects of the service workflow and technologies used. However, informal patients' feedback to health professionals was feeding the co-creation process throughout the entire study period. Moreover, we stimulated synergies between the clinical teams delivering prehabilitation and the technological partners developing the digital tools.

The approach aimed to provide overview, ownership, and involvement of stakeholders on the intervention processes, while encouraging management responsibilities to ensure focus, pace, and self-discipline in the process. Moreover, the pragmatic nature of the adopted PDSA methodology provided flexibility to develop interventions according to stakeholder's feedback ensuring fit-for-purpose solutions, while providing the opportunity to build evidence for change and engage stakeholders as confidence in the intervention increased. The multidisciplinary composition of the co-creation teams at site level aimed to facilitate a good understanding of the complex interactions among multiple non-technological factors, internal and external, that modulate adoption of digitally enabled integrated care services in real life settings.

DESIGN-THINKING SESSIONS

The co-creation process included experience-based co-design and quality improvement process in the form of several Design Thinking (DT) sessions [27–31] which were carried out during October-November 2017; on 22th June 2021; and, on 13th December 2021. While 2017 encompassed three sessions assessing the service in a comprehensive manner [32], 2021 encompassed two sessions focused on the specificities of the interplay between the hospital-based prehabilitation team and professionals from different collaborating sports centres in the city of Barcelona, highly encouraged in the conclusions of the 2017 DT sessions. Main traits were as follows:

2017 Design-Thinking (DT) sessions – Were preceded by a **Preliminary fieldwork** analysis with the surveys done to professionals and patients. It contributed to define the characteristics of the three DT sessions, as displayed in Table 1 wherein objectives, tools and results of each session are summarized. A detailed description of the design-thinking sessions can be found in **Section 1** of the on-line supplementary material. Three DT sessions, each of a four-hour duration, aiming to address the core aims of the study, were carried out. Core objectives of the workshops were: i) to identify actionable factors modulating regional scalability of prehabilitation; ii) to enhance efficiencies of the service with the use of digital tools, and, iii) to design a business model contributing to sustainable adoption of the service. The final goal was to generate a roadmap to foster regional scalability of prehabilitation in Catalonia (ES) (7.7 m citizens).

The content of the three DT sessions covering: Immersion, Ideation and Validation (Sessions I-III, respectively), was based on preliminary work consisting of two actions. Firstly, we performed a survey aiming at gaining insight into the organizational aspects of the prehabilitation structure (Prehabilitation Unit) and service workflow at HCB. The survey was carried out with professionals involved in the design and management of the service. It also included other healthcare professionals having direct contact with the patients enrolled in the service, namely: anaesthesiologists (n = 5), physiotherapists (n = 3), nurses (n = 10), nutritionists (n = 2), psychiatrists (n = 2) and psychologists (n = 2). Secondly, we carried out in-depth face-to-face interviews with five patients and their respective caregivers who had participated in prehabilitation, aiming at capturing the patient experience perspective of the service. Patients surveyed in this phase had been candidates for cardiac transplantation, resection of lung parenchyma or major abdominal oncological surgery. It is of note that the additional collaborative methodology applied in [19] including patients', professionals' and managers' surveys, generated input material for the DT sessions.

The three DT sessions included all the stakeholders' profiles, namely: healthcare professionals (n = 13), managers (n = 3), designers (n = 6), health-technology agents (n = 3), business school representatives (n = 2), innovation agents (n = 10) and policy makers (n = 2) (sessions' details are reported in **Table 1S**).

The first session, Immersion, contributed to identify several different factors with potential impact on the service scalability. The most relevant ideas were clustered into the three dimensions: i) Users' satisfaction; ii) Technological viability; iii) Economic viability that were identified as key areas of action to foster prehabilitation scalability and adoption. It was agreed that actions should converge toward the service definition depicted in Table 1 (second row, third column). Overall, five areas for action were formulated: i) Personalization of interventions based on surgical risk assessment among other factors; ii) Stimulation of a pro-active role of patients, aiming at empowerment for self-management and promotion of physical activity; iii) Enhanced flexibility of interventions through a highly modular service design, facilitating service personalization; iv) Improved accessibility and logistics; and, v) Achievement of financial sustainability of the services to ensure long-term adoption of cost-effective healthy lifestyles interventions.

The second session, Ideation, was initiated with a short inspirational presentation, 10 min, to update the audience on the status of the prehabilitation service. A second talk, 15 min, was geared towards exploring previous experiences in other fields that have solved similar challenges. It was followed by ten simultaneous small group creative sessions, 4–5 persons each, that approached the main previously identified challenges under the following success criteria: i) Allow scalability while preserving the quality of the service; ii) Allow reproducibility of the service outcomes in different sites, that is, service transferability; iii) Enhance the adherence of patients to the work plan; iv) Provide key performance indicators to track service effectiveness; v) Foster accessibility to the program; vi) Ensure economic viability for sustainability; and, vii) Conceive the service within a LEAN approach [33, 34] to allow agile implementation and management using minimal resources. The ideas resulting from the creative sessions were debated by the whole group and then prioritized and pooled into a positioning map. Finally, the ideas incorporated in the positioning map were used to generate a general overview for the refined prehabilitation service workflow to be assessed during the third session, Validation. The categories displayed in the priority map were further debated and elaborated in three subgroups of attendees: i) group A: End-user touch points; ii) Group B: Digital tools; and, iii) Group C: Business, to achieve a well-defined action plan for scalability of the service, as summarized in Table 1 (fourth row, third column).

2021 Design-Thinking sessions – Two three-hour sessions carried out on 22nd June and 13th December 2021 involved core members (on average 18–20 persons in each session) of the clinical prehabilitation team, representatives of three different sports centers and technological experts of three digital small and medium enterprises (SME) and one technological institute. The focus of the June session was on the design of operational aspects of the interplay among the hospital-based team, collaborating sports centers and primary care health professionals.

The DT session held on 22nd June 2021 was focused on the design of pilot study to explore patient acceptability and practicalities of the interplay between the hospital-based team and different sports centres willing to collaborate to increase the weight of community-based execution of the program, as well as to generate a population-based approach to prehabilitation.

	AIMS	TOOLS	RESULTS
PRELIMINARY FIELDWORK	• To capture the patient experience perspective of the service. • To identify factors of the prehabilitation service at HCB that may limit scalability.	• In-depth interviews to patients and caregivers. • Surveys to professionals involved in the prehabilitation unit.	• Identification of actionable areas to be addressed in Session I – Immersion (**see text**).
IMMERSION *(Session I)*	• To gain further insight on organizational and actionable factors of to enhance scalability of the existing prehabilitation to: **a)** Optimize service workflow. **b)** Identify ICT-support to scalability. **c)** Explore financial needs for adoption.	• Elaboration of the following material contributing to refinement of the PreHab service (*): ◦ Experience map ◦ Empathy map ◦ Context map ◦ Priority map	• Agreement on the main challenges to face and solve in Sessions II and III. Main outcome of the Immersion was ***"to provide an accessible, round-the-clock personalized and modular service that the patients should be able to use autonomously during the PreHab period. The service should combine remotely controlled actions and face to face interactions with health professionals".***
IDEATION *(Session II)*	• To generate, develop and assess ideas and plans to solve the challenges identified in Session I.	• Two inspirational presentations (**see text**). • Small group creative sessions. • Positioning map (*)	• Generation of a customer journey that should contribute to define a viable strategy for regional deployment of prehabilitation. To this end, an overview of the prehabilitation service workflow was produced, as a visual map depicting the end users touch points and needs for both ICT-support and business model.
VALIDATION *(Session III)*	• To consolidate the proposals and refine the actions resulting from Session II aiming to define a viable strategy for regional deployment of a refined service workflow.	• Three working groups to separately tackle specific areas and final overall group meeting to generate consensus on specific proposals for each area: ✓ Implementation strategies. ✓ Technology-related aspects. ✓ Business model & reimbursement incentives.	• Fulfil end-user touch points (**see text for more details**) • Creation of a capillary network of healthcare/wellness centres to enhance accessibility. • Mobile app fostering tailored patient empowerment for self-management and remote monitoring. • Interoperability of ICT-enabling tools with existing HIS. • ACM system to support prehabilitation knowledge intensive processes for enhanced service management. • To drive patient interactions and data collection through an AI assisted chat *(i.e. Chatbot)*. • Cost-savings generated by prehabilitaton should cover the operational costs of the service. Investments needed to launch the service, as well as reimbursement incentives, could be covered by innovative PPP models.

Table 1 Objectives, tools and main results of the three 2017 design thinking sessions.

HCB: Hospital Clínic de Barcelona; ICT: Information and communication technologies; HIS: Hospital Information Systems; ACM: Adaptive case management; AI: Artificial intelligence; Chatbot: A computer program designed to simulate conversation with human users, especially over the Internet; PPP: public-private procurement; (*) See description in on-line supplementary material.

The final DT session on 13th December evaluated preliminary data of a two-month pilot experience partly transferring the intervention to sports centres. Two main outcomes were confirmation of feasibility and proposal of a three-layer service design covering the entire spectrum of patient's risk. Accordingly, the service is being organized as follows. i) low risk patients are candidates for an educational intervention and remotely supported behavioural change; ii) patients situated at the medium risk layer are also candidates for promotion of daily-life physical activity and community-based, partly remotely supported, physical training; and iii) high risk patients add to the previous two levels of intervention an initial period with hospital-based face-to-face supervised high-intensity exercise training followed by community based physical training. The December DT session confirmed the potential for transferability aiming at launching the community-based prehabilitation service during the first quarter of 2022.

LARGE-SCALE SUSTAINABLE ADOPTION

The process of implementation of prehabilitation during the study period was assessed using the Consolidated Framework for Implementation Research (CFIR) [35]. Moreover, in the initial phase, we evaluated the ecosystem maturity for digital transformation and deployment of integrated care services using the Scirocco Maturity Model for Integrated Care [36].

The CFIR information was grouped in five different areas, namely: i) Intervention characteristics; ii) Outer setting; iii) Inner setting; iv) Characteristics of the individuals; and, v) Characteristics of the process. It is of note that lessons learnt from CIFR, as well as knowledge from existing literature [8, 9, 37–39], were useful to identify key performance indicators (KPI) for the program long-term follow-up after adoption.

The implementation process following the five items of the CFIR approach [35] is summarized below (Table 2) and in Figure 1 (co-creation process). Briefly:

Intervention characteristics: We identified modularity and personalization of the prehabilitation program as key attributes of the service which will influence the success of implementation. However, the following core components of the program must be acknowledged: (i) High-intensity exercise training; (ii) Promotion of physical activity; (iii) Nutritional support; (iv) Behavioural intervention, as reported in [8, 9]. Besides that, the program will also require the adaptability of non-core components such as psychological support, smoking cessation programs and haemoglobin optimization, among others.

Another key aspect for a successful implementation of prehabilitation programs is an enhanced logistics and better health risk assessment. These components will not only lead to early identification of candidates for prehabilitation but also it will enhance the personalization of the interventions included in each patient work plan.

The evolution toward a community-based service to overcome the current constraints of prehabilitation (i.e., limited capacity of hospital facilities, convenience of facilities closer to patients' residency, efficiencies of care continuum) is cornerstone to achieve service scalability and transferability. However, quality standards of the intervention should be maintained. Finally, the importance of a continuous quantitative & qualitative build-in evaluation of the prehabilitation service, using well-identified KPI, must be highlighted. Transition from a hospital-based intervention to a community-based delivery of prehabilitation was planned during the 2021 DT sessions and currently assessed through a pilot program.

Outer setting – We understand that a patient-centred orientation considering patients' preferences, facilitators and barriers, should be a core trait of the prehabilitation program. Moreover, although clinical site customization is required, networking across different prehabilitation experiences enriches the programs.

Inner setting – Bottom-up & top-down interactions are needed for a successful implementation of the service. Moreover, key resources to generate and reinforce a positive climate change within the Institution are needed.

Characteristics of the individuals – There is a need to stress continuous monitoring of satisfaction levels. Consideration of feedback from patients and professionals is highly recommended. In that sense, PDSA cycles, DT sessions and focus groups are interesting tools to introduce for the guiding of the implementation process.

Characteristics of the process – We recommend facing the implementation process of a modular prehabilitation programs within a building-blocks strategy. This implementation approach will facilitate site customization and will also help to prioritize the engagement. Moreover, we also recommend the continuous evaluation of results during this process. As mentioned, elaboration and follow-up of an appropriate Quality Assurance program is a must.

It is of note that the Scirocco assessment indicated a high level of maturity of the Health District for adoption and further evolution of the prehabilitation service [40].

QUALITY ASSURANCE IN A REAL-WORLD SCENARIO

The evaluation of the prehabilitation service in a real-life setting at HCB during a thirty-month period, from mid-2017 to December 2019, as well as existing literature [6–9], provided the basis for proposing KPI structured using the Avedis Donabedian's model [41], as indicated in Table 2, second column.

Future validations of the proposed KPI in real-life settings should facilitate continuous quality assessment of the service using user-profiled dashboards, useful for clinical and administrative management of the service, aiming at optimization clinical outcomes and/or value generation of the prehabilitation. Cost-consequence

CFIR CONSTRUCTS	CFIR MAIN POINTS	KEY PERFORMANCE INDICATORS	CHALLENGES & RECOMMENDATIONS
Intervention Characteristics	- Prehabilitation as an integrated care component of ERAS pathways (enhanced recovery after surgery) - Core components: ◦ Management multimorbidity ◦ Trimodal intervention ◦ Service workflow defined ◦ Define target patients' profiles ◦ Personalize the service - Adaptability of non-core components is required - Continuous quantitative & qualitative build-in evaluation is needed	**STRUCTURE** **Coverage** **PROCESS** **Rate of dropouts** **Rate of adherence** **Quality assurance scoring** **POST-OPERATIVE OUTCOMES** **Comprehensive Complications Index** **Hospital length of stay** **Use of healthcare resources at 30 days**	• Increase service efficiency & value • Building capacity & Refinement of service delivery • Enhanced risk assessment & program prescription • Improving digital support • Transfer to the community
Outer Setting	- Patient-centred orientation, a core trait - Networking across experiences needed - Site customization is required to minimize potential negative impacts of external factors		
Inner Setting	- Bottom-up/Top-down interactions are needed for success. Champion driven programs show high success rates - Key resources to generate/reinforce a positive climate change are needed		
Characteristics of Individuals	- Continuous monitoring of satisfaction levels and consideration of feedback from patients and professionals is highly recommended		
Process	- A building-blocks implementation strategy, with appropriate site customization prioritizing engagement, is required - Continuous evaluation of results		

Table 2 Implementation of prehabilitation at HCB, KPI and recommendations for scaling-up.

analyses done using data from the reported RCT [8, 9] and from assessment of the service in a real-life setting [42] strongly indicate financial sustainability of prehabilitation in high-risk patients paid by healthcare providers. However, delivery of the service in low and medium risk candidates deserves further studies.

DISCUSSION

The current study addressed major prehabilitation service challenges for large-scale sustainable adoption of the intervention, through a co-creation process that used experience-based co-design tools to identify key elements to be considered for regional scalability and site transferability. Other priority areas also being addressed, but not described in the current report, were: i) Continuous quality improvement of the service in real world settings, aiming at ensuring long-term reproducibility of the initial study results; ii) Enhanced risk assessment for personalization of the service; and, iii) Evolution of prehabilitation toward a population-based approach, which implies tailoring the intervention according to a subject-specific health risk assessment, as well as extending the scope of the intervention to also enhance post-surgical care recovery. It is of note that, during the entire study period, we explored the potential for generalization of the approach to other use cases, namely: rehabilitation of chronic patients, including support to oncologic patients, and early prevention of multimorbidity in high-risk citizens.

We believe that service co-creation and adoption based on the combination of experience-based co-design and a quality improvement process facilitated a stepwise progress towards identifying the three pivotal dimensions requiring intervention: i) Enhanced service design; ii) Digital support; and, iii) Financial sustainability. It is acknowledged that site customization of the service will be required for large scale implementation at regional or international levels. Personalization and modularity of the prehabilitation service have been stressed as two core traits needed for successful site implementation. Likewise, empowerment of patients for self-management of their condition constitutes an essential goal of the service. The requirements for digital support in the scalability of prehabilitation have been formulated in detail in [43] and commercial promotion will be initiated within 2021 through the spin-off company Health Circuit [44]. It is of note that the technological support facilitating service modularity and personalization as well as interoperability between community-based facilities, including patient's home, and hospital-based information systems has been achieved in the health district of Barcelona-Esquerra (520 k inhabitants).

Beyond prehabilitation, we believe that the current study indicates a high potential of co-creation, and DT methodologies, for contributing to the refinement and site adaptation of integrated care service workflows in a broad spectrum of complex interventions as often encountered in the integrated care scenario [40].

LESSONS LEARNT

The co-creation process described in the current report allowed to identify the following areas for action aiming at optimizing value generation and large-scale adoption of prehabilitation:

- *Capacity building and refinement of service delivery* – It involves actions on service re-design using a LEAN approach aiming at enhancing patients' accessibility and adherence, as well as broadening the scope of service delivery to different settings (i.e. health clubs and sport centers), beyond a hospital-centered approach described in the current report.
- *Enhanced risk assessment for personalization of interventions* is needed to facilitate fine-tuning of the three-layer service design described above.
- *Maturity of digital support constitutes a high priority to optimize prehabilitation outcomes* [26, 43].
- *Future co-creation initiatives aiming at service refinement should address specific, and narrower, targets to ensure short-term achievements.*

CONCLUSIONS

The current report provides three well-defined outcomes. Firstly, it illustrates the potential of evidence-based co-creation, specifically using DT methods, and quality improvement methodologies with iterative PDSA cycles to achieve large-scale implementation of integrated care services for chronic patients, taking as a use case prehabilitation. As a second outcome, it identified factors influencing prehabilitation results and the determinants of adoption of the service, using the CFIR framework. Finally, from the lessons learnt, we propose a list of Key Performance Indicators for long-term quality assurance of the intervention after adoption. Overall, the co-creation approach shows high potential for service refinement in other complex healthcare interventions.

ADDITIONAL FILE

The additional file for this article can be found as follows:

- **Supplementary File 1.** Design Thinking Sessions and CFIR Description. DOI: https://doi.org/10.5334/ijic.6503.s1

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COMPETING INTERESTS

The authors have no competing interests to declare.

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Original Paper

The Assessment of Medical Device Software Supporting Health Care Services for Chronic Patients in a Tertiary Hospital: Overarching Study

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Abstract

Background: Innovative digital health tools are increasingly being evaluated and, in some instances, integrated at scale into health systems. However, the applicability of assessment methodologies in real-life scenarios to demonstrate value generation and consequently foster sustainable adoption of digitally enabled health interventions has some bottlenecks.

Objective: We aimed to build on the process of premarket assessment of 4 digital health interventions piloted at the Hospital Clinic de Barcelona (HCB), as well as on the analysis of current medical device software regulations and postmarket surveillance in the European Union and United States in order to generate recommendations and lessons learnt for the sustainable adoption of digitally enabled health interventions.

Methods: Four digital health interventions involving prototypes were piloted at the HCB (studies 1-4). Cocreation and quality improvement methodologies were used to consolidate a pragmatic evaluation method to assess the perceived usability and satisfaction of end users (both patients and health care professionals) by means of the System Usability Scale and the Net Promoter Score, including general questions about satisfaction. Analyses of both medical software device regulations and postmarket surveillance in the European Union and United States (2017-2021) were performed. Finally, an overarching analysis on lessons learnt was conducted considering 4 domains (technical, clinical, usability, and cost), as well as differentiating among 3 different eHealth strategies (telehealth, integrated care, and digital therapeutics).

Results: Among the participant stakeholders, the System Usability Scale score was consistently higher in patients (studies 1, 2, 3, and 4: 78, 67, 56, and 76, respectively) than in health professionals (studies 2, 3, and 4: 52, 43, and 54, respectively). In general, use of the supporting digital health tools was recommended more by patients (studies 1, 2, 3, and 4: Net Promoter Scores of −3%, 31%, −21%, and 31%, respectively) than by professionals (studies 2, 3, and 4: Net Promoter Scores of −67%, 1%, and −80%, respectively). The overarching analysis resulted in pragmatic recommendations for the digital health evaluation domains and the eHealth strategies considered.

Conclusions: Lessons learnt on the digitalization of health resulted in practical recommendations that could contribute to future deployment experiences.

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KEYWORDS

chronic patients; digital health; health technology assessment; implementation research; integrated care

Introduction

Over the past years, substantial progress has been made toward the adoption of digital technology for health or digital health [1]. Health programs using digital technology are increasingly being tested, evaluated, and, in some instances, integrated at scale into health information systems [2], considering its unique methodological challenges [3-6]. Investment in digital health requires evidence to support its value and expected benefits from the perspective of key stakeholders, that is, patients, professionals, health service providers, policy makes, and payers [7].

Assessment of digital health interventions has been conceptualized by a range of different evaluation frameworks [8,9]. A common factor in all of them is that digital health interventions should show benefit from all stakeholders' perspectives during design and development [10], as well as after adoption. However, while such evaluation frameworks may serve as relevant guidelines, only recently, few of them have been extensively applied for the assessment of mature digital health tools [11-14]. Moreover, current medical device regulatory guidelines for digital health technologies [15-17] are, de facto, establishing their own evaluation constraints.

Common requirements are that digital health tools must be safe and must generate value to be successfully adopted in health care. Current medical device software (MDSW) regulations aim for successful links between privacy and information security, as well as for patient safety and clinical benefit [18,19]. It is of note that recent regulatory frames [14], aiming for fast-track assessment of digital applications, define a full set of requirements with respect to user friendliness, robustness, interoperability, and reimbursability.

The main objective of this research was to generate recommendations and to report lessons learnt from separate assessments of MDSW with the aim of bringing together the premarket experience from the cocreation of digital health interventions at the Hospital Clinic de Barcelona (HCB) during the period 2017-2019 [20] and the postmarket experience of MDSW after regulatory compliance in the European Union and the United States through MDSW recalls during the past 5 years (2017-2021). Due to the proliferation of innovation projects involving digital health interventions, there is a clear need for concerted efforts to harmonize and learn from both premarket piloting and postmarket surveillance experiences to foster applicability and standardization of the assessment of digital health tools in real-life settings.

It is of note that the premarket co-design experiences from the HCB [20] benefited from the combined input of all the stakeholders, including end users, aiming to prevent failures when reaching the market, and that the HCB has a dual role as a university center and as a driver of large community-based integrated care in the city of Barcelona (Área Integral de Salud de Barcelona Esquerra [AISBE]; 520,000 citizens) [21,22], falling within the activities of the Catalan Open Innovation Hub on Digitally Enabled Integrated Care Services, which is 1 of the 4 original EU Good Practices in the European Joint Action JADECARE [23].

Methods

Premarket Analysis of the Four Digital Health Prototypes Piloted at the HCB

Cocreation and quality improvement methodologies reported previously [20] were used to consolidate a pragmatic assessment protocol that was applied in the 4 digital health prototypes supporting the interventions (studies 1-4) described below.

Study 1 involved home-based noninvasive ventilation (NIV) of patients with hypercapnic respiratory failure. The study addressed enhanced management of chronic patients requiring specialized respiratory care for home-based NIV by means of a mobile app for patient self-management [24].

Study 2 involved prehabilitation of high-risk patients undergoing major abdominal surgery. The study assessed the potential of the supporting digital health tool, PREHAB [25], to enhance collaborative work among health professionals and patients using a mobile app for self-management at the community level.

The third cluster involved community-based care of frail chronic patients. This cluster of digital health interventions included 2 studies addressing specific objectives: (1) Study 3 assessed an adaptive case management platform [26] for community-based care of chronic patients; and (2) Study 4 investigated the potential of a secure communication platform, prototyped during 2019, for enhanced management of frail chronic patients [27] (Table 1). The details of the digital health interventions are provided in Multimedia Appendix 1.

Table 1. Details of the 4 digital health interventions (studies 1-4) piloted at the Hospital Clinic de Barcelona.

Study	Design	Inclusion and exclusion criteria	Digital health intervention
1	Single-blinded single-center RCT[a] with 2 parallel arms (1:1 ratio): (1) control group (n=34) and (2) digital health intervention during a period of 3 months (n=33).	• Inclusion criteria: Adult patients under home-based NIV[b] at the HCB[c] and having a mobile phone or tablet in the intervention group. • Exclusion criteria: Patients with severe psychiatric or neurological diseases, as well as those hospitalized at the time of assessment.	MyPathway app (TRL[d] 5) [28] was used for bidirectional interaction with the research team. It consisted of positive feedback or reinforcement messages in response to the number of hours of NIV use reported by the patient daily. Moreover, general advice on specific NIV clinical problems was automatically provided by the app according to the patients' weekly input.
2	Prospective cohort study with 16 candidates for the prehabilitation service at the HCB.	• Inclusion criteria: Candidates of major elective surgery in at least 4 weeks, age >70 years, an ASA[e] score of III/IV, and access to a mobile phone or tablet with internet connection. • Exclusion criteria: Physical or psychological problems affecting use and not having a career.	A digital health tool (TRL 6) [25] was used by health care professionals to prescribe and monitor tasks for patient self-management supported by an app, including physical activity goals, nutritional advice, mindfulness exercises, and predefined data collection instruments for patient-reported outcomes and experience.
3	Prospective cohort study with 20 clinically stable chronic patients recruited in 1 primary care unit from AISBE[f] and followed-up for a period of 1 month.	• Inclusion criteria: Acceptance to participate and having an appropriate smartphone or tablet. • Exclusion criteria: Physical or psychological problems precluding the use of the app and not having a career.	Patients were given access to the platform (TRL 5) through their smartphones, and a pedometer was provided to track adherence to a personalized daily physical activity prescription, with remote support from a case manager.
4	Cluster RCT by primary care teams from AISBE, with an intervention (n=31) to control ratio of 2:1 and follow-up for a period of 3 months.	• Inclusion criteria: Acceptance to participate and having an appropriate smartphone or tablet • Exclusion criteria: Physical or psychological problems precluding the use of the digital tool and not having a career.	A case manager nurse used the Health Circuit (TRL 5) communication channel to trigger bilateral or group conversations, including health information exchange among specialized care, social care professionals, and community-based services, to agree on a goal-oriented and personalized health plan to manage both expected and unexpected events communicated by study participants [27].

[a]RCT: randomized clinical trial.

[b]NIV: noninvasive ventilation.

[c]HCB: Hospital Clinic de Barcelona

[d]TRL: technology readiness level.

[e]ASA: American Society of Anesthesiologists.

[f]AISBE: Área Integral de Salud de Barcelona Esquerra.

The premarket assessment of the 4 digital health interventions (Table 1) piloted during the period 2017-2019 primarily focused on assessment of technical robustness and usability. The former was assessed with a technical log book on the cloud that was updated daily with technical issues and suggestions for improvement from all study participants. The end users' perceived usability and satisfaction were assessed by means of the System Usability Scale (SUS) [29] and Net Promoter Score (NPS) [30], alongside general questions about satisfaction.

Besides the technical and usability assessments mentioned above, compliance with other operational aspects, such as privacy and security, interoperability, transferability, and value generation of the accompanying integrated care services, was part of an overall evaluation framework [31], but the premarket analysis did not systematically analyze this. It is worth mentioning that digital support for the 4 digital health interventions (Table 1) was designed to operate on top of existing hospital information systems to minimize the need for ad-hoc integration via standard application programming interfaces.

When writing this manuscript, we adhered to the Consolidated Criteria for Reporting Qualitative Research (COREQ) [32]. All information retrieved from the technical and usability assessments of the 4 digital health interventions (including the end users' interviews) was processed according to the protocol-specific ethics statement mentioned in the Ethics Approval and Consent section.

MDSW Regulations and Postmarket Surveillance Analysis

In recent years, digital health technology has developed rapidly in the market as software-only novel therapies or has been embedded into medical devices or clinical workflows as a companion MDSW device in the market. MDSW is defined, under EU Regulation (EU) 2017/745-MDR [16], as a software, used alone or in combination, that is intended by its manufacturer as a medical device for human beings for a specific medical purpose: diagnosis, prevention, investigation, monitoring, prediction, treatment, alleviation, prognosis, and prediction.

The analysis of the European MDSW regulatory frame was focused on the EU Regulation 2017/745-MDR [16] and the fast-track process generated by Germany's Federal Institute for Drugs and Medical Devices, known as the "BfArM" guidelines for the evaluation of digital health applications (DiGA) [14]. Likewise, for the United States, we considered the FDA 21 CFR Part 820 [15]. Moreover, the EU General Data Protection Regulation (GDPR) [18] and its American counterpart, the US Health Insurance Portability and Accountability Act (HIPAA) [19], were also considered in the analysis.

Within the postmarket surveillance analysis at the EU level, we collected the numbers of devices that had been recalled, irrespective of their risk level and the product end user, over 5 years (January 1, 2017, to December 31, 2021) from the German BfArM website [33]. The results included malfunctioning software that may result in a severe adverse event, device deficiency, incident, or serious incident.

For the postmarket surveillance analysis in the United States, we collected data from the following 2 public databases: Manufacturer and User Facility Device Experience (MAUDE) database [34] and MEDSUN Reports [35]. Considered MDSW recalls included software failures in terms of security flaws, privacy risks, internal controls, technical controls, physical controls, and implementation.

Overarching Analysis

As a result of the experience-based cocreation process [20], 4 domains of digital health system validation (Table 2) and 3 eHealth contextual strategies (Table 3) were considered essential for the assessment of digital health tools. Therefore, they were used to guide a thematic analysis on the assessment results of the 4 digital health interventions, by the author EB, as well as on the overview of the MDSW current regulations and the analysis of MDSW recalls of the past 5 years (2017-2021) in the European Union and the United States, by the author HWH.

Then, the author EB discussed the findings with the participants of each digital health intervention, the final users of the supporting digital health tools, and all other coauthors. For each of the 4 digital health interventions, the evaluation results were judged by the author EB according to the contextual eHealth strategy, defined by the role of the digital tools in the health care service.

Finally, we evaluated the thematic analysis results to generate recommendations for assessment of the sustained adoption of future digital health interventions.

Table 2. The domains considered essential for the validation of digital health systems [20].

Domain and component	Description
Technical	
Robustness	Testing of performance when compared to a technical gold standard
Privacy and security	Testing of privacy and security requirements
Interoperability	Testing of interoperability requirements
Transferability	Potential to adapt to other services and implementation scenarios
Smartness	Testing of innovative features powered by artificial intelligence
Clinical	
Safety	Critical appraisal of technology impact on patient safety outcomes
Medical benefit	Evidence of positive health care effects
Usability	
Ease of use	Whether digital health systems can be used as intended by users
Feasibility	Whether digital health systems work as intended in each context
Cost	
Value generation	Anticipated cost impact on the clinical outcome of interest
Affordability	If the costs of digital health systems can be made affordable

Table 3. The eHealth contexts considered essential for the validation of digital health systems.

eHealth strategy	Description
Telehealth	Digital support to well-established service workflows to enhance health care efficiencies. Typically, clinical evidence is not required. Not a medical device.
Integrated care	Digital support to enable innovative service workflows with a care continuum approach. Clinical evidence is required. Requires regulatory clearance or approval.
Digital therapeutics	Medical device software–driven therapeutic intervention for prevention, management, or treatment. Evidence and regulatory approval are required.

Ethics Approval and Consent

Letters of medical ethics approval of the Ethics Committee for Medical Research of the HCB and signed informed consent forms were obtained for the 4 studies (study 1, HCB/2019/0510; study 2, HCB/2016/0883; study 3, HCB/2018/0803; and study 4, HCB/2018/0805).

Results

Premarket Analysis of the Pilots

A total of 99 chronic patients and 9 health care professionals were assessed during the interaction and cocreation process of the 4 different digital health interventions piloted at the HCB (studies 1-4). Assessment results of the technical and usability performances are summarized in Table 4. See Multimedia Appendix 2 for further details.

Table 4. Usability performance and summary of the technical log book reported by patients and professionals with respect to the digital health tools supporting the 4 digital health interventions piloted at the Hospital Clinic de Barcelona.

Study	Patients' experience			Professionals' experience			Technical log book[a]
	n	NPS[b]	SUS[c] score	n	NPS[b]	SUS[c] score	
1	33	−3%	78	1	N/A[d]	N/A	Recurrent login with a username and a password that are easy to forget (patients).
2	16	31%	67	2	−67%	52	Technology bugs (health professionals) and system enforcement for a random password after reset (patients).
3	19	−21%	56	1	1%	43	Problems connecting the pedometer via Bluetooth with some Android smartphones (patients).
4	31	31%	76	5	−80%	54	Lack of robustness of the multimedia communication channel with some Android smartphones (health professionals).

[a]Main reported issues from patients or health professionals.

[b]The Net Promoter Score (NPS) is a known questionnaire used to assess satisfaction with a product, which includes a key question: "How likely is it that you would recommend our system to a family member or friend?" Patients can give an answer ranging from 0 ("not at all likely") to 10 ("extremely likely"). Individuals scoring 9 or 10 are called "promoters," individuals scoring 7 or 8 are called "passives" (or neutrals), and individuals scoring 0 to 6 are called "detractors." The NPS is computed as percent promoters − percent detractors, and ranges from −100% to 100%.

[c]The System Usability Scale (SUS) was developed by John Brooke in 1986 and consists of a 10-item questionnaire scored on a 5-point Likert scale from 0 (strongly disagree) to 5 (strongly agree). The overall score is calculated from the sum of all item scores multiplied by 2.5 and can range from 0 to 100. A system or product that receives a score of 68 or above is considered to have good usability.

[d]N/A: not applicable.

Study 1: Home-Based NIV of Patients With Hypercapnic Respiratory Failure

Most (20/27, 74%) reported incidences by end users had to do with the need to login with a username and a password that were easy to forget, which precluded the ease of use. However, on a Likert scale from 1 (very bad) to 10 (very good), the general impression of patients was scored 7.5, user friendliness was scored 8.2, and the ability to use the app without assistance was scored 8.5. This was in line with the mean patient usability score (78 out of 100).

Study 2: Prehabilitation of High-Risk Patients Undergoing Major Abdominal Surgery

Fifty percent (5/10) of incidences were due to comfortability and accessibility (the system forced the use of a random password when the password was reset) and 30% (3/10) were due to technology robustness. The remaining 20% (2/10) of incidences were due to various factors. As in study 1, the general impression and user friendliness was scored 8 (out of 10) and the ability to use the app without assistance was scored 7.5 (out of 10). In contrast, the patient usability score had a mean value of 67, which is considered an average usability grading. With respect to the experience of professionals, a neutral experience using the web backend for professionals was reported, with an overall satisfaction score of 5 (out of 10) and a mean SUS score of 52.

Study 3: Community-Based Care of Frail Chronic Patients With the CONNECARE Platform

Most (4/7, 57%) observations during the pilot were due to lack of robustness of the Bluetooth connection with the pedometer. Reported observations regarding motivation, reliability, comfortability, and accessibility reached 14% (1/7) each. In general, patients had a slightly positive experience (6/10) using the system, but its usability was graded low (SUS score of 56). In case of professionals, perceived usability was graded lower (SUS score of 43); thus, the professionals involved would not recommend the CONNECARE system.

Study 4: Community-Based Care of Frail Chronic Patients With the Health Circuit Prototype

High proportions of observations were due to usability (11/18, 61%), and comfortability and accessibility (6/18, 33%) issues, mostly due to lack of robustness of the multimedia communication channel. In general, most patients had a positive experience using the system, which was reinforced by the fact that the median overall satisfaction score was 7.8 (out of 10) and the mean patient usability score was 76. However, the NPS reported by professionals (n=5) was negative (−80%), but since

the median overall satisfaction score was 5 and the perceived usability score was 54, we could consider that professionals had a neutral experience using the prototype.

Comparability Analysis of EU and US MDSW Regulations

Data Protection

Both the EU and US regulatory frames (GDPR [18] and HIPAA [19], respectively) provide clear guidelines for manufacturers, health professionals, patients, and users in general, to assess how medical devices protect private information and security. The GDPR governs the use of and applies to all personal data from an individual person who is in an EU country at the time the data are collected, while HIPAA has a much narrower scope and only applies to protected health information. However, both the regulations are established keeping in mind the public interest and security of sensitive information [36]. In addition, potential risk management assessment and cyber security are essential to consider the stage of design, development, clinical investigation, and postmarket surveillance. Since the primary focus is on data security, privacy, and integrity, all the measures necessary to comply with the regulations are broadly similar. Thus, MDSW that are already GDPR or HIPAA compliant will have in place most of the security measures required to protect data privacy.

Medical Devices

To ensure the safety and efficiency of medical devices while supporting innovation, the European Union and United States have established their own transparency route to internal markets and a procedure for verification and validation (Medical Device Regulation [MDR] [16] and Food and Drug Administration [FDA] [15], respectively). Medical device regulatory compliance under both the FDA and MDR is a complex path involving processes that need constant monitoring and maintenance. For example, the recent requirements of the MDR are much closer to those of the FDA in terms of (1) prerequisites for the conformity assessment; (2) a quality management system in-place compliant with ISO 13485; and (3) use of consensus standards that are relevant to the development and design of interoperable medical devices. With that said, there are some key differences. The FDA's classification system is based upon 3 risk classes, while the EU MDR has 4 device categories and 5 risk-based classifications.

The risk classification assigned will determine the depth and amount of clinical data required under the MDR to get approval for the medical device, whereas under the FDA, Class I and some Class II devices do not require clinical testing, and only proof is required that the medical device is substantially equivalent to a legally marketed product.

Toward Digital Therapeutics

Perhaps the biggest challenge facing EU and US MDSW regulations is reimbursement. With evidence supporting the efficacy of digital therapeutics stacking up, more payers are coming round to the idea of MDSW reimbursement and the business case for offering it [37]. With it becoming ever clearer that MDSW, in general, and digital therapeutics, in particular, can play significant roles in the treatment of many conditions around the world, both the European Union and FDA are creating regulatory frameworks for the safety and efficacy of digital therapeutics. Germany launched a fast-track process for digital health applications (DiGA) [14], which is the first in the world for digital therapeutics reimbursement. DiGA is a pathway for doctors to prescribe digital therapeutics to publicly insured patients and receive reimbursement in much the same way as traditional treatment. This catapulted Germany to global leadership in digital therapeutics regulation. No other country has yet made prescription digital therapeutics so widely available to such a high percentage of the population. Beyond EU MDR standards, DiGA defined further requirements, such as interoperability, robustness, and ease of use, among others.

Postmarket Surveillance Analysis

The review of the German regulatory framework (BfArM) retrieved a total of 556 postmarket events that fitted the research requirements focused on digital health tools (representing 13% of all events that included drugs, assays, and medical devices). Likewise, the review of the MAUDE and MEDSUN databases (United States) found a total of 114 software-related issues, representing 18% of all queried events. See Multimedia Appendix 3 for details.

The vast majority of reported issues were related with software problems, incorrect results, data mismatch, error codes, system unexpected shutdowns, incorrect procedures, and cybersecurity-related aspects, which folded into the *robustness* (620/665, 93.2%) and *privacy and security* (26/665, 3.9%) components of the technical domain mentioned in Table 2. Therefore, software technical defects were reported to have the highest potential risk of harming end users.

No issues were reported with respect to *transferability*, *smartness*, *safety*, or *medical benefit*, whereas very few issues were reported in relation to *interoperability* (2/665, 0.3%), *ease of use* (8/665, 1.2%), and *feasibility* (9/665, 1.3%).

Overarching Analysis

The overarching analysis of the process of premarket assessment of the 4 digital health interventions piloted at the HCB, as well as the analysis of current MDSW regulations and postmarket surveillance in the European Union and United States provided a source of experience-based knowledge that is described below and summarized in Tables 5 and 6 in terms of recommendations for each of the 4 digital health evaluation domains (Table 2) and lessons learnt toward sustained adoption in the 3 eHealth contexts considered (Table 3).

Table 5. Recommendations for the assessment of medical device software for sustained adoption of future digital health interventions.

Domain	Recommendations
Technical	• A high technology readiness level is key for sustained adoption of MDSW[a]. • Data privacy, security, and interoperability need to be addressed for regulatory compliance. • MDSW should evolve to support collaborative work.
Clinical	• A dedicated change management team is required for integrated care eHealth strategies. • A unified evaluation protocol facilitates comparability among digital health interventions. • Key performance indicators need to be adopted for continuous assessment.
Usability	• Cocreation facilitates design while minimizing the need for user training and enhances adoption. • Cognitive behavioral therapy techniques enhance user adherence to digital health applications.
Cost	• Evidence on health care value generation of digital health interventions precedes cost containment. • Bundle payment approaches based on service performance are advised.

[a]MDSW: medical device software.

Table 6. Lessons learnt for the assessment of medical device software for sustained adoption of future digital health interventions.

eHealth strategy	Lessons learnt
Telehealth	Digital health tools that engage consumers for lifestyle, wellness, and health-related purposes, which typically do not require regulatory oversight, do not ensure value generation.
Integrated care	Evidence-based MDSW[a] that allow all stakeholders in the care continuum to collaborate and to access, share, aggregate, and visualize meaningful data daily, are expected to contribute the most to health care efficiency generation.
Digital therapeutics	Digital therapeutics that win public reimbursement must have solid proof of their efficacy/effectiveness. A market strategy or a MDSW regulation that helps build that proof is therefore essential. Real usage data for digital therapeutics and associated evaluations should determine national health coverage.

[a]MDSW: medical device software.

Technical Domain

Optimization of health care value generation and sustainability of the digitally enabled integrated care services explored in the 4 pilot studies were limited by the lack of technical robustness of the prototypes tested during the period 2017-2019, with technology readiness levels [38] within the interval 5-6.

It is of note that data privacy, information security, and data standardization are essential for enabling interoperability with health information systems from different providers or health information exchange platforms across providers within a geographical area. However, many privacy and security features are known to reduce user satisfaction.

In terms of interoperability and transferability, MDSW should evolve to support collaborative work among stakeholders across community and hospital services (ie, vertical and horizontal integration), using shared care plans that incorporate patient goals, which will foster the digital transformation of health care within a care continuum scenario.

Clinical Domain

Overall, digital support should be embedded into properly defined health care service workflows, particularly relevant for integrated care and to some extent digital therapeutic eHealth contexts. Moreover, implementation of adaptive case management for the management of care pathways is highly advisable to face the challenge of unexpected events within well-defined care paths. Telehealth tools not embedded into properly defined health care service workflows, focused on engaging consumers for lifestyle, wellness, or any other health-related purposes, which typically do not require regulatory oversight, do not ensure value generation.

The implementation of digitally enabled integrated care is disruptive and requires transformational change at all levels of an organization. This requires careful and solid strategic planning considering all the obstacles that may be encountered, as well as developing incentives and ongoing change management with a dedicated change management team. Pragmatic application of the same evaluation protocol is highly recommended to facilitate comparability among deployment experiences and to identify key performance indicators for long-term follow-up quality assessment of the service, beyond the initial deployment. In this regard, the use of profiled dashboards could be an efficient strategy for the assessment of cost-effectiveness in real-life settings, especially for MDSW using eHealth strategies that require evidence of efficacy and effectiveness (ie, integrated care and digital therapeutics).

Usability Domain

Flexible adoption of patient-centered cocreation methodologies during the premarket studies was useful to identify factors that generate bottlenecks, facilitating design and adoption of timely action plans. In general, cocreation efforts represented a success factor in terms of perceived usability by patients, but generated high expectations by health care professionals that were not met due to lack of technical robustness of the prototypes tested,

which was a negative factor in terms of perceived usability. Efforts must be devoted toward the development of digital health applications that support patient empowerment for self-management with cognitive behavioral therapy to foster the long-term effectiveness of digitally enabled interventions.

Cost Domain

Digital transformation of health care must be based on cost containment. Operational costs of innovative, digitally supported, integrated care services are expected to decrease, so transitional costs should be covered by savings generated through decreases in operational costs. To this end, bundle payment approaches based on service performance are advised. Evidence-based MDSW embedded into properly defined health care service workflows with an integrated care approach are expected to contribute the most to health care efficiency generation. MDSW delivering a therapeutic intervention must have solid proof of efficacy in controlled clinical trials, but real usage data should be used to monitor cost-effectiveness in a real-world setting and ultimately determine national health coverage.

eHealth Strategies

Digital health tools have become integral to the prevention, diagnosis, treatment, and management of health and diseases. Clinicians use digital health tools to gain insights into patient outcomes, conduct telehealth visits, treat aspects of diseases otherwise unaddressed by traditional medications, and, ultimately, ensure health care efficiency generation. It is crucial to describe the landscape of available digital health tools in addition to the level of clinical evidence and regulatory oversight that correlates with each eHealth category in this quickly evolving industry. End users, clinicians, and payers should understand the difference between the purpose and function of various MDSW, since this differentiation determines the risk level assumed for clinical evidence generation alongside the technical requirements for regulatory oversight.

Discussion

Summary of the Results

The study aimed to update health professionals on the current landscape of MDSW for enhanced management of chronic patients. The research generated recommendations on target evaluation domains and eHealth categories through an overarching analysis of 3 sources of information: (1) premarket evaluation of 4 pilots carried out at the HCB, using ongoing technological developments; (2) assessment of the regulatory frames of MDSW in the United States and Europe; and (3) postmarket surveillance reporting from the same 2 areas of the world.

Evaluation results of the 4 digital health interventions piloted at the HCB showed that patients tended to score higher than professionals in terms of the experience with supporting digital health tools, and in general, they would recommend the use of supporting digital health tools. This can be partly explained by the fact that the technology readiness level of the assessed digital health interventions was rather low at the precommercial stage, which most likely had a negative impact on the perceived usability by health care professionals who had to lead with technical issues at the same time than with the inherent complexities of case management. Moreover, the lack of integration with existing hospital information systems influenced the poor results with respect to the experience of health professionals. The 4 premarket digital health interventions were not considered mature for integration with existing health information systems, and in general, hospital information technology departments tend to reject integration of noncommercial digital health tools, which precludes usability, especially among health professionals who are not strongly motivated.

As mentioned above, EU and US MDSW regulations include premarket MDSW assessment with respect to clinical data, product information, performance testing, labeling, benefit-risk assessments, residual risks, etc. However, MDSW manufacturers should also plan, establish, document, implement, maintain, and update a postmarket surveillance system in a manner that is proportionate to the risk class and appropriate for the type of device. This system should be an integral part of the manufacturer's quality management system and should be notified to the corresponding regulatory body.

Overall, the postmarket surveillance review of both German and US regulatory frameworks confirmed the crucial role of software verification and validation, the voluntary testing of cybersecurity, and the need for testing user interfaces.

Strengths and Weaknesses

The inherent heterogeneity of the 4 digital health interventions considered in this study represents both a strength, because it reinforces transferability of the assessment approach, and a limitation, because it precludes comparability of the results among the 4 study protocols. However, the cocreation process and the application of the same structured evaluation protocol over the 4 digital health interventions contributed to the evolution of the mindset of health professionals toward the use of digital health tools. Specifically, the participation of all stakeholders in the overarching analysis concluded with the generation of a set of general recommendations for adoption in routine clinical practice.

The evaluation protocol focused on technical and usability performance because the primary objective of the 4 digital health interventions piloted at the HCB was to demonstrate the feasibility of the approach. If large-scale deployment is the primary aim, other functional, technical, and ethical aspects of the supporting digital health tools will need to be assessed.

The 4 digital health interventions were piloted within the context of research and innovation projects. This represents a clear advantage for stimulating cocreation of the supporting digital health tools, but establishes the threshold of required technological maturity at the prototype level and limits the transferability of the results beyond the boundaries of pilot settings.

Considered MDSW regulations in the European Union and United States neglect the tools and general requirements of other countries or regions of the world. Although similar premarket approval applications and postmarket surveillance tools are

being put in place in recent years [11-14], they do not apply to the full range of technology readiness levels, that is, they are intended to be used to evaluate mature technology. In this respect, development and production phases of digital health tools (focus of the 4 digital health interventions assessed in this study) may help to generate more mature and robust digital health tools that are ready to be assessed by corresponding health technology assessment frameworks [11-14].

Toward the Adoption of MDSW

Technical performance and usability are arguably among the most important considerations with patient-oriented mobile and digital-based solutions [39,40].

The overarching analysis showed a clear link between premarket assessment and postmarket surveillance in terms of technical failures hindering stakeholder adoption, regardless of usability and acceptability success. Such technical failures can be overcome by generating not only robust and secure products, but also online open access databases (the likes of clinical registries for single diseases) where basic MDSW approval information, medical specialty, and algorithm details can be publicly shared, thus enhancing transparency and collaborative work. Two recent studies [41,42] explored this concept when applied to artificial intelligence MDSW.

Moreover, digital health apps must be easy to use for their intended purpose, require minimal effort to complete tasks, have minimal data entry burden, and allow the user to control preferences when appropriate (eg, notifications). Since systems can be designed for users with disabilities (eg, impaired vision, motor deficits, and cognitive dysfunction), design considerations must ensure that accessibility compliance reflects the target user audience and different potential users, including family members and caretakers. Moreover, to maximize acceptability, digital health solutions require input from clinicians.

Developing digital health tools not only implies technological robustness and usability, but also guarantees data privacy. It requires thinking about how the newly collected data will need to be shared with health care professionals and whether the intended use of the technology ethically makes sense. During the long process of creating and validating a digital health application (starting with an idea, followed by its implementation and dissemination in different application markets), many stages must be achieved, and each one has its own particularities and methodologies.

Accordingly, a redefinition of the digital health ambit is needed. While some evaluation models in terms of the maturity of digital health interventions have been proposed [43], they are either very “technology specific” or “hospital oriented.” Moreover, as acknowledged previously [43], none of the identified models can be used as an overarching tool to encompass the wide range of digital tools used in a complex context such as integrated care. Moreover, they highlight the lack of a holistic approach to identify influencing factors.

The maturity grading criteria for digital health explored in this study cover a wide scope of tools and policies that correspond to the abovementioned new model of the comprehensive understanding of digital medicine. Recently, a review was conducted on the use of digital technologies in health care [44], and not surprisingly, it proposed an approach similar to the one proposed in the 4 domains and 3 eHealth contexts (Tables 2 and 3) to assess the different elements of MDSW adoption.

Conclusions

Usability performance was consistently perceived higher by patients than by health care professionals. This can be partly explained by the fact that the technology readiness level of the supporting digital health tools was within the interval 5-6, and health care professionals had to lead with technical issues at the same time than with the inherent complexities of case management.

However, the active participation of health care professionals in the co-design and application of the evaluation protocol contributed to the evolution of the mindset of the health professionals toward the use of digital health tools in routine clinical practice.

The overarching analysis resulted in lessons learnt and recommendations that could contribute to the large-scale adoption of digital health tools.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Details of the digital health interventions.
[DOCX File , 1461 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Details of the premarket analysis of the 4 pilot studies.
[DOCX File , 17 KB-Multimedia Appendix 2]

Multimedia Appendix 3

Details of the postmarket surveillance analysis.
[DOCX File , 152 KB-Multimedia Appendix 3]

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Abbreviations

BfArM: Federal Institute for Drugs and Medical Devices
FDA: Food and Drug Administration
GDPR: General Data Protection Regulation
HCB: Hospital Clinic de Barcelona
HIPAA: Health Insurance Portability and Accountability Act
MAUDE: Manufacturer and User Facility Device Experience
MDR: Medical Device Regulation
MDSW: medical device software
NIV: noninvasive ventilation
NPS: Net Promoter Score
SUS: System Usability Scale

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DISCUSSION

The current "perfect storm" of COVID-19 pandemic is severely affecting in a disproportionate manner the rising number of older and multimorbid population [123]. It has led to a dangerous burden on the healthcare systems, not only in the acute care setting, but mostly, at the ambulatory setting [124,125]. It is no surprise that during the past two years the classical healthcare systems had to evolve to cope with health provision demand in very different settings, generating diverse approaches to healthcare delivery with varying levels of complexity. In the new scenario, communication technologies became a cornerstone to pave the way to integrate varying elements of health and social care away from the hospital or usual doctor's office [126,127].

As is natural with evolving technologies, some of the solutions have not undergone rigorous evaluation and it is not known if they are sustainable in the long term. Moreover, the Collingridge dilemma directly applies to the current pandemic reality in health and social care: early in a new technology's development, uncertainty and minimal evidence about its impact impede policymaking, but once the technology has diffused and harmful effects have become clear, it may be too late to act [128].

But the leading ethos during the current situation has emphasized that above complex referral pathways or policy conundrums, the patient should always be at the center. Only if the patient's needs within a well-defined context are thoroughly evaluated, then the use of properly tested technology can support personalized care in the long term, leading to sustainable healthcare systems, in the face of new and old challenges. Digitally enabled integrated care has thus become even more relevant today and is poised to become a main driver of healthcare change in the post-pandemic world [129,130].

It is of note that despite all the difficulties, most of the systems have learnt to develop enough flexibility to adapt to the current situation, naturally leading or accentuating areas of uncertainty within the integrated model of care. It is in this respect that the concepts worked in this Thesis contribute to the existing knowledge on the evaluation process of a complex clinical intervention such as digitally enabled Integrated Care.

The first uncertain area that we address in the Thesis, refers to the need for comprehensive evaluation of complex interventions from their inception through the usual process of proof of

efficacy, to the more complicated implementation process, proof of effectiveness in the real world, and key performance indicators development for sustainable scalability and transferability. The second issue that we deal with is the need for the (mature) digital transformation of the healthcare systems. Not only from a technical point of view, but from a more systemic change, in terms of i) creation of new professional roles while involving all relevant actors to create and sustain changes in management and regulatory policies, ii) using advanced tools to supply healthcare providers with fast and meaningful clinical solutions at individual and population level and iii) to provide patients and careers with tools leading to empowerment and preventive strategies, safeguarding privacy and user safety.

By addressing the first item, we have given form to a comprehensive framework built from existing evaluation tools that have the potential be become adaptable to different contexts and research questions in real-life settings. The main findings from the evaluation framework and co-creation studies are fourfold: i) the generation of health value in digitally enabled integrated care models can be assessed qualitatively and quantitatively within the same timeframe of any given project. The evaluation tools proposed by us are clearly defined and articulated at the planning phases and flexibility during the implementation phases is also acknowledged; ii) such flexibility is addressed using robust plan-do-study-act (PDSA) iterations where multidisciplinary teams have to be involved, including co-creation schemes that incorporate all involved stakeholders; iii) by using PDSA and co-creation procedures during the implementation, the gap between efficacy and effectiveness of the intervention in real life is successfully addressed; and, iv) after using the proposed framework alongside PDSA and co-creation techniques, the evaluation and implementation of a complex intervention can be transferred and compared to other settings by using standardized key performance indicators derived from the comprehensive assessment.

It is of note that the use of the three main broad concepts explored in our studies, namely: i) the intervention outcomes, ii) the maturity of the ecosystem where the intervention is applied and, iii) the implementation strategies used within the defined ecosystem, align with the different EU funded projects on Integrated Care. CORDIS, TeNDER and PROCare4Life are centered on neurodegenerative diseases. In our case, frail elderly patients were the main focus in Badalona Serveis Assistencials (BSA) which was a site that formed part of our proposed comprehensive assessment. Recent reports in this setting demonstrate effectiveness of digitally enable integrated care approach [131–133]. Other EU funded projects have generated evidence in areas of chronicity and healthy aging (CHRODIS-JA) or scalability of integrated care (ACT@Scale,

SCIROCCO). The prehabilitation service deployed in the Area Integral de Salut Barcelona Esquerra (AISBE) seeks the promotion of healthy lifestyles (among others) thus forming part of the evaluation framework and co-creation experiences. It also took part in ACT@Scale and since then, this Catalan program has demonstrated effectiveness [134–136]. Finally, part of the works presented in this Thesis were done within the EU projects SELFIE and CONNECARE which looked at two different angles of integrated care: novel modalities of health delivery assessment and enhanced digital support, respectively. As such we consider that by coordinating the EU projects with the Thesis main lessons, we have managed to add practicalities to the current developments on Integrated Care in Europe.

The second item addressed in the Thesis, the digital transformation of healthcare, is already a reality [137–139]. In some EU initiatives the use of digital tools in integrated care is explicit. But their assessment within the clinical care pathways, the healthcare system or/and the political, social, or economic background of the region(s) involved in the pilots has suffered from the lack of standardized ways to enable successful scaling and transferability. By using maturity grading criteria, we have been able to elucidate manifold relevant findings regarding the digital transformation in several European countries. Firstly, the implementation of digital tools varies widely in different countries, lending to heterogeneous uptake of the technologies involved in digital care. Secondly, a lack of policies defining and supporting the digital transformation has hampered the large-scale implementation in many sites. Notwithstanding these barriers, many countries have in place robust health data analytics and assessment programs. Most of the works presented here took place before the COVID-19 pandemic. Since then, some of the barriers identified by us have been overcome, such as the use of the telephone as the main teleconsultation tool or lack of willingness by regulatory or policy stakeholders. We believe that the robust capacity for digital health assessment and follow-up identified by us, smoothed the rapid and sometimes chaotic transition from “classic” care to digitally enabled care during the pandemic. In our opinion, some of our findings are now even more relevant that a few years ago, given this rapid and unexpected transformation. Namely, i) the realization that digital health care should move beyond telemedicine. The use of adaptive case management and risk assessment will help guide clinical decision making and simplify workflows when the patient is not physically present but a trove of his/her data (e.g., wearables, EMR, -omics) is easily accessible and not siloed; ii) the use of patient-reported outcomes (PROMS) and patient reported experience measures (PREMS) have to be taken into consideration within the digital tools including apps, in order to help guide quadruple aims outcomes and quality control process; iii) the use of simple assessment metrics such as usability and acceptability help us learn about the

uptake of the intended technology among patients and healthcare providers, as intended by tech developers; iv) the generation and acceptance of new roles and change management (e.g. tech savvy nurse case manager) is a consequence of successful adoption and implementation of digitally enabled integrated care; and, v) regulatory frameworks across countries and agencies should be understood and adapted in order to make technology accessible while safeguarding individual privacy.

The two concepts covered in the Thesis strive to include mechanisms to elucidate facilitators and barriers in real-life scenarios. The goal is to delineate practical actions to overcome implementation challenges and boost successful initiatives to consolidate the digital transformation, while maintaining the quality of the overall clinical intervention.

Even though the Thesis focuses only on Integrated Care as use case model for complex healthcare service, we are confident that our proposed approach, in terms of service evaluation and ICT assessment contributes to scenarios different from integrated care. Examples such as single acute diseases, or organ transplants, can benefit from the same line of action. Likewise, a health care system who is not considering an integrated care approach but strive to deliver care using clinical pathways that rely on predictive risk stratification and adaptive case management should also benefit from the use of standardized ICT co-creation and assessment in the long term.

The works presented in the Thesis delineate future challenges in some key areas. Firstly, we present a model from where the next generation medicine can draw insights. Data collection in a standardized way, from different sources such as patient reported outcomes, wearables, EMRs, structured and unstructured input from medical or wellness applications alongside -omics data can help the development of novel research methodologies using real-life data. This will contribute to overcome the efficacy-effectiveness gap and to lead the way for more personalized medicine. Secondly, this new approach can help reshape privacy and regulatory issues that, although necessary, should strive for a balance between data protection and the elimination of data silos. Lastly, this new paradigm opens a door for a change in clinical thinking were signs and symptoms are just a part of a broader approach integrating well defined clinical algorithms based on risk prediction and artificial intelligence embedded in diagnostic decisions and treatments based not only on RCTs, but in real-life data previously enriched by machine learning research results.

A comprehensive evaluation framework

While clear consensus and methodologies exist to evaluate effects of drugs and conventional clinical interventions, the same is not yet well defined for clinical programs where complex or integrated care interventions are developed and deployed. To prove clinical effectiveness is deeply embedded in the medical community. But, so far using classical tools to prove value generation in integrated care has been elusive, in part due to the complexity of the care management programs, the differing target populations and the contexts where they are conceived.

The Medical Research Council guidance for developing and evaluating complex interventions published in 2008 [140] gave an initial approach to tackle the problem. Since then, it has been recognized that it lacked enough granularity to carry out specific evaluations, although some papers have tried to add specific recommendations to make it a practical guideline [141]. Moreover, it covered mainly the implementation process' aspects of the intervention. Therefore, our main aim in exploring applicability of a comprehensive framework for Integrated Care derived from the fundamental question: does this care management program works?

And since the aim was to present a useful framework for a real-world scenario, the work was based on the Catalan experience and fully aligned with regional implementation [142,143] plans for digitally supported Integrated Care. The evolution of the framework built upon previous experiences on Integrated Care, where randomized controlled trials shed light on the efficacy of such interventions [105,107,108]. But, on further analysis, effectiveness was not demonstrated [84,110], prompting the need for the evaluation framework presented in the Thesis. The analysis on this regional Integrated Care experiences led to the identification of key modulating factors such as change management, the need of digital integration on the clinical workflows and the proper use of risk stratification for service selection. These reports used classical clinical outcomes (i.e., mortality, readmissions, etc.) alongside patient-reported outcomes and technology assessment tools (for example the MAST), paving our way to harmonize the needed elements to generate the framework explored in the first paper of the thesis.

As mentioned earlier, the framework proposed in the Thesis is based on three main elements: i) intervention outcomes, ii) ecosystem maturity and, iii) implementation strategies, which all should lead to identification of barriers, enablers, quality control measures and ultimately KPIs

for long term sustainability.

Within each of the framework three elements, several existing, or novel tools can be adapted according to user preference, experience with their use or context needs. In our case we explored well regarded tools, but it is important to discuss here some caveats in order to help guide future adopters of the framework.

Firstly, we chose the Quadruple Aim approach [25,26] to evaluate the intervention outcomes. While the first three aims (outcomes, patient experience and costs) are straightforward and measurable, the fourth aim, healthcare provider well-being, can be considered more troublesome. Physician burnout has the potential to reduce emotional energy for job demands, emotional detachment from one's job and presumably patients, and a reduced sense of successfully achieving work-related goals [144]. While it is tempting to attribute a direct negative impact on the (un)successful achievement of the Triple Aim on burned out healthcare workers, so far there is no conclusive evidence in that direction. A well conducted systematic review on physician burnout and patient outcomes showed some very interesting results [145]. First of all, it showed that the effect of burnout on patient outcomes may include moderators and/or mediators. Moderators such as staff support, or organizational support could influence observed relationships between burnout and patient outcomes. Another intriguing finding was that burnout did negatively affect patient satisfaction as a whole, but on examining more closely, burnout did not affect (and even has positive influence) on certain attributes of the physician-patient encounter. This may suggest that organizational process or structures (such as care co-ordination) can affect both the patients and the healthcare workers. Another relevant finding was that burn-out healthcare workers communicate poorly with the patients, affecting patient-centered outcomes. We can infer that the relationships between the different components of the Quadruple Aim are complex and affect one and other, making it a holistic tool suitable for a comprehensive evaluation framework, although it should be acknowledged that many interactions within the different "aims" cannot be individually analyzed to draw conclusion for very specific aspects in an Integrated Care system.

Secondly, the decision to use the CFIR [28,29] was based on the potential to address a wide range of implementation issues during planning, evaluation and follow-up. Nonetheless, it is well recognized that the CFIR can be cumbersome, vague in some definitions, difficult to use in complex interventions and many of its elements can vary by time, location and organizational process [28,29]. Thus, limiting its usefulness as a comparison tool in differing contexts. On this

Thesis we suggest that using the CFIR as part of a more comprehensive framework, and not as a standalone tool may help overcome some of its limitations. The main lesson learnt relates to the need and capacity of the CFIR to undergo changes and adaptations according to the specific evaluation needs for any given Integrated Care intervention. Accordingly, a recent report sought to adapt the CFIR (as a standalone tool) for the evaluation of a complex intervention in primary care [146]. By tailoring and respecifying construct definitions, they managed to produce a "patient-centered" evaluation and thus creating insights on important drivers such as leadership changes.

In terms of feasibility, we believe that the framework is flexible enough to be adapted in different contexts and to diverse populations. Also, the tools proposed for the framework, are mature and have been used as standalone evaluation instruments, thus we do not foresee major compatibility issued in adapting them to users need. Since the writing of some of the papers in the Thesis, recent examples have proven the usefulness of the quadruple aim approach in evaluating eHealth interventions in public health services. Liddy et. al. demonstrated in Canada that using surveys, interviews, usage and administrative data the different components of the quadruple aim can be measured in the setting of health technology implementation, which is in line with the core concepts proposed in the current Thesis [147,148].

Moving beyond the cited past experiences on integrated care evaluation in Catalonia [84,110] three recent (unpublished) reports have adopted the comprehensive evaluation framework proposed in this current Thesis (**Figure 5**) Those experiences have taken part in the context of the Catalan Health System and within the same provider. Although the studies evaluated Integrated Care services, they broadly differ in the intervention, population and timelines, while adapting our evaluation framework to their context and objectives.

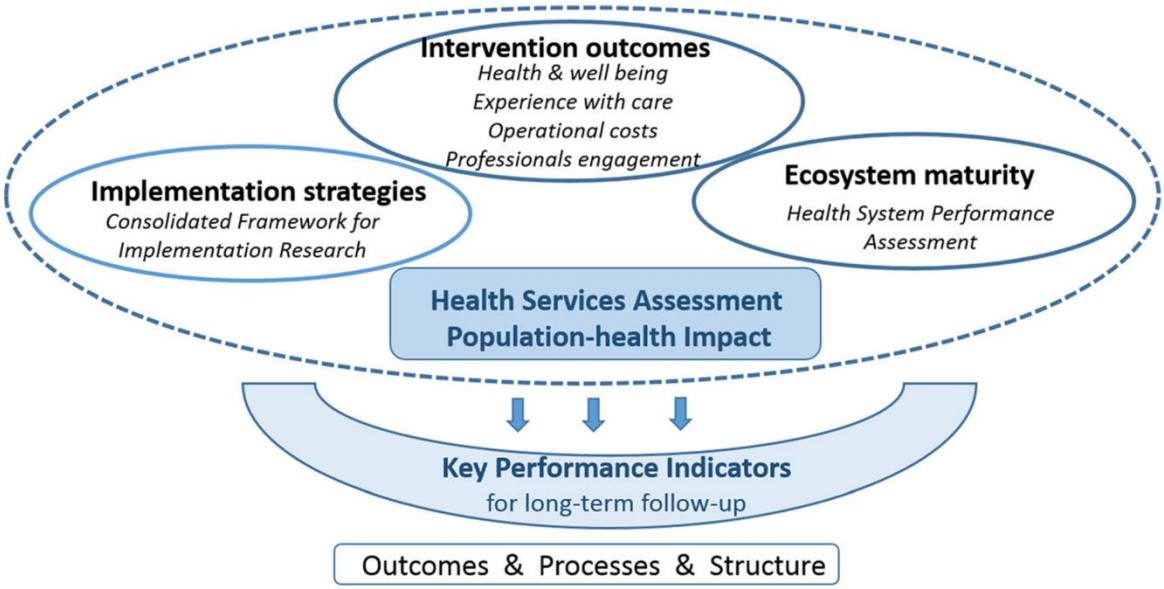

Figure 5. The Evaluation Framework for Digitally Enabled Integrated Care.
Well-defined assessment tools are used within every one of the evaluation areas depicted here. The framework has been shown to flexible enough to allow for adaptation in different real-life settings while being capable of generating key performance indicators to support value-based health services.

The first two studies sought value generation in a hospital avoidance Integrated Care service. Hospital at home had already undergone a real-world pragmatic evaluation during a ten-year period, showing that the service generates value by reducing hospital stay days (a classical clinical outcome) and stakeholders' satisfaction (in line with quadruple aim objectives) [109]. Building on that, the two complementary studies (one prospective, the other one retrospective) used classical outcomes such as mortality, readmissions, and cost-consequence analysis. Novel tools such as patient-reported outcomes and multi-criteria decision analysis (MCDA) [70] were introduced as a way to measure quadruple aim outcomes in a similar way to the Canadian experience [147,148], therefore proving to be a flexible and adaptable framework in light of new developments.

Using this framework, the studies showed a reduction in costs benefiting the Integrated Care intervention. The main driver of this cost reduction was in the form of innovation and change management, in turn affecting (positively) patient satisfaction. This is a clear example on the potential of the framework to clearly identify key barriers and enablers that were previously suggested but not completely demonstrated [110].

The third study explored the implementation outcomes of a complex prehabilitation program (which included several interventions) for patients undergoing major surgery. Previously, the efficacy and cost-effectiveness of prehabilitation were demonstrated [134,135]. The real-world

adaptation of our framework in this Integrated Care scenario showed that while only a third of the enrolled patients completed the prehabilitation program, their health-related outcomes were significantly better than the control group, thus generating (cost) efficiencies, alongside patient and provider satisfaction. Among the evaluation tools was the CFIR, which helped unveil barriers as to why only a third of patients completed the program, proposing future intervention areas in order to improve adherence to the program. Alongside the use of quantitative outcomes, the qualitative approach helped refine key performance indicators for future follow-up. Also, this constitutes a clear example on how the framework can help foster personalized medicine by helping identify the correct population that will mostly benefit from a well-defined clinical care pathway, thus giving real sense and practicality to risk stratification at population health level.

It is of note that the CFIR used by this study has recently been updated to include several important addendums [149]. Interestingly, the two main points underlined by Damschroder et. al. [149] reinforces our message on how a complex intervention should be evaluated. Namely:

i) The two different main phases of the implementation: first, the planning and initial execution phase (as described by Damschroder et. al. [149] as implementability and/or sustainability) and the more stable phase of an already implemented or sustained healthcare intervention. The distinction is important in terms of anticipated and actual implementation outcomes. This broad concept aligns with our proposed use of co-creation techniques (PDSA, SWOT analysis) and use of KPIs, which will be discussed later.

ii) Innovation outcomes are introduced as an integral part for the evaluation. The outcomes impact the recipients (e.g., patients, caregivers), deliverers (e.g., healthcare professionals) and key decision-makers. As we see, all the stakeholders are taken on account therefore emphasizing the need for coherent interplay between the quadruple aim and context maturity for a successful implementation of new interventions such as digital health.

Finally, some commonalities can be found in the Catalan studies, which, as mentioned early, concern to the planning and development phases of a complex intervention. As show in this Thesis, the use of co-creation and quality control (using PDSA) lead to value generation as well as patient and provider acceptance of the complex interventions. In this sense, patient empowerment may lead to value co-creation behaviors, such as the stimulation to participate in physical activity outside the hospital and/or enhance responsibility for chronic management for multimorbidity among others. Ultimately, the proposed framework should lead to generate

drivers for co-creation, patient engagement and effective communication between stakeholders. But implementers of qualitive methods (such as co-creation) should be aware that without coupling them with clear and well-defined quantitative methods (such as clinical outcomes based on previous RCTs) may lead to incomplete identification of key implementation enablers.

One of the main challenges of using the PDSA method is that the tool mainly results in a learning process about the intervention to be implemented or scaled up if not used as a rigid and standalone instrument. It has the capacity to generate evidence of effectiveness if during its implementation is combined with other instruments such as SWOT [150,151]. Therefore, it makes sense to use it as part of a well-designed evaluation framework as was demonstrated by the previous examples in prehabilitation and hospital at home services, as well as during the current implementation at JADECARE.

It is in this respect, that the SWOT analysis should complement the PDSA. This kind of analysis, derived from the marketing industry which is based on the listing of strengths, weaknesses, opportunities, and threats applies in our case to the development, deployment, implementation and scaling up of integrated care programs. As discussed by Minsky et. al. [152], the proper way to apply SWOT analysis is by firstly take into account external or environmental conditions (threats and opportunities) and then integrate internal conditions (strengths and weaknesses) into the plot. In this way, the PDSA analysis, alongside the implementation tools used (e.g., CFIR) are first put into relevant external context, which is crucial for scaling up and transferability. We see how the different elements of the proposed evaluation framework in this Thesis should interact with one another, not generating redundancies but synergies.

Within the current perspective for the evaluation of digitally enabled Integrated Care, the practicality of a harmonized framework is reflected by the EU joint action project JADECARE. This project is already implementing many of the concepts developed and discussed in the current Thesis. As presented in the Introduction, and since JADECARE constitutes a pragmatic approach to the scaling up of Integrated Care practices we believe that the framework presented here must become one of the main tools used for assessment before, during and after implementation of the original good clinical practices by the next adopters.

The methodology adopted by JADECARE is in full accordance with the principles set by this Thesis. Namely, i) a framework used to evaluate digitally enabled Integrated Care; ii) the evaluation of effectiveness in terms of clinical and process outcomes; iii) the establishment of a

mechanism of continuous quality assurance and co-creation from the pre-implementation up to the post-implementation phases, and iv) the generation of key performance indicators to allow for effectiveness follow-up upon transfer of clinical practices between different geographical regions.

Not only the Thesis contributes on evaluating the roll-out operation and implementation during JADECARE, but also sets a standardized form to report on the implementation process and transferability, making it a suitable tool for comparability. Recommendations derived from our experience during the development of the framework include the use of simple metrics from data sources in order to derive population-based outcomes; to employ simple and brief questionnaires or surveys for patient and provider experience (we also propose the use of artificial intelligence-powered questionnaires [153]); to adapt novel costs analysis based on stakeholders differential perspectives on the same program (e.g. discrete choice experiments and MCDA [70,154]); to integrate all relevant stakeholders during the co-creation and PDSA phases, creating focus core groups, such as a technical group with a few key clinicians or a clinical group with a few key administrators and so on; and finally to consider the innovation process as an opportunity to generate new professional roles and lead a change in management of the classical clinical pathways.

Key Points
• Initial efficacy studies on specific integrated care services triggered further analyses that contributed to generate recommendations for building the comprehensive evaluation framework proposed in the current PhD Thesis to be applied in real-life settings. • Such evaluation framework aims to shed light on facilitators and barriers for large scale adoption and transferability of complex clinical interventions. The results of the evaluation framework feed Task 2 (create matrices of change) out of the five tasks of the Implementation Mapping Process *(Fernandez ME et al. (2019) Front. Public Health 7:209. doi: 10.3389/fpubh.2019.00209).* • The use of PDSA cycles and SWOT analysis is critical for the intended stakeholders to efficiently designing and implement innovative care pathways, alongside usable and acceptable digital tools to support value-based Integrated Care services. • Through the flexible use of the proposed evaluation framework during the deployment process of specific integrated care services, the impact of clinical outcomes, implementation strategies and ecosystem maturity lead to the identification of KPIs which can be used in user-profiled dashboards for service monitoring after sustainable adoption. • After completion of this Thesis, real life studies in prehabilitation and hospital at home have demonstrated the value of using framework-derived dashboards to highlight costs

containment while preserving service quality alongside the pivotal role of co-creation in order to deliver efficient care to the right group of patients.

The digital health transformation in Integrated Care

During the last decades, the digital transformation has slowly evolved leading to a wide array of concepts usually encompassed by the term "digital health". Areas such as telemedicine, mobile health & wearables, information technology management & EMRs, medical imaging, artificial intelligence and machine learning are part of the digital revolution in medicine. But research and clinical application derived from many of these areas have advanced separately from one and other leading to heterogeneous implementation thus generating barriers for comparability.

A good example is a recent published article by Marques et. al. [155] where the authors try to systematically review the digital transformation in healthcare. The paper reflects the difficulty on making a coherent narrative on the digital transformation. At the end the authors present several papers as separate experiences.

Nonetheless, valuable information can be inferred from this extensive review, namely: i) in the field of information technology and EMRs, there has been a clear shift from implementing simple programs for data input to more sophisticated systems were interoperability between different healthcare tiers (e.g. hospital departments, community and hospital providers, etc.) has become the focus in recent years; ii) mobile health began before the widespread use of mobile phones, basically using personal digital assistants as means to receive information and rapidly respond accordingly, or to facilitate literature search "on-the-go". With the advent and generalization of mobile phones at first and then wearables, the mobile health area has expanded, and medical staff are not the only ones using it, but, in many cases, patients and healthy populations are adopting it as means for empowerment, wellness and healthy lifestyle promotion. iii) telemedicine has grown from stand-alone and disease-centered applications to a broader concept (in part fueled by the COVID-19 pandemic) of patient-centered services that are part of well-defined care pathways. According to a recent digital health consumer survey, the use of digital tools by patients such as e-prescriptions, follow-up or preventive services messaging, managing doctors' appointments online, using telemonitoring devices for recording own health indicators or using video-chat with providers has greatly increased from 2016 to 2019 [156].

Last but not least, it is in our opinion that the most valuable lesson from the evolution of digital health in the last few years is that the boundaries between the above-mentioned digital territories are disappearing and moving forward to a more comprehensive digital medicine. Examples such as the use of artificial intelligence and machine learning within EMRs for risk prediction, commercialization of mobile apps on different platforms (android, iOS) to deliver behavioral therapies (e.g., digital cognitive behavioral therapy for insomnia is already recommended in clinical practice [157]) or using big data on pharmacogenetics studies are only a small sample of the redefinition of digital health.

Accordingly, and in line with our proposed scheme for the assessment of the maturity of digital health, a redefinition of the digital health ambits is needed. While some evaluation models in terms of the maturity of the ICT intervention have been proposed (as reviewed in [158]), they are either very "technology specific" or "hospital oriented". And, as acknowledged in [158], none of the identified models can be used as an overarching tool to encompass the wide range of digital tools used in a complex context such as integrated Care. Moreover, they highlight the lack of a holistic approach to identify influencing factors.

Our proposed maturity grading criteria for digital health covers a wide scope of tools and policies which corresponds to the abovementioned new model of comprehensive understanding of digital medicine. Lately a paper by Senbekov [159] has reviewed the use of digital technologies in healthcare, and not surprisingly, they propose a similar way to the one proposed in the current Thesis to understand the coverage of the different elements of digital health.

A manner of adapting our proposed maturity grading to the everyday reality to make it more practical and comparable among sites is to change focus from the tools to the environment where they are applied, namely,

i) *At the hospital and at primary care level,* the EMRs are the basis for big data collection to generate clinical prediction tools which will in turn feed EMRs and mobile devices used by healthcare providers. Also, artificial intelligence and machine learning will support areas such as diagnostic imaging and adaptive case management to deliver more personalized medicine. Interoperability and data integration must be planned ahead during the implementation of those systems.

ii) *The pharma industry* will also use big data and will benefit from "virtual clinical trials" where patients are telematically recruited and followed, using mobile devices and wearables for vitals monitoring and recording. Also, drug delivery and logistics

should benefit from the use of patient data integration. Finally, cost effectiveness in real life studies will benefit from claims data use at large scale.

iii) *The laboratory & research community* will use biomarkers data alongside -omics and clinical data derived from EMRs to produce fast and reliable results that can feed the pharma industry for drug development or repurposing.

iv) At *the ambulatory setting* telemedicine will help close the gap in rural communities or secluded frameworks such as prisons or disaster areas. Also, the integration with other horizontal or vertical settings, such as the hospital or social care services will benefit from adaptive case management built on machine learning protocols and risk prediction rules.

v) *Medical education* will gain from the use of distance learning and the flexibilization of processes using augmented reality and artificial intelligence for clinical problem solving and simulation training.

It is of note that the above-mentioned scheme falls in line with the proposed Blueprint on Digital Transformation on Health and Care and its proposed roadmap [86]. Arguably, one of the central aspects of the Blueprint is the focus on interoperability and data sharing. Without it, all the information from the digital tools is not actionable, stays in siloes and undercut the transformative power of the digital era. The early adoption of the EMRs in the United States is a clear example on how (justified) concerns on privacy alongside private interests on network referrals led to a trove of independent EMRs, thus alienating healthcare providers, leading to burnout and generating siloed information.

Interoperability should occur in many of the maturity categories proposed in our model. The Blueprint shed light on this, firstly, all data collected from the everyday digital tools should be normalized using a common coding scheme such as LOINC, ICD or SNOMED. Secondly, the use of healthcare communication standards such as HL7, DICOM, FHIR is essential to harmonize IT systems across providers.

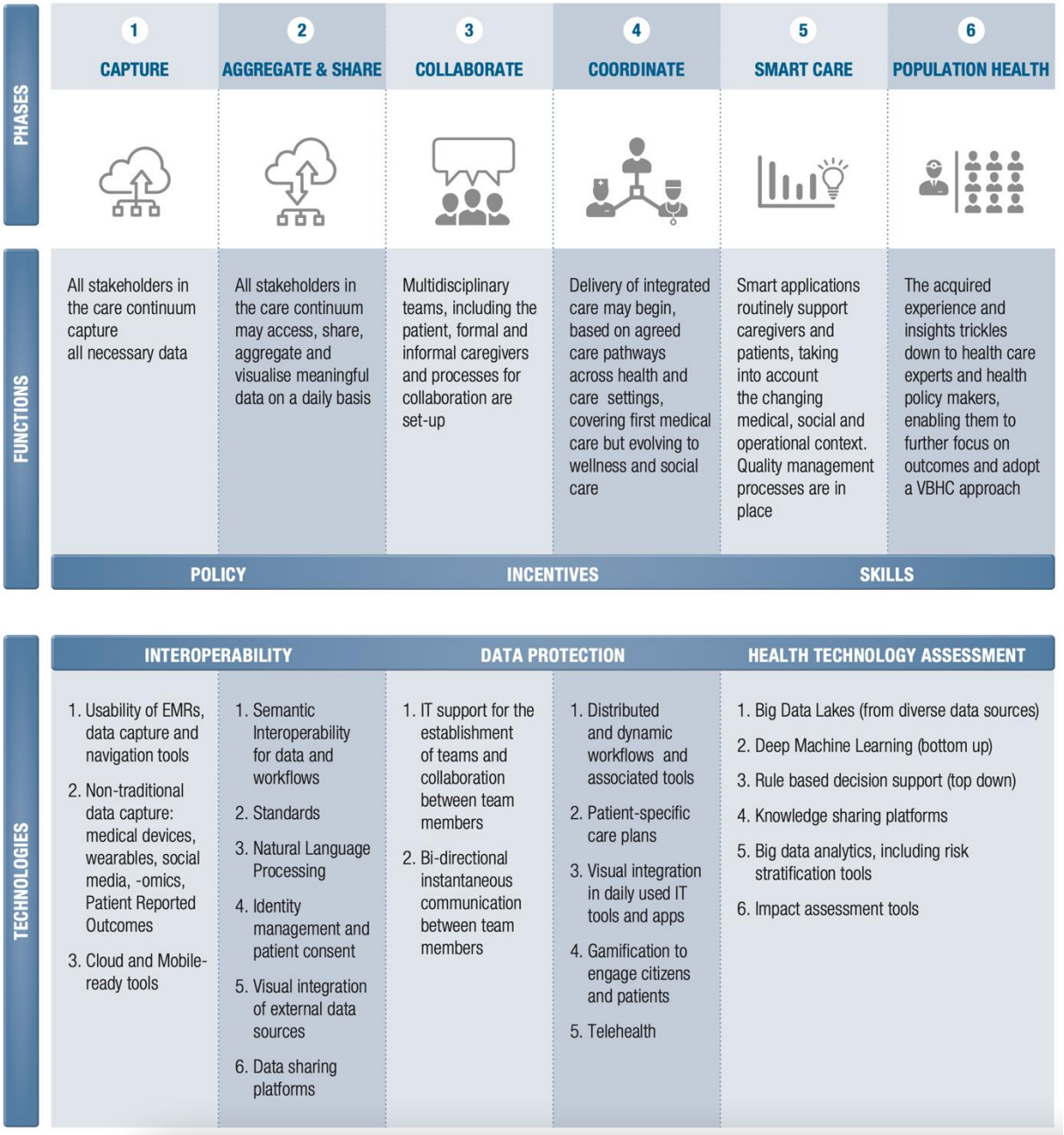

Figure 6. The Digital Health Roadmap to Support Integrated Care.
The building blocks, from data collection up to big data analysis using machine learning, are depicted alongside the proposed changes in management to support the transformation. Interoperability, data protection and health technology assessment are outlined as necessary technical steps to adopt and sustain the implementation of digital tools in value-based healthcare interventions. The main messages of the thesis are compatible with this roadmap, as described in the text. Taken from [86].

New professional roles within public organizations and private biopharma enterprises may help tackle interoperability issues. Lately one of such figures is becoming prevalent: the Chief Digital Officer. One of the important lessons learn from the fourth study in the Thesis [160] was that the involvement of a specialty nurse with IT knowledge helped solve many end-user problems. The role of the digital officer should focus on interoperability and privacy challenges, and at the development and post-marketing phase of a digital health intervention.

At national level, initiatives such as the 21st Century Cures Act Final Rule (rule 85 FR 25642) in the US directly states the need for interoperability and free patient access to all their electronic health information. It even penalizes institutions not complying with interoperability standards. At European level, the European Health Data Space initiative (to start working during 2025) also seeks to align widespread access to health data irrespective of transnational barriers, while enabling individual citizens better control and use of their own data. It should be noted that such initiatives can foster competition and innovation, since private vendors will strive to make better and easier to use interoperable systems, that if adopted by most institutions create a monetary incentive.

Alongside interoperability comes privacy challenges. Medical apps and devices do not only have to work as intended (safety), but by analyzing huge amounts of data, privacy can be compromised. As previously mentioned, data collection is just the first step on the roadmap for digital transformation, making privacy and regulatory issues an important part of the maturity model proposed by us. A recent analysis and expert opinion from different US centers, Estonia and Mexico has also identified the regulatory and reimbursement issues as barriers for the implementation of digital medicine [161].

In this respect, the recently adopted General Data Protection Regulation (GDPR) constitutes a milestone to tackle privacy challenges. Being a positive step in data collection, processing and protection, the regulation also creates a new role, the Data Protection Officer, showing similarities to interoperability challenges. Nonetheless, the regulation possesses specific challenges in the research arena [162], especially on how patients give consent when biological samples are taken and how data is anonymized, particularly in big datasets, need for data mining, AI building or/and biobanking. One of the proposed digital tools to overcome these issues is the use to block-chain solutions. The unique characteristics of this technology (i.e., decentralization, transparency and anonymity) make it difficult for any user to control or change information, thus having the potential to be used on clinical trials, shared medical records and biobanks [163,164].

As shown by us several similarities exist between the GDPR and its American counterpart, the US Health Insurance Portability and Accountability Act (HIPAA). Nonetheless, a lot of confusion and complexity exists when dealing with the regulatory aspects of medical devices. A current situation exists where consumer devices such as wearables are being marketed as health-promoting aids but in the end, clinicians are faced by patients with troves of data as if

such technology is regarded as medical device, leading to professional and ethical dilemmas. Also, the GDPR implementation has added layers of complexity for data usage at clinical level and for research or innovation endeavors. First of all, it is of note that although the DGPR is a European directive, thus not applying directly to countries outside the EU, it does mandate that any global website having users and/or offering services should comply with it. This situation creates discrepancies between the GDPR and other regulations, such as HIPAA. Thus, anyone seeking to exploit databases (e.g., a clinician using AI on sleep hygiene habits collected by wearables) may have to treat the same datasets in different ways. Secondly, the simple fact where the GDPR is a regulation and not a law, algo generates heterogeneities in its implementation within the EU space. Clearly, challenges on how to anonymize and de-identify data for research purposes have created barriers for the creation of large transnational databases. Notwithstanding, the GDPR has led the way forward at the international level by offering clear rules on how to manage and safeguard health-related data, making every provider (public or private) accountable for the provenance of their data in the daily clinical practice, or for research purposes. When it comes to innovation and/or quality assurance auditing to strengthen healthcare service provision, these same GDPR directives have been more difficult to apply, requiring an individualized case-by-case approach thus helping overcome implementation barriers.

Another area where the clinician is faced with difficult terminology is the technical aspects of the regulatory policies. We showed a clear link between pre-market app development and post-market surveillance in terms of technical failures hindering stakeholder adoption, regardless of usability and acceptability success. Such technical failures can be overcome not only by generating a robust and secure product, but also generating online open access databases (on the likes of clinical registries for single diseases) where FDA/CE approval, date of approval, medical specialty and algorithm details are shared, thus enhancing transparency and collaborative work. Two recent reports from npj Digital Medicine and Lancet Digital Health [165,166] have explored this concept.

After sorting out interoperability and regulatory issues within a mature digital health ecosystem, the next step, and partially resolved issue so far, relates to the capacity and willingness of a given healthcare system to scale-up digital health solutions. Several lessons derived from the works in the current Thesis contribute to solve this unmet need.

Firstly, is that digital tools that are usable and well-accepted among the different stakeholders, have more probability of being successfully adopted generating potential for scalability. We

propose that the success of a digital health tool is dependent on the user's experience with it. Tools that win are those that help stakeholders accomplish better health goals (outcomes) at individual and/or system level. Arguably, usability testing is the preferred way to ensure that digital health tools deliver value to its stakeholders ("people get what they pay for").

Hand-in-hand with the usability, is the acceptability of the digital health tool. The usability and acceptability of a digital health tool are seen as direct consequence of a patient-centered vision: if the patient (or caregiver) cannot use an app as intended, then the system holds no value for his/her needs. This is critical when the intended user population has chronic and sometimes disabling diseases such as hearing/visual impairment, neurological or orthopedic hand coordination problems or general cognitive decline, among others, or must use health-supporting machines such as non-invasive positive pressure ventilators. It is also crucial to embed a useable digital tool within the care pathway and not as a separate element. A natural flow within EMRs where the clinician doesn't have to "jump" from one app to another helps reduce adoption resistance. Also, if the patients see the tool embedded and smoothly working within the healthcare provider web portal, they will fell more assured to use it, boosting their engagement.

Secondly, is that a multidisciplinary co-creation team and the use of quality control processes (i.e., PDSA co-design cycles) lends the digital tool flexibility to be adapted in different contexts and changing environments. The co-creation process where several stakeholders are involved assures that the digital tool answer different needs while overcoming well-known barriers at user level. Patients and health professionals can feel a lack of trust and even a sense of a threat from the new technologies. Professionals can even feel that the new technology increases the workload without a clear benefit. By using co-creation processes and technical logbooks during implementation, alongside users' reassurance by a technology-capable case manager (a new role highlighted by us) we have demonstrated a good acceptance a digital tool supporting an integrated care intervention.

A recent expert commentary [167] on enablers and barriers for scaling-up digital health innovations identified and grouped several themes recognized by the authors as contributing to the ongoing debate of scalability. Many of these themes coincide with the elements and consideration made by us in the previous paragraphs. The authors organize the enablers and barriers in overarching, macro, meso and micro groups. Coinciding with the scheme developed by in the current Thesis, at the overarching level they identify interdisciplinary co-creation, siloed knowledge, care management and the gap between tech developers and health care

practice as main factors influencing scale-up. At the macro level they recognize legal and regulatory barriers, including safety issues. At the meso level, interoperability issues and change in management are proposed as enablers. Finally, at micro level the negative perception by health care professional (lack of trust and motivation, addition a workload and perceived threats from health innovations) can hinder adoption and scaling-up.

Lately, a natural development from the lessons learnt from this Thesis took form in creation of a digital platform for integrated care management based on collaborative work and digital support (www.healthcircuit.es). Health Circuit was built using co-creation and co-design processes where clinicians, IT experts and digital health innovators were part of the team [136]. The platform features instantaneous bidirectional communication with patients, the ability to incorporate PROMs and PREMs for assessment and follow-up while creating customizable and personalized care pathways supported by adaptive case management leading to digital prescription of non-pharmacological interventions and recommendations for behavioral change, self-management, and patient empowerment. Thus, the digital platform follows one of the main principles highlighted through the Thesis, that is, digitally enabled Integrated Care should be patient-centered and not disease oriented to improve patient outcomes, improve sustainability, and generate value in health care.

Key Points
• The maturity level of digital transformation in Europe is heterogeneous. • Digital technologies act as facilitators for deployment and adoption of Integrated Care services. • Our studies revealed substantial challenges for mature implementation of digital tools embedded into integrated care services, in terms of: i) interoperability with health information systems, ii) change management, and iii) health risk assessment for service selection. • The use-case of home-based non-invasive ventilation where adaptative case management was explored, helped to delineate facilitators to overcome the challenges mentioned above. • The knowledge gained, through the co-creation process undertaken in the PhD Thesis, on digital support to various Integrated Care services, as well as the examination of current regulatory frameworks, enables the formulation of recommendations for pre- and post-marked evaluation of digital health products. • E-health products regulation is highly dependent on the products' intended function. Thus, the thorough understanding on how the digital solution works should naturally lead to proper clinical study design to prove effectiveness in real life.

	TELEHEALTH	INTEGRATED CARE	DIGITAL THERAPEUTICS
DEFINITION	Technologies, platforms, and systems that engage patients for lifestyle, wellness, and health-related purposes; capture, store or transmit health data; and/or support life science and clinical operations without suggesting specific treatments.	Digitally supported Integrated Care includes evidence-based software and/or hardware products that measure and/or intervene in the service of human health.	Digital therapeutic (DTx) products deliver evidence-based therapeutic interventions to prevent, manage, or treat a medical disorder or disease.
CLINICAL EVIDENCE	Typically, do not require clinical evidence.	Clinical evidence is required.	Clinical evidence and real-world outcomes are required for all DTx products.
REGULATORY OVERSIGHT	These products do not meet the regulatory definition of a medical device software (MDSW*) and do not require regulatory oversight.	Require clearance or approval. Products used as a tool to develop other drugs, devices, or medical products require regulatory acceptance by the appropriate review division.	DTx products must be reviewed and cleared or certified by regulatory bodies as required to support product claims of risk, efficacy, and intended use.
EXAMPLES	**Data & information capture, storage, and display** - Lifestyle apps - Nutrition apps - Medication reminder apps - Scheduling apps - Online repositories - Personal health records - Patient portals **Data & information transmission** - Telemedicine virtual visits - Remote care programs that do not include remote monitoring - Decision support software that: • presents information for independent clinician review • Does not make recommendations that the user could not find through other channels	**Measurement products** - Digital diagnostics tools - Digital biomarkers tools - Patient Reported Outcomes / Experience tools - Remote patient monitoring - Decision support software that: • Relies on data inputs from medical imaging or in vitro diagnostic devices • Process or analyze this information without clinician input **Measurement & intervention products** - Digital companion component integrated with either a drug, a device, or a medical intervention - Digital products that measure and intervene without human intervention (e.g., pacemaker, CPAP, etc.)	**Software that delivers a therapeutic Intervention, including:** - Treating a disease - Managing a disease - Improving a health function **Core principles:** - Conduct clinical trials and publish results - Employ design, manufacture, and quality best practices - Ensure end user engagement - Implement privacy and security protections - Apply product deployment and maintenance best practices - Undergo applicable regulatory reviews - Make appropriate claims - Utilize real world outcomes

* MDSW: Software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the Medical Devices Regulation (MDR) or per Section 201(h) of the Food, Drug, and Cosmetic Act.

Figure 7. e-Health Overarching Scheme.

As reported, digital health systems have many different purposes and functions. End users, clinicians, and payers should understand these differences and know what to expect from each product in terms of function, clinical evidence, and regulatory oversight. The thesis proposes three well-defined eHealth strategies depicted in the table below. This categorization is based on products' primary mechanism of action at the functional level and should be updated regularly to reflect the quickly evolving eHealth regulatory framework.

Personalized healthcare on the cross-roads: Integrated Care meets Systems Medicine

Integrated Care and Systems Medicine share many commonalities at the individual level (i.e., patient-centered care) and at population health level. Although their current practical approach tackling these areas differs, we believe that some key future developments derived from the concepts explored during the current Thesis will help overcome challenges for the implementation of functioning Systems Medicine within an Integrated Care scenario.

Both areas seek to address the practice of medicine in a holistic way where the understanding of disease mechanisms at molecular, cellular, and physiological level leads to targeted treatments for similar individuals, each in his/her own context and circumstances, never being exactly the same between two patients.

The following determinants can be seen as key factors on how integrated care and systems medicine are synergistic: i) preventive services, ii) citizen empowerment, iii) services optimization and iv) patient-centered treatment. As we see, these determinants cover the whole spectrum from a healthy to a physiologically altered state. As such, the role of the digitally enabled Integrated Care will help narrow the gap between the theory and practical implementation of computational models [168,169] for i) risk prediction leading to tailored preventive strategies; ii) harnessing the power of telemedicine and wearables to engage people using behavioral interventions, leading to empowerment; iii) using huge databases (clinical, claims, etc.) to feed data analytics in order to improve clinical services while containing costs, and; iv) generating -omics tailored approaches to different kind of patients with the same disease. The clinician can offer them targeted therapies while taking on account their clinical and social risk factors that modulate future clinical decisions and transitional care. The ultimate goal is to offer every individual the right healthcare strategy at the right time.

By articulating complex clinical and social scenarios with Systems Medicine the “next generation medicine” (**Figure 1**) have the real potential to generate value-based care. From -omics applied research and into stakeholders’ direct intervention on the clinical process, the integration of community and specialized services at tertiary hospital (vertical integration) and different healthcare sectors (horizontal integration) should lead to more efficient communication and continuity of care. The use of mature technologies which were co-created at early development phases, alongside the capacity of the medical and regulatory establishment to

generate comprehensive evaluation frameworks and long-term monitoring KPIs will allow for more sustainable healthcare systems. In the long term, a real "health fellowship" is forged where prevention, empowerment and personalized services become the new norm.

Beginning with preventive service strategies, the classical medicine paradigm is based on a series of "one size fits all" approach (e.g., chest CT for long-standing present and past smokers). Although based on a firm evidence base, many of these strategies leads to false negative and false positive results, resulting in dangerous reassurance or unnecessary invasive procedures. Therefore, the importance, and the call for, powerful risk prediction tools alongside well-defined biological traits to create coherent clusters of individuals which can benefit from tailored preventive strategies. In this sense, technologies such as artificial intelligence have the potential to be integrated within well-defined clinical pathways that have been previously proven to be effective and efficient in real life. Thus, having the potential to be implemented at wide scale by using evaluation strategies such as the ones described by the current Thesis. In turn this must create the amount of data necessary to feed technologies needed to better stratify the population by risk, prognosis or potential responders to defined therapies [170]. Following the initial example, -omics, social and clinical data from EMRs of a past smoker can be combined with artificial intelligence analysis of chest CT images in order to determine the present and future risk of developing lung cancer, alongside the best course of action in case an abnormality is noted. Predictive risk analysis is therefore a step forward from simple risk stratification for preventive purposes.

The use of predictive risk analysis, which in part is feed by data generated by the individual (via wearables, web portals, health apps, etc.) should empower individuals to self-manage their own health and control risk factors (e.g., sedentarism) alongside the spectrum from full health to a disease state. While the vast majority of the population will need simple interventions such as proactive encouragement and behavioral change, the predictive risk analysis will also generate intermediate and high-risk groups where adaptive case management, clinical decision support systems or more intensive interventions must lead to better population health.

By providing a clear picture of the population by means of predictive risk analysis, the combination of Integrated Care and Systems Medicine will help organizations manage their resources and personnel. A learning health system that uses data lakes feeding artificial intelligence can help identify relevant outcomes and/or KPIs that in turn feed the predictive risk model [171,172]. In this way the clinical services can contain costs and increase patient

satisfaction (e.g., early interventions to reduce emergency room visits). It should be noted that this scheme is fully compliant with the Triple/Quadruple Aim approach.

Finally, some strategies may be proposed to achieve the mentioned change in paradigm, namely i) Sample collection should be done with ease: biological samples such as blood, urine or saliva, or usable apps alongside friendly wearables; ii) Research cohorts should tackle some of the limitations of the RCTs by being purposefully heterogenous including minorities or patients with pathologies usually excluded in RCTs. Novel statistical methods and/or research designs should be used (for example, propensity score matching). Results should be validated in different populations and in real-life settings; iii) Privacy issues and informed consent should be openly discussed and adapted in ways that the population understand the importance of balancing overzealousness on personal (including biological) data and the wider need for health and welfare at societal level; iv) In the case of siloed information that cannot be deanonymized or aggregated due to regulatory constraints, the use of federated learning to train machine learning algorithms at local level to share between different hubs can generate synergies and generate shared knowledge on physiology and disease at multicentric level; v) Creation of new professional roles were a clinician or healthcare worker is also knowledgeable in technological development and regulatory aspects concerning new technologies, and; vi) Stakeholders willingness to adopt successful digitally-enabled integrated care pathways may have to accept changes on the implementation process derived from well-designed evaluation strategies using combined quantitative and qualitative approaches.

We can synthetize this new novel approach to the practice of medicine as the conjunction of the holistic way to see individual patients, the understanding of health and disease mechanisms from molecule to whole physiological systems in parallel to their interactions, and the input from digital tools for the acquisition and analysis of huge amounts of data to pave the way forward a new paradigm. While personalized medicine can be seen as “the right treatment for the right patient”, the consolidation of a Systems Medicine and Integrated Care approach should lead to the “correct clinical pathway for the correct group of people with similar clinical and social needs”. It is of note that ongoing initiatives like EUSTANDS4PM: European Standardization Framework for Data Integration and Data-driven *in-silico* Models for Personalized Medicine (https://www.eu-stands4pm.eu/) are generating ISO standards for biomedical research and for clinical practice that should contribute to pave the way toward Precision Medicine with an Integrated Care approach.

It is at this point where the authors (Pulmonary physicians) must reflect on the exceptional circumstances during which this Thesis evolved. While most of the works presented here took place immediately before the COVID-19 pandemic, some of them and most of the Thesis writing took place during the different waves and "calm" times in-between. As such, we find ourselves in a privileged position to witness how many of the lessons learnt here took place in real life. The digital transformation rolled in place, sometimes in a very coordinated and purposeful way, some others in a more improvised one. Also, we witnessed how the use of large quantities of data were collectively shared and used to feed clinical decision systems to make therapeutic decisions even when big, randomized trials were just beginning or at the planning phases. Time was of essence, resources scarce and a high level of uncertainty paved the way to implement rapid and standardized methods to evaluate a complex situation in which most of the moderate and severe patients were elderly and/or multimorbid ones. We saw how people, in the face of an emergency, were less occupied on stringent policy and regulatory issues, thus granting healthcare organizations more margin to collect data on vaccine efficacy and safety (e.g., the vaccine roll-out in Israel). The current climate in Europe has been a fertile ground for the development of the JADECARE project which indubitably has gained a lot from the pandemic experience. The removal of several barriers, especially in terms of stakeholders' acceptance to change in management withing digitally enabled integrated care models will smooth the way forward for large scale adoption by the "next adopters".

After more than two years into the pandemic, with several vaccines and antiviral medications having a positive effect at population and individual level, we can focus on the natural developments taking place right know. We bring to attention to the example of Israel, where the main author of the Thesis practice medicine. The Chaim Sheba Medical Center built a technology hub leaded by clinicians. ARC (https://arc.sheba.co.il) has several departments: AI, telemedicine, virtualization medicine, precision medicine, innovation in surgery and rehabilitation. Within them, clinician led-initiatives get support in form of technical knowledge, search for technical partners or solutions (star-ups or well consolidated businesses) and serving as the leading interphase between physicians, investigators, and the hospital IT staff, including EMR support. Examples such as telepsychiatry replacing hospital stay or the use of AI to assist radiology residents during the nightshifts are already part of the daily practice at the hospital. Moreover, a close collaboration between engineers sitting physically side by side with the treating physicians at the Internal Medicine wards has led to the development of AI and big data tools to create differential diagnostics in case of unusual and/or difficult cases to help guide diagnostic workup and treatment. Finally, in the same hospital sits Sheba Beyond, also led by

physicians (https://beyond-en.sheba.co.il), which is the unit in charge of scaling-up all the technological developments to contain costs, enhance patient satisfaction and contribute to the sustainability of the public healthcare system.

CONCLUSIONS

The research work undertaken within the current PhD thesis generated the following conclusions in three areas:

SERVICE ASSESSMENT

1.The evaluation framework proposed in the thesis facilitates scalability and transferability of the integrated care services in real-world scenarios.

2. The identification of key performance indicators, encompassing different service dimensions, enables the creation of user-profiled dashboards for post-adoption service monitoring.

DIGITAL TRANSITION

3. The thesis examined digital transformation maturity in Europe and highlighted the crucial role of digital tools in enabling integrated care services. Significant challenges were identified in terms of change management, interoperability, integration of digital tools into clinical workflows and health risk assessment for service selection.

4. The results confirm both the high potential and current limitations of digital health tools for supporting collaborative adaptive case management.

5. The analysis of existing regulatory frames, allowed the formulation of recommendations for pre- and post-marked evaluation of digital health tools.

CO-CREATION

6. The combination of experience-based codesign and quality improvement methodologies, with involvement of the relevant stakeholders, helped to efficiently design and implement innovative care pathways with digital support, leading to adoption of value-based integrated care services.

7. A valuable lesson learned during the research was the need for optimization, and simplification, of future co-creation processes through a building-blocks strategy.

8. We can conclude that future developments of the achievements of the current research should have a positive impact beyond integrated care for chronic patients by paving the way toward personalized welfare medicine within a digital society.

SUMMARY IN ENGLISH

Integrated Care is acknowledged as an effective and efficient (value-based) approach to cover health and social care needs of patients with chronic disorders. However, its large-scale adoption requires solving unmet needs in two main fields: evaluation of service implementation in real-world settings, and achievement of mature digital support for integration among the different complexity levels of healthcare assistance, in addition to the stakeholders involved in the process.

The current research was performed in the context of the Catalan original Good Practice of the European **Joint Action on implementation of digitally enabled integrated person-centered care** (www.jadecare.eu), an initiative launched to address core aspects of health system transformation in the European Union. The PhD thesis involves five studies that encompass the two main blocks of unmet needs for health system transformation.

The rationale behind the first block is that clinical medicine relies on evidence of efficacy produced by randomized clinical trials. However, proven efficacy-effectiveness gaps seen in complex interventions, such as integrated care, are limiting adoption, as well as comparability among sites. The first manuscript (*BMC Health Services Research. 2019; 19:370. 10.1186/s12913-019-4174-2*) hypothesized that a comprehensive, highly applicable, evaluation framework should foster adoption and transferability of integrated care services in different contexts, as shown for prehabilitation and hospital at home services in Catalonia. Moreover, the identification of key performance indicators, encompassing different service dimensions, should lead to creation of user-profiled dashboards to facilitate service monitoring after adoption. Likewise, the co-creation process conducted to shape the prehabilitation service (*IJIC*, 2022; 22(4): 1, 1–12. 10.5334/ijic.6503), combining design thinking techniques and quality improvement methodologies (PDSA cycles, SWOT analysis and assessment of maturity of the landscape) with contributions of the relevant stakeholders, showed its crucial role to efficiently shape and implement innovative care pathways, as well as to create usable and acceptable digital tools to support value-based integrated care services. The approach proposed was useful for solving maturity gaps facilitating sustainable adoption of novel services. A lesson learnt during the research lifespan was that future co-creation processes could be optimized by adopting a building-blocks strategy wherein each block addresses a specific target.

The second objective of the thesis was to explore the pre-pandemic technological ecosystem supporting integrated care in terms of maturity and integration with the aim to generate actionable recommendations for the different stakeholders. The rationale behind the technological block was that digital transformation in healthcare is already a reality in every day

clinical practice. Nonetheless its implementation has been uneven and is still immature. Therefore, the second block of the thesis addresses three core aspects: i) Performs a structured descriptive approach of the status of digital transformation in Europe (*J Med Internet Res 2019;21(8):e14956. 10.2196/14956*); ii) Explores the potential and the limitations of mHealth in a specific use case – Home-based non-invasive ventilation (*JMIR Mhealth Uhealth.2020;8(4):e16395. 10.2196/16395*); and iii) Generates recommendations for evaluation of digital health tools (*J Med Internet Res. 2023 Jan 4;25:e40976. 10.2196/40976*). The three studies confirmed the key role mHealth tools to support collaborative adaptive case management and identified major pending challenges of digital transformation, namely: change management, interoperability, integration into clinical workflows, and health risk assessment for service selection. The experience acquired with the development of digital solutions supporting different integrated care services, and the analysis of existing regulatory frames, allowed the formulation of recommendations for pre- and post-marked evaluation of digital health tools.

While acknowledging that relevant challenges still need to be faced, it is concluded that the evaluation framework and the co-design strategy proposed in the thesis demonstrated their usefulness to facilitate scalability and transferability of the integrated care services, whereas the second block of the thesis constitute a valuable contribution towards digital health transformation.

RESUM EN CATALÀ

L'Atenció Integrada és un model assistencial eficaç i eficient (generador de valor) que cobreix les necessitats d'atenció sanitària i social dels pacients amb malalties cròniques. Tot i això, la seva adopció a gran escala requereix millores significatives en dues àrees rellevants: l'avaluació de la implementació de serveis d'atenció integrada en entorns reals i la consecució d'un suport digital madur per a la integració entre els diferents nivells assistencials, tot plegat amb un paper proactiu dels pacients i dels diferents actors involucrats.

Els estudis de la tesi doctoral es van fer en el context de l'activitat del programa d'Atenció Integrada de Catalunya, dins de l'**Acció Conjunta Europea sobre Implementació de Serveis d'Atenció Integrada, amb suport digital, centrats en el pacient** (www.jadecare.eu). JADECARE és una iniciativa generada per abordar aspectes centrals de transformació dels sistemes de salut a la Unió Europea. La investigació inclou un total de cinc estudis que s'agrupen en les dues àrees referides anteriorment: avaluació de serveis i transformació digital.

Els dos estudis efectuats al bloc d'avaluació de serveis parteixen del fet que, de manera tradicional, l'evidència clínica d'eficàcia es basa en els resultats generats per assaigs clínics aleatoritzats. Tot i això, la bretxa entre eficàcia i efectivitat observada molt sovint en intervencions complexes, com els serveis d'atenció integrada, limita l'adopció i el potencial de transferència de les intervencions. El primer article *(BMC Health Services Research. 2019; 19:370. 10.1186/s12913-019-4174-2)* planteja la hipòtesi que un marc d'avaluació integral, i aplicable, hauria de facilitar la adopció i transferibilitat de serveis d'atenció en diferents contextos, com es va demostrar per a la prehabilitació i l'hospitalització a domicili a Catalunya. A més, la identificació d'indicadors clau de rendiment, que considerin diferents dimensions del servei, permetria la creació de panells, perfilats segons les necessitats de l'usuari, útils per a la gestió i el manteniment de la qualitat del servei després de l'adopció. En el segon article, el procés de co-creació realitzat per dissenyar el servei de prehabilitació *(IJIC*, 2022; 22(4): 1, 1–12. 10.5334/ijic.6503*)*, combinant tècniques de "design thinking" i metodologies de millora de la qualitat (cicles PDSA, anàlisi DAFO i avaluació de la maduresa de l'ecosistema), comptat amb contribucions dels actors rellevants, va tenir un rol crucial per implementar de forma eficient aquesta intervenció innovadora per a la prevenció de complicacions quirúrgiques. També va contribuir al desenvolupament d'eines digitals útils com a suport a l'atenció integrada, amb la reducció consegüent de la bretxa entre eficàcia i efectivitat. Una lliçó apresa en aquest estudi va ser que futurs processos de cocreació es poden optimitzar si augmentem el focus, de manera que s'abordin objectius més específics.

El segon bloc de la tesi va explorar, abans de la pandèmia, l'ecosistema tecnològic de suport a l'atenció sanitària amb l'objectiu de generar recomanacions operatives que ajudin a assolir un nivell de maduresa digital més gran. Els estudis realitzats assumeixen que la transformació digital dels serveis sanitaris ja és una realitat a la pràctica clínica diària, però la seva implementació ha estat desigual i immadura. En aquest apartat, es van abordar tres aspectes centrals: i) Realització d'un estudi descriptiu estructurat de l'estat de la transformació digital a Europa *(J Med Internet Res 2019;21(8):e14956. 10.2196/14956)*; ii) S'ha explorat el potencial i les limitacions de mHealth en un cas d'ús específic: ventilació no invasiva a domicili (*JMIR Mhealth Uhealth.2020;8(4):e16395. 10.2196/16395*); i iii) Es van generar recomanacions per a l'avaluació d'eines digitals de suport a l'atenció sanitària *(J Med Internet Res. 2023 Jan 4;25:e40976. 10.2196/40976)*. Els tres estudis van confirmar el paper clau de les eines de mHealth com a suport de la gestió col·laborativa i adaptativa de casos i van identificar els principals desafiaments pendents en l'àmbit de la transformació digital, és a dir: gestió del canvi, interoperabilitat, integració de la tecnologia en els fluxos de treball clínics i en el suport de la predicció de risc com a ajut a les decisions clíniques i a la personalització de l'assistència sanitària. L'experiència adquirida en el desenvolupament de solucions digitals per al suport de serveis d'atenció integrada i l'anàlisi dels marcs normatius existents va permetre formular recomanacions per a l'avaluació, la pre- i la post-comercialització, d'eines de salut digital.

Tot i que encara hi ha reptes importants per assolir plenament els objectius últims de la tesi, es conclou que el marc d'avaluació i l'estratègia de codi-disseny proposats faciliten l'escalabilitat i la transferibilitat dels serveis d'atenció integrada. Així mateix, els estudis tecnològics efectuats constitueixen contribucions valuoses per assolir la maduresa en la transformació digital dels serveis de salut.

RESUMEN EN CASTELLANO

La Atención Integrada está ampliamente aceptada como un modelo asistencial eficaz y eficiente (generador de valor) que cubre las necesidades de atención sanitaria y social de los pacientes con enfermedades crónicas. Sin embargo, su adopción a gran escala requiere mejoras significativas en dos áreas relevantes: la evaluación de la implementación de servicios de atención integrada en entornos reales, y la consecución de un soporte digital maduro para la integración entre los diferentes niveles asistenciales. Todo ello con un papel proactivo de los pacientes y de los diferentes actores involucrados.

Los estudios de la tesis doctoral se realizaron en el contexto de la actividad del programa de Atención Integrada de Catalunya, dentro de la ***Acción Conjunta Europea sobre Implementación de Servicios de Atención Integrada, con soporte digital, centrados en el paciente*** (www.jadecare.eu). JADECARE es una iniciativa generada para abordar aspectos centrales de transformación de los sistemas de salud en la Unión Europea. La investigación incluye un total de cinco estudios que se agrupan en las dos áreas referidas anteriormente: evaluación de servicios y transformación digital.

Los dos estudios efectuados en el bloque de evaluación de servicios parten del hecho que, de forma tradicional, la evidencia clínica de eficacia se basa en los resultados generados por ensayos clínicos aleatorizados. Sin embargo, la brecha entre eficacia y efectividad observada muy a menudo en intervenciones complejas, como los servicios de atención integrada, limita la adopción y el potencial de transferencia de las intervenciones. El primer artículo *(BMC Health Services Research. 2019; 19:370. 10.1186/s12913-019-4174-2)* plantea la hipótesis de que un marco de evaluación integral, y aplicable, debería facilitar la adopción y la transferibilidad de servicios de atención en diferentes contextos, como se demostró para la prehabilitación y la hospitalización a domicilio en Cataluña. Además, la identificación de indicadores clave de rendimiento, que consideren diferentes dimensiones del servicio, permitiría la creación de "paneles de control", perfilados según necesidades del usuario, útiles para la gestión y el mantenimiento de la calidad del servicio después de la adopción. En el segundo artículo, el proceso de co-creación realizado para diseñar el servicio de prehabilitación *(IJIC*, 2022; 22(4): 1, 1–12. 10.5334/ijic.6503*)*, combinando técnicas de "design thinking" y metodologías de mejora de la calidad (ciclos PDSA, análisis DAFO y evaluación de la madurez del ecosistema), contando con contribuciones de los actores relevantes, tuvo un rol crucial para implementar de forma eficiente dicha intervención innovadora para la prevención de complicaciones quirúrgicas. También contribuyó al desarrollo de herramientas digitales útiles como soporte a la atención integrada, con la consiguiente reducción de la brecha entre eficacia y efectividad. Una lección aprendida en este estudio fue

que futuros procesos de co-creación pueden optimizarse si aumentamos el foco, de forma que se aborden objetivos más específicos.

El segundo bloque de la tesis exploró, antes de la pandemia, el ecosistema tecnológico de soporte a la atención sanitaria con el objetivo de generar recomendaciones operativas que ayuden a alcanzar un mayor nivel de madurez digital. Los estudios realizados asumen que la transformación digital de los servicios sanitarios ya es una realidad en la práctica clínica diaria, pero su implementación ha sido desigual e inmadura. En este apartado, se abordaron tres aspectos centrales: i) Realización de un estudio descriptivo estructurado del estado de la transformación digital en Europa *(J Med Internet Res 2019;21(8):e14956. 10.2196/14956)*; ii) Se exploró el potencial y las limitaciones de mHealth en un caso de uso específico: ventilación no invasiva a domicilio *(JMIR Mhealth Uhealth.2020;8(4):e16395. 10.2196/16395)*; y iii) Se generaron recomendaciones para la evaluación de herramientas digitales de soporte a la atención sanitaria *(J Med Internet Res. 2023 Jan 4;25:e40976. 10.2196/40976)*. Los tres estudios confirmaron el papel clave de las herramientas de mHealth como soporte de la gestión colaborativa y adaptativa de casos e identificaron los principales desafíos pendientes en el ámbito de la transformación digital, a saber: gestión del cambio, interoperabilidad, integración de la tecnología en los flujos de trabajo clínicos y en el soporte de la predicción de riesgo como ayuda a las decisiones clínicas y a la personalización de la asistencia sanitaria. La experiencia adquirida en el desarrollo de soluciones digitales para el soporte de servicios de atención integrada, y el análisis de los marcos normativos existentes, permitió formular recomendaciones para la evaluación, pre y post comercialización, de herramientas de salud digital.

A pesar de que aún existen importantes desafíos para alcanzar plenamente los objetivos últimos de la tesis, se concluye que el marco de evaluación y la estrategia de co-diseño propuestos facilitan la escalabilidad y transferibilidad de los servicios de atención integrada. Asimismo, los estudios tecnológicos efectuados constituyen contribuciones valiosas para alcanzar la madurez en la transformación digital de los servicios de salud.

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