CONNECARE

WP6 – DEPLOYMENT OF CLINICAL STUDIES

D6.2: RESULTS FROM CASE STUDY 1

H2020-EU.3.1: Personalised Connected Care for Complex Chronic Patients

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Responsible Author	Maarten M.H. Lahr	**Email**	m.m.h.lahr@umcg.nl
Partner	UMCG	**Phone**	+31 50 53614386

Abstract	This deliverable focuses on Implementation Study 1 and describes the implementation studies carried out in all four sites along with interim results. The deliverable is divided into five sections: 1. Introduction 2. Overall Concept of Implementation Study 1 3. Implementation Study Performance Report 4. Final results of the deployment of CONNECARE in all four sites

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Executive Summary

CONNECARE – "Personalised Connected Care for Complex Chronic Patients" is a HORIZON 2020 Research and Innovation Project funded under Call: H2020-PHC-2015 – Topic: PHC-25-2015. CONNECARE is essentially a technologically-oriented initiative aiming at exploring digital tools to support two key requirements of integrated care services for chronic patients, namely: (i) Smart adaptive case management (SACM) of patients with multimorbid conditions; and, (ii) Collaborative work among the various stakeholders, including patients and their families across health and social care tiers, involved in the services. The CONNECARE model consists of two major components: an organizational model for integrated care and a technological platform to support the integrated care organizational processes. From the outset, the aim of the project has been to deploy the CONNECARE model in real life situations in each of the sites. Consequently, the CONNECARE approach has been an implementation research approach, using an observational study design focused on implementing the CONNECARE organizational model and technology in real life situations with an intervention group and matched control group in four implementation sites: Barcelona, Lleida, Israel and Groningen. The CONNECARE platform has been deployed in two situations:

- Community-based prevention of unplanned hospital-related events in chronic complex patients with high risk for hospitalization (Implementation Study 1)
- Preventive patient-centered intervention in complex chronic patients undergoing elective major surgical procedures. (Implementation Studies 2 and 3)

The aim of Implementation Study 1 of the CONNECARE project was to develop, test, and implement a novel ICT management system in order to prevent unplanned hospital-related events in frail complex patients in a real-life setting. This document describes and summarizes the activities performed in Implementation Study 1 in all clinical sites, divided in four section:

1. Introduction of the context and the rationale of the CONNECARE project, taken from a perspective of the developments in both integrated care and digital technology.
2. Overall Concept of Implementation Study 1 – describes the rationale and development and implementation of the CONNECARE ICT systems and connected devices to support community-based prevention of unplanned hospital-related events in frail complex patients with high risk for hospitalization in real-life settings.
3. Implementation Study Performance Report – describes in detail the implementation in each of the four sites – site by site - addressing the following components:
    - Site adaptation of the Concept
    - Pilot description, inclusion criteria and main study variables
    - Pilot experience - progression and changes over time
        - Brief description of the intervention
        - Recruitment process and participants

    - Difficulties, problems and barriers – how they were overcome and the changes they necessitated to enable successful deployment
  - Summary of Implementation Study Performance in all four sites
4. Results of the deployment of CONNECARE in all four sites – site by site - The results reported in this deliverable include:
  - Recruitment results and main reasons for failure to recruit and for patient drop out.
  - Patient assessment of the implementation of the integrated care service and model.
    - Patients rating of the integrated care services using the Person Cantered Coordinated Care Experiences Questionnaire (P3CEQ and the Nijmegen Continuity Questionnaire (NCQ).
    - Organisational and Process Issues that were reported in the implementation logs and the evaluation of implementation process indicating those that were successful and could be replicated and those that did not work.
  - Patient and staff engagement and actual usage of ICT tools.
  - Patient and staff satisfaction with the technology.
  - Issues with the digital tools recorded in the implementation log.
  - Intervention effectiveness - Patient outcomes and use of resources.
  - Cost – benefit analyses.

The following deliverables are highly recommended to be read:

Number	Title	Description
D2.1	Cook-book	The document provides an overall view of the CONNECARE project, and describes the procedures for its development. The deliverable indicates the different phases of the project, with an emphasis on how PDSA cycles will be structured. Overall, the CONNECARE project does not aim at a rigid integrated care solution that needs to be adopted by all potential deployment sites but to a flexible solution that has high potential for generalization at the EU level. In this sense, innovative methodologies involving both global and local stakeholders have been adopted.
D6.1	Study release feasibility for the three clinical studies	The CONNECARE document D6.1 covers the operational aspects required to: i) Initiate the implementation studies at site level; ii) Do a proper follow-up of their progress until the final release of the system at the end of the second co-design period; iii) Perform assessment of the five main dimensions of the project (1. Service workflows design & cost-effectiveness; 2. Technological developments; 3. Health risk assessment & service selection; 4. Innovative assessment aspects;

		and 5. Transferability analysis & service adoption); and, iv) Prepare the elements required for accomplishment of Tasks 7.4 and 7.5 (Recommendations of final services and proposals for scale-up integrated care) which constitute the core activity of the third co-design period, from M36 to M42.
D7.1	Evaluation plan for the entire project	The document defines the steps and tasks required for the entire project evaluation. It analyses the criteria used for identification of the different modalities of indicators, the methodological approach including clinical study designs, as well as the three main phases: (i) Initial co-design process; (ii) Clinical studies; and, (iii) Refinement & fine tuning process, defining and overall strategy for CONNECARE assessment. The document also indicates synergies established with other EU projects showing complementary goals, namely: ACT@Scale and SELFIE. Assessment of the value generated by the CONNECARE approach and identification of determinants of scale-up of the clinical studies are central goals of the project. Moreover, the document identifies the two final outcomes of the project: (i) refined CONNECARE ICT-supported integrated care services; and, (ii) generation of guidelines for transferability of CONNECARE to other EU sites beyond the project life span.
D7.2	Evaluation results of the initial co-design phase until Study Release	The D7.2 document summarizes the results of the first co-design period, from the project start to month 18th, for the main project dimensions, namely: i) Implementation studies covering service workflows design, effectiveness and operational cost analyses; ii) Technological developments to support integrated care services; iii) Health risk assessment and service selection; iv) Innovative assessment aspects proposed by the project; and, v) Transferability analysis & recommendations for service adoption at European level. The document summarizes the lessons learnt.

1. Introduction

With the increasing life expectancy of the world population, particularly in the developed world, there has been an increasing burden of chronic illness and disability that, together with increasingly limited resources, has necessitated a change in the way we view and provide health and social care. Integrated care has been seen as a response to the fragmented delivery of health and social services being an acknowledged problem in many health systems [1-3]. While the notion of integrated care was discussed in the late 1990s, a first attempt to define integrated care was offered by Kodner and Spreeuwenberg in 2002 [4]. In 2016 WHO proposed the following definition: "Integrated care is a concept bringing together inputs, delivery, management and organization of services related to diagnosis, treatment, care, rehabilitation and health promotion. Integration is a means to improve services in relation to access, quality, user satisfaction and efficiency." (WHO Europe, 2016). The integrated care literature distinguishes between different ways and degrees of working together and between horizontal integration (linking similar levels of care like multi-professional teams) and vertical integration (linking different levels of care like primary, secondary, tertiary and social care).

Side by side with the movement toward integrated care, the rapid development of information and communication technology has provided new digital tools that are catalysing the transformation of health care and gives the concept of integrated care new meaning. There is technology for sharing medical and care information between professionals and institutions. In addition, there is increasing attention and work directed towards terms of patient-centred care supported by digital tools. The digital transformation of health care is high on the agenda in all developed countries and is receiving especially high visibility in the European Union with its publication on 25th April 2018 by the European Commission of the Communication on Digital Transformation of Health and Care in the Digital Single Market. One of the three major priorities is citizen empowerment with digital tools for user feedback and person-centred care using digital tools to empower people to manage their own health and well-being, stimulate prevention and enable feedback and interaction between users and healthcare providers. There is a growing conviction and preliminary evidence that, for instance, the use of mobile apps can support chronic disease management [5-7].

Within this context, the CONNECARE project takes its role and aims to develop and implement a model and platform for digitally enabled integrated care, specifically for elderly, chronically ill patients. The CONNECARE platform was intended from the outset to be implemented in two situations:

1. Community-based prevention of unplanned hospital-related events in chronic complex patients with high risk for hospitalisation
2. Preventive patient-centred intervention in complex chronic patients undergoing elective major surgical procedures.

2. Overall Concept of Implementation Study 1

The main aim of the interventions in Implementation Study #1 is to prevent unplanned hospital-related events: (i) unplanned hospitalisations; (ii) emergency room consultations; and (iii) early re-admissions after hospital discharge by implementing digitally enabled integrated care. To support deployment of CONNECARE in real-life settings two requirements for integrated care services were focused upon, (i) Smart adaptive case management (SACM) of patients with multimorbid conditions; and, (ii) Collaborative work among the various stakeholders, including patients and their families across health and social care tiers, involved in the services. As such the organizational model of CONNECARE and a technological platform to support the integrated care organizational processes were main components.

The CONNECARE approach has been an implementation research approach, by bringing the CONNECARE organizational model and technology to real life situations and integrated into existing care pathways. The dedication to real life implementation in each of four clinical implementation sites has led to a high level of heterogeneity among the implementation scenarios, in order to meet real life challenges, with the intent that major aspects of the implementation will continue to evolve after project's end. Already from the start of the project onwards, there were apparent differences between the clinical sites in the level of maturity of the organizational model and the maturity of local and regional IT system to support delivery of integrated care service throughout the region. For example, Barcelona and the region of Catalonia were more advanced in terms of their maturity of the organizational model and associated digital systems as part of delivery of integrated care models, and in terms of the development of region-wide IT systems to supports such innovative integrated care services. Accordingly, Barcelona has tested the CONNECARE platform stressing the analysis of its potential for supporting the ongoing large scale deployment of the services. Moreover, as described in detail in D6.4 "Results from Case Study 3", Barcelona has been exploring the potential of other digital tools, following the CONNECARE concept, with a twofold purpose: (i) as a contingency plan to overcome risks associated to technological developments, and, (ii) to optimize the digital support of the ongoing services.

The target group is patients with high risk of hospitalisation identified in each of the four sites. Two subgroups of high risk patients have been identified: patients identified in a hospital setting – either in the emergency room or in the hospital who are then discharged back to their home in the community in a transitional care context or in a primary care context; or patients living at home but receiving (intensive) medical services due to the complexity of their condition. While the objectives and desired outcomes are the same in all sites, the organizational model for integrated care has been adapted to the specific needs of each site. Hence, in the first subgroup – patients identified in a hospital setting, Barcelona focused on home hospitalisation as the mechanism for transitional care with a subgroup that received integrated follow-up post home hospitalisation for prevention of unplanned hospitalisation, whereas Lleida and Israel implemented a post-discharge (from the ER or inpatient hospitalisation) case management model for integration between the hospital and care in the community. In the second subgroup, Groningen focused

on integration and continuity of care between primary care, specialists and social care in the community for complex asthma and COPD patients living at home, while Barcelona focused on: (i) home hospitalization and transitional care (implementation study 1); (ii) home-based non-invasive ventilation (implementation study 2); and, (iii) optimization of vertical and horizontal integration (implementation study 3). All of the community-based integration models have been supported by some form of digital ICT. In Lleida, Israel, Groningen, and Barcelona in subgroup 2, the focus of the ICT implemented was on patient empowerment through the use of a mobile application (either the CONNECARE SMS, MyPathway® from partner ADI or Health-Circuit, as described in detail in D6.4 “Results from Case Study 3”) that provided patient reminders and alerts as well as supporting communication between patients and clinicians. Consistent with the different orientations among sites regarding technological testing, Lleida, Israel, and Groningen used the CONNECARE clinician case management platform (SACM) as a stand-alone tool, while Barcelona also focused exploring the potential for large scale implementation of the digital tools. To this end, integration with existing IT systems both at provider and at regional levels was a core priority. In all cases, the aim was to strengthen and support care integration with ICT. Thus in all cases, there is an intervention group receiving integrated care supported by ICT and a control group for comparison in order to assess usability, user satisfaction, patient outcomes, and cost-effectiveness.

3. Implementation Study Performance Report

3.1 Barcelona

The implementation studies addressing management of multimorbidity in frail complex patients with high risk of hospitalization, Case Study 1 (CS1), in Barcelona are grouped in three articulated clusters of protocols, as described below, with a threefold aim:

- To perform a comprehensive assessment of the process of deployment of digitally-supported services covering the spectrum of vertical (specialized vs community-based care) and horizontal (within community-based care) integration of health and social care in the health district of Barcelona-Esquerra (AISBE, 520k citizens).
- To investigate applicability of technological developments generated during the lifetime of the project.
- To explore the potential of the CONNECARE concept through adaptation and testing of other digital health tools.

The seminal plan for CS1 protocols in Barcelona was reported in D6.1 “Study release feasibility for the three clinical studies”, but the ambition of the implementation plans slightly expanded during the project lifetime. The protocols finally undertaken fit with the report in [9], wherein the study on Long-Term Oxygen Therapy (LTOT) has been substituted by home-based non-invasive ventilation.

The protocols explored different digital health tools aiming at supporting at least one of the three key requirements identified in CONNECARE to effectively support integrated care services for complex chronic patients, namely: (i) smart adaptive case management (SACM) for collaborative work among the various stakeholders across health and social care tiers involved in the services; (ii) patient empowerment for self-management; and, (iii) enhanced clinical decision support for personalization of care. In most cases, we tested the performance of digital health tools embedded into mainstream integrated care services with previously proven potential for health value generation [14] [15] [16] [11] . The studies were mostly carried out in real-life settings wherein large scale adoption of digitally supported services is a central objective.

Well-accepted goals of the digital support to services are: (i) safety, (ii) robustness, (iii) usability and acceptability by both patients and professionals, (iv) added-value in terms of service efficiency and cost-effectiveness; (v) enhanced clinical decision support for personalization of the service; and, (vi) potential for supporting scalability of the service. Despite the fact that not all of the above traits were formally tested in the implementation studies, all the six dimensions were considered in the final evaluation of the digital support. The results of the technological testing are briefly summarized for each of the protocols composing CS1 in Barcelona.

As alluded to above, the three clusters of studies done in Barcelona are:

Home hospitalization and early discharge (HH/ED). The aim was the analysis of the HH/ED service during one-year period, from 30th September 2017 to 1st October 2018. This study period corresponds to the expansion of the service, from twelve to fifty-four home-based beds per day, aiming at progressively covering the needs of the health district of Barcelona-Esquerra (AISBE, 520 k citizens). It is of note that, since March 2019, the team at Hospital Clinic de Barcelona (HCB) has a leading role in a task force set by the regional single-public payer (CatSalut) with a twofold objective: i) standardization of home-based hospitalization services across the region (7.5 M citizens); and, ii) optimization of vertical & horizontal integration for enhanced management of chronic patients with high risk of hospitalization. The first cluster includes two protocols:

- **Protocol IA –** Evaluation of hospital avoidance (HH)
- **Protocol IB –** Health risk assessment of candidates to HH/ED

The deployment of home-based hospitalization as an integrated care service involves two additional interventions of high interest in CS1, that is: (i) transitional care during the period of 30-days after discharge; and, (ii) identification of needs for shared agreements between specialized and primary care or with other community-based services. These two interventions are explored in detail in Protocol IIIA, described below as part of the third cluster of studies done in Barcelona.

Home-based non-invasive ventilation of patients with hypercapnic respiratory failure (home-based NIV). This cluster only includes one protocol (**Protocol II)** addressing management of frail chronic patients requiring specialized respiratory care for home-based NIV. The service displays a clear need for enhanced interactions between specialized care and different community-based services such as: (i) primary care professionals; (ii) companies providing technical support to the home-based service; and, eventually, (iii) social support services. The study protocol aimed to include the entire universe of patients under home-based NIV at HCB. The use case has commonalities with other respiratory therapies such as long-term oxygen therapy (LTOT) [10] and sleep-related disorders, but it also displays key elements representative of unmet needs for others home-based services.

Community-based care of frail chronic patients. The third cluster of studies includes three protocols addressing specific objectives. As alluded to above, **Protocol IIIA** analyses the needs in terms of vertical and horizontal integration for a subset of 400 patients followed-up at 30 and at 90 days after discharge from HH/ED (Protocol IA). **Protocol IIIB** assesses patients and professionals' perceptions of usability and acceptability of the CONNECARE platform in 20 chronic patients recruited in primary care. Finally, **Protocol IIIC** investigates the potential of a new prototype (Health-Circuit, see D6.4 "Results from Case Study 3"), developed during 2019, to provide digital support for management of frail chronic patients following the CONNECARE concept. To this end, we recruited a subset of 40 patients from Protocol IIIA in whom the current study was carried out approximately one year after hospital discharge.

Evolution of the technological approach during the project life span

During the two initial PDSA cycles (M1-M6 and M7-M12, respectively), Barcelona heavily contributed to the co-design process supporting the technological developments of the project. But, the technological risks identified in terms of: timeline, robustness and potential for scalability, triggered the following proposals to the consortium that have been progressively activated, since March 2018, at site level in order to comply with the needs of CONNECARE in Barcelona, namely:

1. To ask the technological partners to agree to the possibility of testing the CONNECARE platform as a whole, but also to address the different elements separately. Specifically, SACM, SMS and risk predictive modelling.
2. To explore alternative digital health tools, complying with the CONNECARE concept, easily adaptable to the site requirements in order to foster large scale deployment of digitally-supported services, and
3. To take into account the interoperability requirements at site level in order to address both technical and functional integration with local health information systems during the lifetime of the project.

The team in Barcelona has been keeping track of the evolution of the CONNECARE platform as a whole throughout the project lifetime, but the site has focused also energies toward development and/or adaptation of different digital health tools ensuring two key CONNECARE functionalities. To this end, besides testing the elements of the CONNECARE platform (Protocol IIIB), adaptations of two different digital tools have been addressed in CS1, namely: (i) MyPathway® in Protocol II (Home-based non-invasive ventilation); and (ii) Health-Circuit in Protocol IIIC (Vertical and Horizontal integration). Likewise, an adaptation of the SMS has been worked out by partner EURECAT to support CS2 and 3.
The detailed description of the assessment of the overall digital support to the target services, CS1 to 3, in Barcelona is reported in detail in D6.4 “Results from Case Study 3”.

3.1.1 Implementation studies description

The specificities of the protocols included in CS1 are briefly described below:

Protocol IA - Home Hospitalization & Early Discharge (HH/ED) in AISBE

Background & Aims – The HH/ED service was implemented as a mainstream integrated care service at HCB in 2006 [11]. It is defined as a service providing acute, home-based, short-term complex interventions aiming at substituting conventional hospitalization fully, HH, or partially, ED. The service is delivered by trained hospital personnel for a period of time, in general, not longer than the expected length of hospital stay for the patient’s diagnostic related groups involved. Virtual beds are used to support required administrative and clinical processes. Recently (2018), the HH/ED service has expanded to fifty-

four home-based beds per day aiming at progressively covering the needs of the entire AISBE health district.

Such evolution generated the need for a comprehensive assessment of the HH/ED service during one-year period, from 30th September 2017 to 1st October 2018 (Figure 1), which constituted the main objective of the current study. The study protocol was carried out following the evaluation framework reported in [8]; that is, assessing: (i) health outcomes; (ii) the implementation strategy following the CFIR approach(https://cfirguide.org/) [17-19]; (iii) characterizing the maturity of the ecosystem following Scirocco[1]; and, identifying key performance indicators for structure, process and health outcomes [20] to be considered for long-term monitoring of the service beyond the initial deployment phase.

Figure 1 depicts the study group of 620 patients admitted in the emergency room due to a first episode during the study period, 30th September 2017 to 1st October 2018, in whom the hospital avoidance service was administered. The corresponding control group, currently under construction, will be extracted with a propensity score matching technique from the 5,507 patients admitted for conventional hospitalization (usual care), in general wards.

The final analysis will be completed within January 2020. Accordingly, the current document reports complete data analysis for a subset of 200 patients from the intervention group and the corresponding 200 matched controls. Availability of the information for this subset of patients was possible because they followed a particular path for data management since they were included in an ancillary protocol aiming at exploring novel modalities of health delivery assessment[2].

Ancillary objectives of **Protocol IA** are: (i) Identification of subsets of patients with specific healthcare requirements at community level, after HH/ED discharge; and, (ii) generate recommendations for refinement of current transitional care services during the initial 30-day period after discharge, both addressed in **Protocol IIIA**.

[1] Scirocco: Scaling Integrated Care in context. https://www.scirocco-project.eu/

[2] SELFIE (2016-19) – Sustainable Integrated Care Models for Multimorbidity Delivery, Financing and Performance. Available from: https://www.selfie2020.eu/

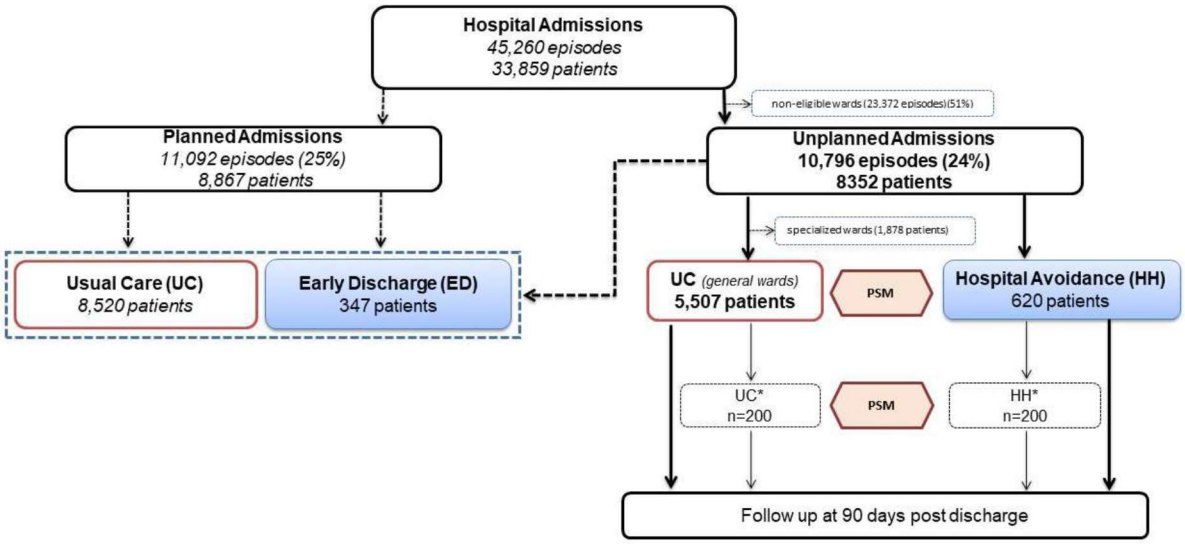


Figure 1. Depicts the distribution of hospital admissions during the study period, from 30th September 2017 to 1st October 2018. Protocol IA focuses on the evaluation of the hospital avoidance (HH) service. The intervention group includes 620 patients hospitalized at home from the emergency room. All recruitments correspond to the first episode during the study period. As described in the text, the document provides complete data analysis for a subset of 200 patients from each group, UC and HH*, in whom full information is currently available.*

Ancillary objectives of protocol IA are: (i) Identification of subsets of patients with specific healthcare requirements at community level, after HH/ED discharge; and, (ii) generate recommendations for refinement of current transitional care services during the initial 30-day period after discharge, both addressed in **Protocol IIIA**.

Study design & measurements: current status and planned analyses – It follows a non-randomized controlled design. The intervention group (HH) was compared with a contemporaneous control group consisting of non-surgical patients admitted from the emergency department at HCB (conventional hospitalization) (1:1 ratio). Comparability among intervention and control groups was addressed using a two-step propensity score matching (PSM) approach. Firstly, a one-to-one PSM is performed using the following five variables: (i) age, (ii) sex, (iii) multimorbidity using adjusted morbidity groups (GMA) grading [21], which is the population-based risk assessment tool implemented in Catalonia; (iv) number of admissions in the previous year; and, (v) polypharmacy. In a second step, comparability between groups is further enhanced by using an inverse probability of treatment weighting (ITPW) approach [22].

Measurements - Standard health outcomes obtained from the electronic medical records, as described in detail in [11], were used. The study will also include an extended set of variables from the primary care electronic health records (eCAP) aiming at informing on different dimensions of frailty and previous use of healthcare resources. Moreover, a third source of information will be the Catalan Health Surveillance System (CHSS) providing additional information on multimorbidity, past use of healthcare resources one year before HH and up to 90 days after home-based discharge.

As described in the legend of Figure 1, the current document reports on health outcomes and costs for a subset of 200 patients from the intervention group, hospital avoidance (HH), and for their 200 matched patients under conventional hospitalization in whom full information was already available for analysis. It is of note, however, that the analysis of combined information from the different data sources, as well as the application of the matching strategies described above, has been delayed due to GDPR constraints, but it is currently being addressed and it should be completed within January 2020.

Cost-effectiveness of the HH intervention was assessed calculating operational costs of the service analysing detailed estimations of the following items for both HH and control groups: (i) Staff; (ii) Non-pharmacological and pharmacological therapy; (iii) Consumables; (iv) Equipment; (v) Transports; and, (vi) Structure. Mean average cost per patient was calculated for all items except pharmacological therapy that will use actual individual information. The health value generation analysis will be carried out taking both the perspective of the provider and the impact at health system level. Finally, patient and health professionals' engagement to the program was done using data collected from routine assessments, but also using the tools provided by the EU project ACT@scale [12] to address these items. Characterization of the implementation process using the CFIR approach [17-18], maturity of the ecosystem[3] and proposals for Key Performance Indicators (KPIs) [20] are also reported.

Characteristics of the intervention - All patients in the intervention group followed a care path described in detail in Hernandez C et al in [11]; whereas, the control group includes patients admitted in an Internal Medicine general ward that followed the standard of conventional care. As indicated in Figure 1, all patients included in the study, both intervention and control groups, were admitted through the emergency department. The remaining inclusion and exclusion criteria for the study were identical to those described [11]. No patients were excluded due to technological constraints.

Technological approach – The existing technological setting to support HH/ED at HCB is explained in detail in [11] and in D6.4 "Results from Case Study 3". Briefly, health professionals performing the home-visits use laptops that provide access to the clinical workstation at HCB. They have access to mobile technology to do measurements and to communicate with physicians at the Hospital for specific consultations. Moreover, we learnt through previous projects that elderly patients in acute conditions are not prepared to do self-monitoring unless a carer takes this responsibility [16]. This is not the case for elderly chronic patients in stable clinical conditions. Consequently, the initial technological objectives to enrich digital support for this specific protocol were twofold:

> *During HH*: (i) facilitate communication between patients/cares with professionals at HCB through access to a call centre/videoconference; (ii) videoconferencing between professionals during the home visit and professionals in the hospital; (iii) videoconferencing between professionals from the HH team and community-based professionals to prepare the post-

[3] Scirocco: Scaling Integrated Care in context. https://www.scirocco-project.eu/

discharge period; and, (iv) identify potential eHealth support that may benefit the patient after HH discharge.

During transitional care: foster collaborative work between specialized and primary care teams aiming; that is, vertical integration, at optimizing implementation of shared care paths during the period, while empowering patients for self-management of his/her conditions.

To this end, we initially explored the potential of the CONNECARE platform as a whole and we deeply analysed the potential of the different components: SACM and SMS separately, as explained in the introductory section of D6.4 "Results from Case Study 3" and in the results section of the current document. Moreover, we also assessed the potential of adapting other existing digital tools in order to explore their potential to fulfil the requirements of Protocol IA.

Additional information and main results of Protocol IA are reported in **ANNEX I on Home Hospitalization & Early Discharge.**

Protocol IB – Health risk assessment for enhanced clinical decision support in patients under HH/ED

An additional component of **Protocol I** was to assess the potential of risk models for the prediction of readmissions and deaths after HH discharge in real-world settings.

As a first step, this protocol have applied machine learning techniques for the elaboration of multilevel predictive modelling tools to assess risk of mortality and re-admissions, both during home hospitalization and 30-days after discharge (Figure 2). For the development and validation (cross-validation) of the predictive models, this protocol has combined clinical, biological and population-based HH/HD data () from a real-world database including 1832 cases having been admitted to the HH/HD program of Hospital Clinic of Barcelona from January 2012 to December 2015. The results show a prediction performance, captured by the Area Under the Curve (AUC), of 0.73 for the prediction of readmissions and of 0.90 for mortality risk.

Please, see **ANNEX II – Health risk assessment for enhanced clinical decision support in patients under HH/ED (Protocol IB)** for the complete manuscript ready for submission to Scientific Reports.

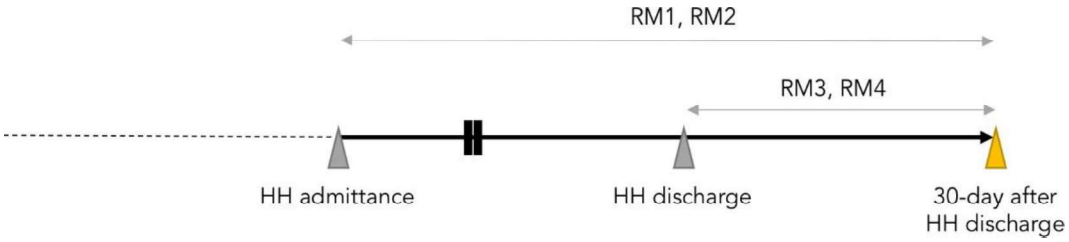


Figure 2 . Implemented risk models. RM1 accounts for the model predicting 30-day readmission at the moment of admission; RM2 predicts 30-day mortality risk at admittance; RM3 and RM4 respectively refer to 30-day readmission and mortality prediction at HH discharge.

This protocol provides a first step to support clinical decision making at moment HH/ED admission and in the proper allocation of transitional care services after HH discharge. However, further work is need towards designing the implementation of this approach in real-world settings so it can provide directions for the translation of health-risk assessment models to daily clinical practice. To this end, this protocol is currently undergoing real world data extraction for the independent validation of the predictive modelling using HH/HD data from the period 2017-2018. In parallel, this protocol will also assess the maturity of health information systems to support the deployment of the decision support tools in the clinical workstation of HH/HD clinicians, as well as the dynamic update of the predictive models. The later will require functionalities of a learning health system (i.e., data-lake versus data warehouse, online training and deployment of multilevel predictive models, etc.). Ultimately, this protocol will propose a roadmap for implementation in real world settings in Catalonia, fully aligned with the regional director plan.

Table 1. List of outcome and input data considered for the generation of the multilevel predictive modelling.

Outcome variables				
ing_hd	Hospital admission during DHOM			
mort_alt	Mortality 30 days after HDOM discharge			
ING_30	Hospital admission 30 days after HDOM discharge			
Input clinical variables				
SEX	Gender	**ANALI_IN***	Blood lab test performed during HDOM	
AGE	Age	**nom_pato**	Knowledge of the name of the disease	
p_entr	Hospital entry	**sig_alar**	Knowledge of the alarm symptoms of the chronic disease	
SERVICE	Service of origin	**ucias_an**	Emergency room visits previous to DHOM (last 12 months)	
DAY_HCP*	Hospital stay (days)	**ing_ano**	Hospital admissions previous to DHOM (last 12 months)	
dias_hdm*	Home hospitalisation (HDOM) stay (days)	**ucias_hd***	Emergency room visits during DHOM	
dias_tot*	Total stay (days)	**VIS_NURS***	Number of nursery visits at home	
ano_cat	Year of admission at HDOM	**VIS_DOC***	Number of clinical visits at home	
diag_cat	Classification by diagnostic group	**VIS_HCB***	Number of hospital visits	
resp_cr_ag	Chronic or acute respiratory health issue	**CALL***	Number of phone call by the health professional	
N_diag	Number of secondary diagnosis	**SEGU_PRE**	Follow-up previous to HDOM	
Charlson	Charlson index	**SEGU_ALT***	Follow-up at HDOM discharge	
Tabaquis	Tobacco habit	**SEGUI_CA***	Follow-up categories	
paq_ano	Cumulated dose (packages/year)	**ABS_new**	Basic (primary care) health area	
Imc	Body mass index	**AGA**	Care management area	
Camina	Walk in a regular basis	**Hospital_ref**	Reference hospital	
Barthel	Barthel index	**proveidor**	Service provider	
sf_36	Applies quality of care (SF-36)	**disease_group**	Disease group classification based on ICD9 codes	
estad_me	Mental status (SF-36)	**Data collected during and after HH/HD*		
EQUI_PRE	Respiratory therapy previous to HDOM			
ocd_domi	Oxygen therapy previous to HDOM			
VENT_PRE	Non-invasive ventilation	**Input lab test data**		
TECN_DOM	Number of techniques at home	**LAB1300**	10^9/L	[4.00 - 11.00] Count of leukocytes
EQUI_HD*	Equipment during HDOM	**LAB1308**	%	[17.0 - 55.0] Lymphocytes % (analit.)
EQUI_ALT*	Equipment remains at home after discharge	**LAB1314**	g/L	[120.0 - 170.0] Hemoglobin concentration
dif_medi	Burden of medicine	**LAB1323**	%	[10.5 - 17.2] RDW (Reed Distribut. Width)
past_dia	Number of daily pills	**LAB2422**	mg/dL	[65 - 110] Glucose
iny_dia	Number of daily injections	**LAB2467**	mg/dL	[0.30 - 1.30] Creatinine
inh_diar	Number of daily inhalations	**LAB2507**	mEq/L	[135 - 145] Sodium
atb_ev*	Intravenous antibiotic during HDOM	**LAB2508**	mEq/L	[3.5 - 5.5] Potassium
furo_ev*	Intravenous furosemide during HDOM			
cort_ev*	Intravenous cortisone during HDOM			
trat_ev*	Requires some intravenous treatment	**Input population-based variables**		
HEPARINA*	Heparin SC	**GMA_new**	Adjusted Morbidity Groups	
curas*	Requires cures during HDOM	**Peso**	Relative patient weight in the Adjusted Morbidity Groups	
ESPIRO*	Forced spirometry performed during HDOM	**EstratP**	Population-based stratification	
GASO*	Gasometry performed during HDOM	**EstratC**	Cohort based stratification by the relative patient weight	

Protocol II - Home-based non-invasive ventilation

Background - Home-based non-invasive ventilation has proven cost-effective. But, adherence to therapy still constitutes a common clinical problem. We hypothesized that a behavioural intervention supported by mHealth can enhance patients' self-efficacy. It is also accepted that mHealth-supported services might enhance productive interactions among the stakeholders involved in home-based respiratory therapies.

Objectives and study design - To measure changes in self-efficacy in patients with chronic respiratory failure due to diverse aetiologies, during a follow-up period of three months after the intervention. Ancillary objectives were assessment of usability and acceptability of the mHealth tool, as well as to learn on its potential contribution to enhance collaborative work among stakeholders.

A single blinded, single centre, randomized controlled trial was performed on 67 adult patients with chronic respiratory failure undergoing home-based non-invasive ventilation, between February and June 2019. In the intervention group, a psychologist delivered a face-to-face motivational intervention. Follow-up was supported by a mHealth tool (MyPathway) which allowed patients to introduce the number of hours of use per day and problems with the therapy. Advice was automatically delivered by the mobile tool in case a problem was reported. The control group received only usual care.

Please, see ***ANNEX III*** for the complete manuscript reporting on Protocol II, accepted for publication, with revisions, to JMIR in November 2019.

Protocol IIIA – Assessment of needs for vertical and horizontal integration

Background Aims – Protocol IIIA assesses the needs for both vertical and horizontal care coordination in 400 patients after discharge either from conventional (n=200) or home-based hospitalization (n=200). The study group was recruited from Fall 2017 to Fall 2018, as part of Protocol IA (Figure 1). For the purposes of the current protocol, the entire group of 400 patients is jointly analysed irrespective of their original recruitment source (usual care, UC, or hospital avoidance, HH).

The study has a threefold aim: (i) to identify subsets of patients with common health and social care needs; (ii) to compare the services' coverage that was provided within a follow-up period of 90 days after discharge, with an optimal use of the care coordination scenario delineated by the Catalan Health Plan 2016-2020[4], as proposed by an independent group of qualified stakeholders; and, (iii) to generate recommendations aiming at enhancing care coordination.

Study design & Pilot description - Information on the 400 patients (UC and HH) regarding: (i) primary and secondary diagnosis at discharge at the hospital and in the primary care medical records; (ii) GMA scoring [21]; (iii) sociodemographic data and social status; (iv) allocation of the patient immediately after

[4] Catalan Health Plan 2016-2020: http://salutweb.gencat.cat/web/.content/_departament/pla-de-salut/Pla-de-salut-2016-2020/documents/health-plan-catalonia_2016_2020.pdf

discharge in terms of community-based services; (v) use of health and social care resources during the previous year; (vi) number of drugs administered; (vii) triple aim characterization after 30-days of the hospitalization event; and, (viii) follow-up health and social care events at 90 days after discharge, will be used to generate patients' requirements profiles. A summary description of the characteristics of the study group is provided within ***ANNEX I***.

Two main study phases are considered: (i) Phase I – Data Analytics and elaboration of a summary report; and, (ii) Phase II – Design Thinking sessions aiming at generating recommendations.

Data Analytics (Phase I) - Three well-differentiated objectives have been identified:

Objective I – Analysis of multimorbidity clustering in order to enhance the potential of the GMA for clinical decision support in primary care. Identifying common clusters of multiple chronic conditions (MCC) may help locate subsets of the population with similar healthcare requirements, facilitating case finding and screening. Relatively small shifts in healthcare delivery for common disease clusters may achieve improved outcomes via joint care pathways for cross-condition management. Once common clusters of MCCs are identified, further information on burden will be developed using modelling of individual health risks, and longitudinal data analyses of healthcare use. Co-occurring chronic diseases within each individual will be identified using a non-hierarchical cluster analysis. Building on the methods described in [23], Multiple Correspondence Analysis (MCA) allows identification of patients with the same clinical characteristics, by representing patients as points in geometric space. K-means clustering will classify patients into clusters from the geometric space created in the MCA, according to proximity criteria from the k-means algorithm. The combination of both MCA and K-means clustering separates patients into homogenous groups while maximising heterogeneity across groups. The objective is planned to be addressed as an exploratory study to be further expanded to a deeper analysis using the CHSS, beyond the project.

Objective II - To make use of network medicine as a methodological approach to assess associations between clinical diagnosis (or identified clusters of MCC) with non-clinical information and use of health care resources. The methodology offers the potential to understand and create potential implications for the design of innovative prevention strategies.

Objective III – The use of cluster analysis, taking into consideration the results of the previous steps (Objectives I and II), should help locate subsets of the population with similar healthcare requirements. For future research, beyond the current project, it is hypothesised that a coalescence of risk-stratification of MCC clusters, combined with predictions of healthcare use, will provide the intelligence needed to predict cluster dependent healthcare pathways for unique patients. This information can be attached the medical records enriching the support for clinicians to make timely decision making for complex patients.

Design Thinking (Phase II) – A detailed report of the results of Phase I will feed design thinking sessions to be carried out with selected groups of stakeholders, including patients, to assess current gaps in care coordination and generate recommendations to foster core aims of the ongoing Health Plan (2016-2020) at health district level, looking for transferability at regional level.

Completion of Protocol IIIA is dependent on merging collected data from these 400 patients with information from primary care (eCAP) and from the CHSS. Such task, similarly to what has been described for Protocol IA, has experienced delays due to GDPR interpretations. It is estimated that the data analytics described above will be initiated by early January and completed within the first trimester of 2020.

The two subsequent protocols correspond to studies assessing specific digital tools aiming at providing support to vertical and horizontal integration that have been completed during the lifetime of the project.

Protocol IIIB – Assessment of the CONNECARE platform in primary care

Study aims & study design - The lessons learnt in Protocols IA and II on the technological potential of the available digital tools prompted the need for testing the final version of the CONNECARE platform in a primary care setting in Barcelona. The main objective of the study was to formally assess acceptability and usability of the digital platform (SAMC and SMS) by patients, as well as to further explore the potential of the most mature version of the tool. To this end, a study protocol carried out with 20 clinically stable patients with multimorbid conditions recruited in one primary care unit, CAP Casanova, from the Barcelona-Esquerra health district (AISBE). They were characterized at baseline, access to the use of the platform through their smart phones and a pedometer (Lifevit AT-250[5]) were provided and the patients were followed-up throughout the period by one case manager. Assessment encompasses: (i) Digital literacy; (ii) System Usability Scale (SUS) [24]; (iii) Safety; (iv) Satisfaction (Net Promoter Score [25]); and, (v) log-book with incidences and user's suggestions.

Protocol IIIC – Assessment of Health-Circuit in primary care

Background - Health-Circuit (see D6.4 "Results from Case Study 3") embraces the new generation of smart collaboration technology to allow patients and health professionals to interact seamlessly from any device. It is a cloud-based, GDPR-compliant, team collaboration platform customized: (i) to empower adaptive case management across healthcare tiers; (ii) to enhance patients' self-efficacy; and, (iii) with potential to implement intelligent bots to assist professionals through well-defined flexible service workflows. It is designed to operate on top of existing information systems. We have undertaken a two-phase study. The current protocol explores acceptability, usability, and safety of the digital tool for patients and professionals; whereas, the subsequent study phase is planned to analyse its potential for health value generation in the management of chronic patients at risk of hospitalization.

[5] http://lifevit.es/ENG/pulseraactividad2.php

Method - Cluster randomized controlled trial, by primary care teams, with an intervention to control ratio of 2:1 and follow-up for a period of three months. Phase I is carried out with patients (n=75) from one provider (CAPSBE, 110k inhabitants) in one health district of Barcelona (Barcelona-Esquerra, AISBE). In the intervention group, patients, and corresponding professionals, are managed using Health-Circuit as supporting digital tool, while the control group will receive conventional treatment. Assessment for users, patients and professionals from the two groups (intervention and control), encompasses: (i) Digital literacy; (ii) System Usability Scale (SUS[27]); (iii) Safety; (iv) Satisfaction (Net Promoter Score[28]); (v) self-efficacy; and vi) log-book with incidences and user's suggestions. Moreover, at the end the protocol, design thinking methodologies will be used to evaluate the potential of the digital tool.

Intervention – Each of the patients, intervention and controls, was comprehensively assessed at baseline and had a motivational interview with one case manager aiming to co-design a personalized and comprehensive care plan, as well as to empower the patient for self-management of his/her conditions. Patients and professionals pertaining to the intervention primary care centres were instructed on the functionalities of Health-Circuit. In the control group, both patients and professionals followed standard of care procedures. The digital tool was used for two main purposes: (i) to facilitate management of unplanned events through a direct access to one case manager who could eventually trigger a shared session with other health professionals (primary care, specialists or both); and, (ii) to empower patients' self-management aiming at increasing self-efficacy by using different approaches: period chats, videoconferencing and/or reinforcing the care plan through shared videos or educational material.

3.1.2 Evolution of ICT support & health technology assessment for Implementation Study 1

The developments associated to the CONNECARE platform: SACM + SMS, while being conceptually attractive, showed three main weaknesses regarding its use in the implementation studies in Barcelona. These limiting factors were: (i) Well justified delays in the technological developments due to several reasons described throughout the project; (ii) Poor robustness of the platform at the end of 2017 precluding its use in the implementation study conceived as a real life deployment initiative; and, (iii) Need for further debates within the consortium regarding materialization of the ACM concept and the requirements of collaborative tools.

For all these reasons, we triggered the contingency plan (March 2018) described in D6.4 "Results from Case Study 3" aiming at covering the technological requirements of the implementation studies, but also to prepare interoperability with the health information system at HCB, as well as scalability of the clinical programs. The following three digital health tools were considered for testing:

MyPathway® - The adaptations began on March 2018 and the clinical testing was initiated in January 2019. It was concluded that the simplicity of the solution, if it were robust, would be attractive to cover current unmet needs regarding interactions between patients and professionals. However, MyPathway®

shows limitations to support two key requirements of the CONNECARE project: it does not show potential to support smart adaptive case management for collaborative work, in a flexible manner, among multiple stakeholders: patient/carer and several professionals.

Adaptation of the CONNECARE SMS - It consists of an adaptation of the functionalities of CONNECARE SMS to the requirements of the multimodal prehabilitation service currently deployed at HCB. The adaptation has been performed by EURECAT with close and continuous iterations with the prehabilitation team at HCB-IDIBAPS. Finally, an operational version of the adapted system was available at HCB for testing by early October 2019. By the end of October, we initiated the use the App on routine basis in the perioperative care program (see D6.3 "Results from Case Study 2" and D6.4 "Results from Case Study 3"). In parallel, integration with the health information system at HCB was implemented in a pre-production environment, as part of the setting developed in the Prehabilitation Unit.

Health-Circuit - The team at HCB-IDIBAPS is currently exploring the adaptation of a new digital tool, HEALTH-CIRCUIT covering collaborative work among multiple stakeholders. Moreover, the tool shows further potential to assist case management through complex care paths and generate decision support using intelligent bots. In this regard, HEALTH-CIRCUIT is conceived as a digital tool complementary to the CONNECARE SMS. We believe that its potential to foster both vertical & horizontal integration for CS1, as well as large scale deployment of prehabilitation.

3.2 Lleida

3.2.1 Site adaption of the concept

The integrated care efforts in Lleida's health region during the last years have focused on the empowerment of primary care professionals for the appropriate management of chronic patients. To enable this, several programs fostering the transfer of knowledge from the specialists located in the University Hospitals Arnau de Vilanova and Santa Maria, both located in the city of Lleida, and the network of Primary Care centres spread across a large rural area (over 4300 km^2), have been established. However, while transferring the know-how of specialists to primary care professionals has been very successful, the whole setting had several flaws that CONNECARE was meant to address. First, the electronic medical records in the Hospitals and Primary Care centres are based in two different systems (Argos SAP and eCAP, respectively), which severely limits the transfer of information (up to date it is only possible to look at data from one system to the other but there is not a bidirectional transfer of information among them). Second, the professionals treating a given patient determined the patient's treatment plan at an individual level, thus without consulting to professionals in the other settings of the healthcare system. Finally, the patient empowerment was very low, as it acted on a mostly passive way throughout the whole care path.

The implementation of CONNECARE in Lleida required, first of all, the deployment of a supporting digital platform common to all settings of the healthcare system. The platform, needed to be the hub were all

the professionals from different settings involved in the management of a given patient could exchange information, agree on the best management plan for each patient, and take specific actions in terms of treatment, monitoring and reactions when needed. Therefore, this implied the need of engaging a broad range of professionals and providing them with a fully functional access to the CONNECARE platform. Moreover, this required the emergence of new roles in the organization of the involved services. The already existing hospital case managers (that used to track a few proportion of patients), needed to be reinforced with a CONNECARE-specific case-manager that took the role of both introducing the patient to the CONNECARE platform, and following-up the monitoring of the patients done by the involved health professionals.

The pilot for Implementation Study 1 in the Health care region of Lleida, Catalonia, Spain, focused on home dwelling patients 55+ with chronic conditions and a past history of visits to the emergency room leading to hospitalizations. Patients were recruited during an unanticipated admission to the hospital through the emergency room. These patients, due to their chronic conditions, require a continuum of care from the hospital towards the primary care centres, hence the focus of the pilot was on providing integrated care, monitoring and follow up post discharge for 3 months, using a case management model supported by the CONNECARE digital platform comprised of a mobile app (SMS) and a smart adaptive case management platform (SACM). The main goal of Implementation Study 1 in Lleida was thus to effectively coordinate the post-discharge care between the University Hospital Arnau de Vilanova and University Hospital Santa Maria (both of them located in the city of Lleida) and the network of 23 Primary Care centres in charge of the day-to-day management of patients (spread through the whole extension of the health care region), while enabling an active role for patients and/or carers in the management of their chronic conditions. The study is thus the spearhead of formal community-based integrated care in the region of Lleida, wrapping-up several pre-existing initiatives into a single program. CS1 assessed: (i) the effectiveness of joint/integrated discharge planning of hospitalized complex patients; (ii) the effectiveness of integrated transitional care in the community post-discharge; and, (iii) the added value of a self-management system app.

The implementation of the CONNECARE platform was adapted to the specific conditions in the Health care region of Lleida:

1. The CONNECARE digital platform (SACM and SMS) was translated into Catalan and Spanish, that are the co-official languages in the territory.
2. The Electronic Medical Records (EMR) systems of the hospitals and primary care centres are not homogeneous. This posed a challenge for the integration of the SACM, as two different integrations needed to be tackled and, therefore, only partial integrations were feasible.

3.2.2 Pilot description, inclusion criteria and main study variables

The aim of Implementation Study 1 was to provide continuity of care to chronically ill patients discharged to the community following an unplanned hospital admission with the objective of improving their medical condition and preventing further exacerbation of their condition leading to emergency room visits and additional admissions to the hospital.

The design corresponded to a pragmatic, prospective, implementation study with parallel groups. The intervention group (post-discharge monitoring and integration of community services) was compared with a control group (regular care in another hospital). Control patients were selected from the same wards were CONNECARE patients were recruited and had similar characteristics.

The eligibility criteria were:

- Admission to the ER of University Hospital Arnau de Vilanova and University Hospital Santa Maria because of a Respiratory or Cardiovascular cause (COPD exacerbation or heart failure decompensation)
- Being assigned to a Primary care center of the region of Lleida
- Age 55 +
- Living at home (not in a nursing home) and being discharged back to the community
- Understanding either Catalan or Spanish
- No Dementia/cognitive impairment (GDS < 5)
- LACE score >7
- Successfully passing a basic technological competence test (to assess connectivity and adherence to the use of technology of the patient and/ or the carer
- To sign the informed consent

Main study variables included:

1. The actual use of the ICT tools by patients throughout the period of the study.
2. Patient satisfaction with the integrated care service as well as the digital tools using the following assessment tools: (i) Person-centred coordinated care experience questionnaire; (ii) System usability scale; (iii) Overall satisfaction and net promoter score; and, (iv) Nijmegen continuity of care questionnaire.
3. Staff assessment of the Integrated Care Service and the digital tools using the following assessment tools: System usability scale; and, overall satisfaction and net promoter score.
4. Patient Outcomes including:
    - Improvement in patient's Health-related quality of life as measured by comparing patient status at baseline and after the 3-month intervention using the SF-12 questionnaire.

- Service utilization and costs including hospital services (emergency room visits, hospitalizations, other hospital services) and visits to primary care during the intervention period.
- Cost effectiveness by addressing the improvement in Health-related quality of life relative to the costs dimension.

3.2.3 Recruitment process and Participants

The patient recruitment period for the project in Lleida was July 2018 – June 2019. Potential participants were identified by either the case managers or medical personnel of the Respiratory and Internal medicine wards of the 2 involved hospitals, based on EMR data. Potential candidates were approached by a case manager that conducted the recruitment process and introduced the patient to the CONNECARE platform (intervention group only). All patients received a face-to-face explanation about the study, its purpose, its benefits and what they would actually receive. Similarly, after the recruitment of each CONNECARE program patient, an active search for a matched control with the required characteristics began, although patients in the conventional management arm were not required to pass the basic technological competence test. The patient's recruitment process included: (i) signature of the patient on the consent form, after reading and receiving an explanation of the main points; (ii) preliminary assessment of the patient's health status using several questionnaires, tests and indexes; (iii) installing the applications and providing guidance on the day-to-day use of the applications; (iv) generating the profile of the patient in the SACM platform, and introducing the information of all the involved medical personnel (Hospital, Primary care and social care); and, (v) providing all the required contact information. After discharge, patients in the control group followed standard management in primary care, while patients on the intervention group embraced the CONNECARE program benefitting of a SMS app during 90 days post discharge. All patients regardless of study arm had a 3-months passive follow-up after the initial 90 days standard/CONNECARE management.

The main characteristics of the patients recruited in the CONNECARE arm (n=52) were: 25 (48%) men, mean (SD) age of 82.4 (6.8) years, median (p25-p75) LACE score of 12 (14-17), and mean (SD) Charlson score of 6.7 (2.0). The main characteristics of the patients recruited in the control arm (n=35) were: 21 (60%) men, mean (SD) age of 82.2 (7.8) years, median (p25-p75) LACE score of 13 (15-17), and mean (SD) Charlson score of 7.1 (2.0). None of the differences between CONNECARE and control patients were statistically significant. Only one included CONNECARE patient interacted on his own with the system, the rest of patients interacted with the system through a carer or family member living with the patient (offspring or partner).

3.2.4 Difficulties, problems and barriers encountered

During the recruitment of patients, some difficulties were found by the case managers and involved medical personnel. However, most of those problems and barriers were successfully resolved through the duration of the study, for example:

a. Difficulties with patients/ families/ caregivers and their smartphones:
   - Because initially it seemed very difficult to find patients aged over 65 years with adequate compliance with the use of technology, the limit age to recruit patients was lowered to 55 years or more.
   - The case managers, who recruited most of the patients, had problems contacting the family members that most often carried out the role of caregivers. Specifically, during the morning when doctors visit their patients in their rooms, family members were not available due to job-related obligations. Therefore, case managers had to arrange meetings with these families during the afternoon, thus adapting to their time schedule.
   - The process of installation of SMS and linking monitoring devices took more time than expected because of frequent technical issues (30-40 minutes). To avoid this issue, SMS installation was decided to be carried out by a trained case manager with the remote assistance from EURECAT technicians when needed.
   - In order to overcome the technological limitations of some patients' smartphones (old versions of Android/IOS and/or smartphone brands with UI personalization layers that interfered with the satisfactory installation and use of the SMS) tablets were supplied to the patients to connect though the Wi-Fi they had already available in their own homes.
   - The case manager sometimes had to visit the home of the patient because there was a problem with some devices (ex: connection of a device to the SMS of a given patient) or she had to solve doubts about the use of the SMS in site.

b. Difficulties with other professionals involved:

   The high number of professionals participating in the recruitment and control of patients through the CONNECARE system (in hospital and in primary care), generated the expected occasional technical or usability issues because of lack of training. However, the case manager that was integrated in the hospital team provided any requested support. Such support can be described as follows:

   - Training professionals in the use of the SACM.
   - Providing information on how to carry out any given phase of the CONNECARE process (Case Identification, Case Evaluation, Work-Plan Definition/Monitoring, and Discharge).
   - Confirming that a response is given to any alert or key message received by the health care team of a given patient.

- Supervising that the report of discharge is performed by the corresponding professional.
- Locating the patient in case of an unexpected hospital re-admission during the follow-up period.
- Helping to solve problems of connectivity of the SACM between hospital professionals and primary care professionals.

c. Difficulties with the performance of the SACM and SMS.

Because of unexpected technological issues, sometimes SMS and/or SACM were shut down or the information on the systems was only partially available or delayed (server fall, dysfunctions, bugs). These problems, although usual and expectable when a new system is created and implemented, are often unforeseen and have an undetermined duration. Therefore, it was crucial to try to avoid any inconvenience to the professionals, patients and caregivers operating with the system. Therefore, a parallel communication system for technical issues was created to ease communication in real time between the case managers, key professionals and key engineers working in the maintenance of the system (EURECAT). The aim was to enable quick and reliable communication channels to exchange information between clinicians and engineers about any problem and the problem-solving process. Finally, special attention was given immediately after system upgrades, as it corresponded to well-known potentially critical periods.

3.2.5 A brief description of the intervention

Before hospital discharge, all medical personnel involved in a given patient's management (both hospital and primary care professionals) agreed upon an initial treatment plan based on the current situation of the patient (assessed in situ by hospital professionals), previous experiences and therapeutic approaches (as described by Primary care professionals), and the patient's needs and expectations (assessed directly from the patient and/or carer). The treatment plan not only included the prescription of any required drugs but also specific tasks and goals.

The hospital case manager and involved health professionals monitored, each patient, at least weekly, for three months, using the SACM system, where they could view all the automatically and manually generated data from the patient's SMS and Fitbit apps and respond with feedback or additional instructions. This resulted in the adaptation of the management plan according to the development of the proposed strategies, thus the tasks and goals could be modified through the follow-up period to respond to changes in the patient's situation. The frequency of any required virtual or in situ interventions was determined by the patient's health status and feedback. The case manager was the primary contact point for any technical issues encountered during the whole process by either patients or professionals.

3.3 Israel

3.3.1 Site adaption of the concept

Despite a technologically advanced health care system, with organization wide central electronic medical records, both at the Community healthcare level (primary and secondary care) and in the hospitals, a major challenge for the Israeli healthcare system has been integration and continuity of care between the hospital and the community. The Israel Ministry of Health published draft regulations in 2015 to address this challenge that included the following requirements for both hospitals and Health Plans (responsible for operating community healthcare services and contracting with hospitals): Transfer of medical information between the hospitals and the health plans, reducing hospital readmissions, appointing people responsible for liaison between community services and hospitals, appointment of positions/units responsible for continuity of care in both hospitals and Health Plans and joint discharge planning. Within this context, Assuta Ashdod Hospital, the newest public general hospital (the first to be built in 40 years) which opened in 2017 had as its vision and mission the actualization of integrated care for its region and together with Maccabi Healthcare Services, the second largest Health Plan, put a number of organizational components in place to implement this vision. These included appointment of one of the deputy hospital directors as responsible for integrated care; setting up a Maccabi Integration Unit on the hospital premises, responsible for transitional care in the community for all patients discharged from the hospital; appointing a joint task force to address the identification and development of necessary interfaces between the EMRs of the two organizations; setting up a joint task force together with the Municipality's social services department to develop and implement processes for continuity of care not only between hospital and community healthcare services but social services as well. CONNECARE was an integral part of the plans of both the hospital and the Health Plan for the implementation of integrated care. Given the emphasis of the Israel Ministry of Health on the nationwide implementation of regulations for continuity of care, the CONNECARE project will make a significant contribution to the scaling up of digitally enabled integrated care in Israel.

The major organizational change that was put into place in Assuta Ashdod/Maccabi as a part of the CONNECARE project was the implementation of a digitally supported nurse case management program within the Maccabi Integration Unit to provide close monitoring and follow up for 3 months for elderly chronically ill patients discharged home after an unplanned admission to the hospital through the Emergency department.

Thus, Implementation Study 1 in Assuta Ashdod Hospital in Israel focused on Maccabi home dwelling patients 60+ with chronic conditions with an unplanned admission to the hospital through the emergency room. These patients, due to their chronic conditions, required multiple services in the community post-discharge, hence the focus of the pilot was on providing integrated care, monitoring and follow up post discharge for 3 months, using a case management model supported by the CONNECARE digital platform comprised of a mobile app (SMS) and a case management platform (SACM). The coordination of post-

discharge care was the responsibility of Nurse Case Managers in the Maccabi Integrated Care Unit that is physically located in the Assuta Ashdod Hospital, beginning with joint discharge planning while the patient was still hospitalized followed by a discharge plan coordinated with hospital medical and nursing staff and the patient's primary care doctor.

The aim of the deployment of implementation study 1 in Israel is to demonstrate the effectiveness of digitally supported integrated care for decision makers in order to facilitate its large scale adoption across the healthcare system. Therefore, Implementation study 1in Israel addresses the following questions:

1. Does integrated care, as defined in the CONNECARE model (digitally supported post-discharge case management) improve post-discharge outcomes including improved physical activity, reduced emergency room visits, and reduced readmissions to the hospital?
2. Are older adults willing and able to use digital technology (Fitbit watch and CONNECARE SMS app) as part of their recovery process post-discharge?
3. Does the close monitoring of the patient post discharge, supported by the CONNECARE digital technology, improve patient adherence to treatment plans?

The implementation of the CONNECARE platform was adapted to the specific conditions in Assuta Ashdod and Maccabi:

1. Due to the high proportion of Russian speaking elderly people within the Maccabi population, the CONNECARE app was translated into Russian as well as Hebrew
2. The Israeli healthcare system is a National Health Insurance System with four autonomous Health Plans (of which Maccabi is the second largest) that have a contractual relationship with hospitals and each Health Plan as well as each hospital has its own Electronic Medical Record System. This posed a challenge to integration of the SACM (the case management platform) with these systems which led to two major implementation decisions:
    a. To use the SACM as a standalone system, not directly integrated with either EMR
    b. To limit the direct use of the SACM to the Nurse Case managers who were responsible for integrating the relevant information between both EMR systems and the SACM.

Coordination with hospital staff on one hand and Maccabi primary care and community healthcare services on the other hand was carried out through the two EMR systems. Thus, communication between the Nurse Case Manager and the primary care physician was mediated by the Maccabi EMR, supplemented by telephone when needed.

3.3.2 Pilot description, inclusion criteria and main study variables

The aim of CONNECARE Implementation study #1 was to provide continuity of care to chronically ill patients discharged to the community following an unplanned hospital admission with the objective of improving their medical condition and preventing further exacerbation of their condition leading to emergency room visits and additional admissions to the hospital.

All patients with an unplanned admission through the ER who met the following conditions were potentially eligible for the study:

- Age 60 +
- Living at home and not in a nursing home
- Maccabi insured member
- No Dementia/cognitive impairment
- Capable of using mobile apps
- Ambulatory – not bedridden
- Expected to require more than two interventions after discharge

The study design is an observational matched control group study. The intervention group (post-discharge monitoring and integration of community services) was compared with a matched control group (regular care in another hospital). For each patient in the intervention group, 2-3 "matching" patients were identified from the Maccabi's database, using a three step matching approach. In the first step, matching between the two groups used the following variables: sex, age group (groups of 5 years), type of hospitalization and/or procedure code, date of hospitalization (same month, or a month before or after). In the second step, additional matching was done between the patients in the two groups based on inclusion in the same disease registries (Cardio, Diabetes, Blood pressure, Cancer, Kidney). In the third step, additional matching was done between the patients in the two groups based on medical costs in the year prior to hospitalization (sum of 12 months) divided into 3 groups of deciles. Main study variables include:

1. The actual use of the ICT tools by patients throughout the period of the study
2. Patient satisfaction with the integrated care service as well as the digital tools using the following assessment tools: (i) Person-centred coordinated care experience questionnaire; (ii) System usability scale; (iii) Overall satisfaction and net promoter score; and, (iv) Nijmegen continuity questionnaire.
3. Staff assessment of the Integrated Care Service and the digital tools using the following assessment tools: (i) ACT@Scale - Advancing Care Coordination and Telehealth questionnaire adapted for CONNECARE; (ii) Clinician support for patient activation (CS-PAM) questionnaire adapted for CONNECARE; (iii) System usability scale and overall satisfaction and net promoter score;4. Patient Outcomes including:
    i. Improvement in patient functional, emotional and health status as measured by comparing patient status before and after the intervention using the following assessment tools:
        - Barthel Index
        - Lawton Index
        - SF12

- HADS
- EQ-5D
- Sweet 16

ii. Service utilization and costs including hospital services (emergency room visits, hospitalizations, other hospital services), visits to primary care and specialist doctors in the community, and pharmacy by the intervention group as compared with the control group.

iii. Cost effectiveness and Cost benefit–Cost effectiveness is measured by comparing the difference in net expenditures for the intervention group and the control group taking into consideration the additional costs for implementing the digitally enabled integrated care intervention. Cost benefit will be addressed by addressing the improvement in patient functional, emotional and health status relative to the cost dimension.

3.3.3 Recruitment process and participants

The patient recruitment period for the project in Israel was July 2018 – August 2019. Every morning the nurse case managers (NCMs) received a list of hospitalized patients, aged 60+ who are members of Maccabi Healthcare Services. In order to decide whether the patient was appropriate for the study according to inclusion criteria, the nurses checked for details on each patient in the hospital's and Maccabi's EMRs. With the list of appropriate patients, the nurses made their daily rounds in the hospital's departments. Patients who were in their rooms received a face-to-face explanation about the study, its purpose, its benefits and what they would actually receive, accompanied by a brochure in Hebrew or Russian. Patients who were not in their room or patients, who asked for time to think and consult, were visited again.

Immediately after the patient's consent to participate in the study or at a time that was suitable and convenient for both the patient and the nurses, the full recruitment process was carried out. Most patients were recruited in the hospital during their hospitalisation before discharge, but in special cases patients were recruited a few days after discharge at the hospital or at their home. The patient's recruitment process included: (1) signature of the patient on the Consent Form, after reading and receiving an explanation of the main points (2) preliminary assessment of the patient's health status using several questionnaires, tests and indexes (3) installing the applications and providing guidance on the day-to-day use of the applications, (4) providing a list of ways to contact the nurses in case of need, and (5) building the initial treatment plan.

3.3.4 Difficulties, problems and barriers encountered

During the recruitment of patients, the nurses encountered some difficulties. Problems and barriers in the process were treated and resolved during the duration of the study, for example:

- The CM needed the help of the nurses on the wards to locate the patients. During the project, staff meetings were held several times with the head nurses resulting in improved cooperation.
- The Maccabi nurse CM encountered an information security problem that prevented them from obtaining lists of hospitalized patients. The Assuta research team manually provided the lists every morning to the CM nurses.
- Initially, the nurses' rounds in the departments conflicted with the rounds of the medical staff, and the patients were not available to talk or were distracted. Subsequently, the nurses' rounds hours were coordinated with the department staff, and the nurses knew the optimal time to visit each department to recruit patients.
- Patients did not find it convenient to come to the nurses' office for the recruitment process, so the procedure was performed at the patient's bedside. For this purpose, two large tablets were purchased for the two nurses, so they could use the SACM system at any location.
- The recruitment process took much longer than expected, between 40 minutes to an hour, mainly because of the amount of time it took to go over the consent form together and to download, install and connect the two applications. In order to shorten and streamline the process, two improvements were made:
    - Some of the questionnaires in the evaluation process were printed on paper and given to the patient to fill out alone (if the patient's condition allowed it), so that the nurse could take care of the other stages of the process.
    - The two nurses performed the recruitment process together (as much as possible) so that one performed the assessment for the patient while the second dealt with the technology installations.

It should be noted that Assuta Ashdod hospital is a newly built hospital that only became fully operational in November 2017. At the time of CONNECARE pilot implementation, the hospital had only been in full operation for 7 months and consequently the project encountered problems due the dynamics of consolidating operational policies and procedures in a totally new hospital with a totally new staff.

3.3.5 A brief description of the intervention

After the patient's recruitment, Maccabi's nurse case manager created an initial treatment plan, in accordance with the medical and nursing discharge plans from the hospital, the patient's data in Maccabi's EMR, and the patient's needs. She also informed the patient's family physician of his/her patient's involvement in the project, and asked for any specific tasks, goals or medical orders that the family physician might want to add.

The nurse monitored each patient, at least weekly, for three months, using the SACM system, where the nurse could view all the automatically and manually generated data from the patient's SMS and Fitbit apps and respond with feedback or additional instructions. During the follow-up period, the nurses added, deleted, and made changes to the treatment plan, as needed. Depending on patient's need and

compliance with the treatment program, the nurse increased the frequency of her interventions, including phone calls and home visits.

The nurse also assisted the patient with any problems or bureaucratic hurdles in the hospital and/or Maccabi, and, when necessary referred the patient's requests to the administrative secretary for individual assistance with scheduling appointments.

Broad professional engagement in the CONNECARE program in Israel, was somewhat lacking. Despite repeated attempts by project staff to build a joint discharge-plan by the nursing staff in the hospitalization department with Maccabi's NCMs, this process was implemented only in a very limited way. Also, other medical or social professionals in the community besides Maccabi's NCMs, were not involved enough, and treated the patient in the traditional way without significant integration that could have been created under this project. The family physicians were aware of the patient's participation in the study, but while they saw the patient and treated him as appropriate post-discharge, most did not participate in planning a personal treatment plan within the CONNECARE framework.

3.4 Groningen

3.4.1 Site adaption of the concept

The ambition of the UMCG as an academic and tertiary hospital in the Netherlands is to provide the right care, for the right patient, at the right time. This means that acute and complex care is centralized in the region, and chronic care patients are managed largely outside the walls of the hospital. Hospital services and expertise will still play an important role, i.e., have a prominent position in society, yet only at the moment a citizen falls ill or has an accident. Care on hospital premises will be limited, whereas ambulant assistance at home will become the norm. In order to provide such a supportive role, supplementation and innovation of care pathways by using digital tools and wearables embedded in a broad e-Health system is of vital importance. The IT systems and Electronic Medical Record (EMR) of UMCG have recently been updated and modernized. This obviously is essential, and provides conditions and opportunities for further development. In the near future communication with Personal Health Records (PHR) will become a reality, and thus a prospect of extremely rich and complex data emerges. This will foster collaborating with experts in AI and big data, and allow further personalization and tailoring of prevention and treatment. Existing research infrastructures such as Lifelines and EPIC may be used to expand and enrich e-Health systems, and support the scaling up of activities in the region. A central theme in the activities outlined may be support of a broad implementation of the Personal Health Environment (PHE) in the UMCG, as a digital system owned and managed by citizens. This PHE will comprise all relevant information on health, well-being and care utilization. In line with this ambition is the development and implementation of CONNECARE, providing a platform for UMCG to develop and test an ICT management system and a self-management system (app) with integrated ambulant equipment

(wearables) for patients. This also entails developing a smart adaptive care management system for professionals to interact and manage patient health.

The aim of CS1 in Groningen is to co-design, develop, and evaluate a novel smart, adaptive self-support integrated care system for care management of the elderly oncological patients in the postoperative period. To this end, the following questions were formulated:

- Is a novel ICT-supported integrated care management system with a mobile application and additional smart-devices for remote home monitoring in asthma and COPD patients' feasibility?
- Under which conditions are patients able and willing to use the CONNECARE IT system and connected devices?
- Does the implementation of the CONNECARE system lead to improvements in disease management and severity?

In Groningen, CS1 focused on asthma and/or COPD community dwelling adult patients (minimal age 18 years) and referred by primary care services. These patients often encounter difficulties in managing their disease, for example by exhibiting low levels of self-management skills and adherence to disease management protocols. Therefore, the aim of this study was to provide use-centred and ICT supported management systems allowing for monitoring disease management at a distance and avoiding exacerbations and ultimately care consumption. The SMS was co-developed with the end-user and used by patients to monitor disease management and patterns in physical activity. Communication with the case manager and information exchange was facilitated by the SACM, allowing also for data capturing used for evaluation purposes. Coordination of activities was performed by the case manager working both in the community at Certe Laboratories and at the department of general practice of the UMCG.

The CONNECARE SMS was executed in an existing well implemented integrated care service for asthma and COPD patients in the North of the Netherlands called the Asthma/COPD-service [13]. In this service, primary care physicians refer patients with respiratory complaints or a diagnosis of asthma / COPD for assessment. Patients receive lung function assessment, evaluation of burden of disease, medication evaluation and other diagnostics. All collected data is transferred through the internet to pulmonologist in a local hospital. The pulmonologist assesses the data and sends diagnosis and treatment advice to the general practitioner.

Implementation of the CONNECARE ICT was done as a stand-alone, as integration with existing IT systems was not possible at the start of the study. We therefore also included patients through the Dutch Lung foundation. These were primary or secondary care patients not treated by the Asthma/COPD-service.

3.4.2 Pilot description, inclusion criteria and main study variables

All patients with an unplanned admission to primary care, advice/diagnosis, return home with integrated follow-up were eligible for inclusion. Also patients diagnosed with asthma or COPD interested in this study

by the UMCG patient panel or the Dutch Lung foundation could participate. A pragmatic longitudinal trial was set up with 90 patients in total. These patients were assessed at baseline, after three months and after six months with different questionnaires. All patients received the CONNECARE SMS including activity tracker (Fitbit). Our hypothesis was that patients who have used the CONNECARE SMS for 6 months are able to manage their asthma or COPD more effectively compared to baseline. Therefore, the COPD health status or asthma control is expected to improve during the intervention.

Inclusion criteria were:

- Adults referred to the AC-service 18 years and older, from the UMCG patient panel and the Dutch Lung foundation
- Confirmed diagnosis of asthma, COPD or asthma/COPD overlap syndrome
- Participants should own a tablet or smart phone
- Comprehension of the Dutch language (reading and writing)
- Willing to sign informed consent and answered the questionnaires that are provided
- In possession of tablet or smartphone

Study variables included:

- The actual use of the ICT tools by patients throughout the period of the study.
- Patient satisfaction with the integrated care service as well as the digital tools using the following assessment tools: (i) Person-centred coordinated care experience questionnaire; (ii) System usability scale; (iii) Overall satisfaction and net promoter score; and, (iv) Nijmegen continuity of care questionnaire.
- Staff engagement and experience with the ICT system and digital tools.
- Intervention effectiveness - Patient outcomes and use of resources
- Costs – benefit analyses

3.4.3 Recruitment process and participants

Patients were included from the Asthma/COPD-service, from the UMCGs patient panel and via the local lung foundation. Potential eligible patients were identified and asked to participate in the study, starting with an explanation of the purpose of the study. In case the patient consented to participate the informed consent form was signed. Next, home visits were made by the case-manager in which and patients received instructions for using the CONNECARE system, including the installation of the CONNECARE SMS and Fitbit app and how to synchronize the devices. Also questionnaires were collected (at T0) as a baseline measurement. The start of the intervention was in January 2019. Last patient in will be July 2019. Last patient out will be September 2019.

3.4.4 Difficulties, problems and barriers encountered

During all stages of development, recruitment and implementation of the CONNECARE system barriers were encountered by either the users, care professionals, case managers, students, and IT personnel. The main challenges are listed below. All items were resolved during the duration of the clinical studies.

- Feasibility studies performed with a mock-up version of the CONNECARE system suggested important bottlenecks with the usability of the app, especially with the location of tabs and the font size of text.
- Preliminary test studies with the CONNECARE SMS showed that the application can be difficult to use especially for elderly. Therefore, it was important to develop the CONNECARE SMS according to the comments of the patients. Therefore, we are training patients in using the application before patients start using the application.
- The navigation in the app improved substantially after the qualitative feedback of patients.
- Attrition is a risk factor because if too many patients stop filling in the questionnaires that power will drop. However, we took into account a 10% attrition rate.
- Time was another limiting factor because the start date of the study was postponed for six months. We had therefore less time to include patients.
- Additional students were attracted between September 2018 and September 2019 to support in patient recruitment, instructions, data collection and evaluation and solving problems with the digital systems used in CONNECARE.

3.4.5 A brief description of the intervention

We have expanded the inclusion of patients to the UMCG patient panel and patients from the Dutch Lung foundation because there were not enough patients that could be approached through the Asthma/COPD-service.

Patients were randomly divided in control or intervention group. Patient inclusion was accompanied by a face-to-face appointment, information letter about the study and its objectives and an informed consent form. During the face-to-face meeting goals were set in terms of self-management and physical activity. Also the GP and, if necessary, the pulmonologist was consulted. All patients received the CONNECARE SMS including activity tracker (Fitbit). Its functionalities were explained. The case manager remained the focal point of contact for questions or problems with the ICT systems experienced by the patient. Patient progress was monitored by the case manager, assisted by students, using the SACM system and by telephone contact if necessary.

We provided 50% of the patients with 2-weekly messages about the benefits of physical activity for respiratory patients and with practical advices. We will evaluate the effects of these messages on their step count and compare them with the 50% of patients who did not receive these messages.

3.5 Summary – all sites

As study deployment was performed in real-life settings all processes and technologies had to be adapted to local settings and procedures currently in place. Also changes occurring during phases of preparation and execution of implementation studies and use of the CONNECARE ICT systems and connected devices needs to be factored in. Still, following the end of patient recruitment a fair amount of homogeneity was observed across clinical sites, for instance in the main study variables included. However, considerable heterogeneity still resided in both the population targeted for the CONNECARE study, and also in the way monitoring and follow-up of patients was organized. We believe that this reflects the action based research approach taken by the consortium, aimed at direct clinical testing of the ICT systems that were developed. Importantly, all clinical sites contributed to the development of the system and its implementation, making important observations and changes to the system and the way it was delivered in its final form. Important advances have been made in customizing CONNECARE ICT systems, fine-tuning functionalities for both patients and professionals to promote optimal usage and satisfaction among end-users. Also, progress can be seen in further developing and testing integration into local EHRs, and the use of data repositories in testing the SACM and recommender systems.

The definitive study protocols used in the implementation studies still displayed marked differences across clinical sites. The most prominent of which was the role of the case manager, responsible for patient identification, recruitment, providing instructions, data collection, monitoring and follow-up. All sites, except Groningen, had a care professional in charge as case manager, sometimes assisted by other professionals. Either a nurse, a clinician or a researcher were in the lead, assisted by other care professionals either located in primary, secondary or community care and in some cases also students to assist in patient recruitment and data collection. As such the role and activities performed by the case manager was largely comparable between the clinical sites, albeit the professional role differed. Importantly, evaluation of the engagement of professionals was performed in all clinical sites, although the definitive number of professionals that were asked to participate varied. This again related primarily to differences in the way CONNECARE was implemented and adapted to the needs and requirements in local clinical settings. Also, as implementation studies differed in their study design, viewing execution of the study protocol either as an observational- or as an intervention study led to different agreements on who was in charge of case management and follow-up of patients.

Throughout the implementation studies, patient identification and recruitment was primarily organized by screening electronic medical records either in primary or secondary care. In addition, collaboration with patient organizations and primary care organizations was set-up in order to improve recruitment rates. Reasons for failure of patient recruitment included discharge to a nursing home or patients suffering from too high disease severity. Also mental burden of using the self-management system and connected devices was mentioned. Continuous refinement of recruitment procedures was executed in all clinical sites, which led to important increases in recruitment rates.

All sites encountered a wide range of barriers and difficulties. One important barrier that was overcome included lowering the age for study inclusion, as was performed in some sites, in order to reach the required recruitment targets. A previously mentioned improvement to pre-install all applications on the devices was successfully implemented by some of the partners. This improved patient adherence to the study protocol. The face-to-face contact between case manager and patients/relatives also proved an effective strategy to improve retention of information, instructions and their willingness to participate. Taken together, implementation studies needed to be adapted to local procedures, needs and beliefs to be successfully integrated in clinical practice.

4. Implementation Study 1 Results

The results of the clinical studies presented here are updated to include all patients in the implementation studies in all sites. As such these represent the final results. Following the general Introduction and overall concept of Implementation study 1, we will provide a detailed description of implementation studies per clinical site, and present the results. The description of the studies includes the site adaptation of the CONNECARE concept, description of inclusion criteria and main study variables, the process of patient recruitment, barriers and challenges encountered and a brief overview of the intervention. The results sections includes (1) actual recruitment rates achieved, (2) reasons for patient drop-out, (3) patient assessment of implementation of the integrated care service and model, (4) issues reported in the implementation log– organization and process issues, (5) patient engagement and actual usage of ICT tools, (6) patient and staff satisfaction with the technology, (7) issues with the digital tools recorded in the implementation log, (8) intervention effectiveness - patient outcomes and use of resources and (9) costs and costs benefit analyses.

4.1 Barcelona

4.1.1 Protocol IA - Implementation of home hospitalization at health district level (AISBE)

Since the end of data collection in November 2018, a substantial part of the activity in this protocol has been devoted to overcome limitations on data management. As already mention, the analysis of the protocol requires articulation of information from three different data sources: (i) SAP at HCB, (ii) eCAP at Primary Care; and, (iii) Catalan Health Surveillance System (CHSS). Potential problems in the application of GDPR were already identified as a risk factor in D6.1 “Study release feasibility for the three clinical studies”, as mentioned in the introductory section of D6.4 “Results from Case Study 3”. Such limitations have been progressively solved, but the final analysis is still underway which has impact on the data analytics of the entire study group (***see* ANNEX I**), as well as in Protocol IIIA.
The current document provides a complete analysis of characteristics of patients’ characteristics, main health outcomes and cost analysis for a subset of 200 patients out of the 620 individuals of the entire study group (Figure 1). Moreover, comparisons between this subset of patients and the entire study group exploring representativeness are displayed.

Value generation of the HH service *(see ANNEX I)* – Table 1S depicts the main characteristics of both home hospitalization and usual care groups in terms of: (i) socio-demographics, (ii) use of healthcare resources from the HCB dataset (SAP) previous to the current hospitalization event, (iii) multi-morbidity, (iv) percentage of patients into the three main top risk categories used in Catalonia within the Health Plan 2011-2015, and, (v) assessment of patient reported outcomes in terms of patients’ experience on transitional care, on continuity of care and on quality of life at 30-days after discharge. Figure 1S displays

frequencies of the top ten diagnoses in the two groups using ICD codes. While identifying some differences between home-based hospitalization and usual care patients, the two groups show reasonable groups for comparability (***ANNEX I***). Moreover, Table 1S indicates that the intervention group of 200 patients is representative of the overall intervention group of 620 patients. Short-term availability of CHSS data will facilitate to build-up a control group for the overall study group of 620 patients using an inverse probability of treatment weighting (IPTW [26]) approach, as mentioned above. This scenario will ensure enhanced comparability between intervention and control groups. Consequently, it will be enriching the current analysis and strengthening our conclusions.

Table 2S provides information on core health outcomes after discharge, as well as on patient reported outcomes on transitional care needs and on frailty. Overall, the analysis carried out shows significantly better health outcomes, and enhanced patient reported outcomes at 30-days after discharge, in the home-based hospitalization group as compared to controls. Moreover, the evaluation of operational costs of the two groups, displayed in Figure 2S, clearly indicates cost savings for the intervention group which shows approximately half-cost compared to the usual care group. It is of note that savings are seen in most of the items analysed in the current study, but two predominant components wherein usual care is clearly more expensive than home hospitalization: personnel and structure.

Despite the current report corresponds to a still ongoing analysis, we can clearly conclude that the hospitalization avoidance offers four major positive outcomes.

1. Health value generation both at provider (HCB) and at health system level (single-public payer, CatSalut).
2. Enhances the potential of HCB for performing more highly specialized interventions due to increased availability of hospital beds
3. Shows sustained high degree of engagement &satisfaction of health professionals and patients formally assessed in [12] and through surveys carried out as part of the QA (see ***ANNEX I***, Table 1S) of the service.
4. Enhances the interactions between hospital and community-based care, as addressed in Protocol IIIA.

Implementation strategy & transferability – The description of the two-steps implementation strategy (2006-215 and 2016-2018) following the CFIR [17-18] is displayed in Table 3S. The exercise provides a comprehensive view of the characteristics of the implementation process followed in order to achieve sustainability of the service and allows identification of facilitators/barriers encountered in the deployment process. Moreover, the analysis performed helps to define the transferability potential of the home hospitalization service and contributes to shape site-specific strategies for transferability. The later must also take into account the maturity of target ecosystem (Scirocco), as analysed in detail in D7.3 “Evaluation of clinical studies deployment and PDSA iterative cycles”.

Finally, proposals of KPIs for long-term follow-up of the home-hospitalization service aiming at monitoring quality of scale-up after the initial deployment phase are reported in Table 4S.

Technological evaluation – As indicated above, and further described in D6.4 "Results from Case Study 3", the digital support to the HH&ED service during the study period was essentially done using already existing technology in AISBE (i.e., call centre/videoconference and laptops connected to the virtual private network of the hospital). The following additional needs for Protocol IA, in terms of technological support, were identified during the project lifetime: (i) a proper adaptive case management approach providing flexibility to professionals for management of multi-morbidity and to select specific tasks to efficiently face unexpected events that often occur in the current scenario; and, (ii) enhanced support to collaborative work among stakeholders. In the later, we distinguish two different phases showing different patterns of interactions among stakeholders: (i) within home-based hospitalization; and, (ii) shared agreements between specialized and community-based care during the transitional care period (30-days post discharge) and on a long-term basis for management of complex cases.

Overall, lessons learnt after testing MyPathway (Protocol II), SMS-xCARE (D6.3 "Results from Case Study 2"), CONNECARE platform (Protocol IIIB) and Health-Circuit (Protocol IIIC) provided solid elements to formulate proposals aiming at facing the needs for digital support embedded into different service workflows involving multi-morbidity management. These proposals are formulated in D6.4 "Results from Case Study 3" and further discussed at consortium level within WP7.

4.1.2 Protocol IB - Health risk assessment for enhanced clinical decision support in patients under HH/ED

Please, see **Annex I** for the manuscript **Predictive Modelling of 30-day Mortality and Readmission Risk from Multilevel Data: A Case Study on Patients Hospitalized at Home**, in preparation for submission to Scientific Reports).

Abstract

Home hospitalization (HH) is a healthcare alternative capable of providing high standards of care in the patient's home. A previous study on the HH program of Hospital Clinic of Barcelona over a 10-year period (2006-2015) clearly demonstrated its effectiveness and high level of user's acceptance. However, health-risk assessment is still needed so as to provide support for clinical decision made at patient admittance and discharge.

To this end, this paper proposes a machine-learning approach for the early-prediction of hospital readmission and death after HH. It is based on a multilevel solution since it relies on the hypothesis that health-risk assessment could be significantly improved by combining clinical, biological and population-based data.

Predictive models were evaluated on a real-world database including 1,832 cases having been admitted to the HH program of Hospital Clinic of Barcelona from January 2012 to December 2015. The results show a prediction performance, captured by the Area Under the ROC Curve (AUC), of 0.73 for the prediction of readmissions and of 0.90 for mortality risk. Moreover, this study provides directions for the translation of health-risk assessment models to daily clinical practice.

4.1.3 Protocol II - Home-based non-invasive ventilation

See **Annex II** for the manuscript **An Integrated Care Intervention Supported by a Mobile Health Tool in Patients Using Noninvasive Ventilation at Home: Randomized Controlled Trial**, (accepted for publication in JMIR).

Abstract

Background: Home-based non-invasive ventilation has proven cost-effective. But, adherence to therapy still constitutes a common clinical problem. We hypothesized that a behavioural intervention supported by mHealth can enhance patients' self-efficacy. It is also accepted that mHealth-supported services might enhance productive interactions among the stakeholders involved in home-based respiratory therapies.

Objectives: To measure changes in self-efficacy in patients with chronic respiratory failure due to diverse aetiologies, during a follow-up period of three months after the intervention. Ancillary objectives were assessment of usability and acceptability of the mHealth tool, as well as to learn on its potential contribution to enhance collaborative work among stakeholders.

Methods: A single blinded, single centre, randomized controlled trial was performed on 67 adult patients with chronic respiratory failure undergoing home-based non-invasive ventilation, between February and June 2019. In the intervention group, a psychologist delivered a face-to-face motivational intervention. Follow-up was supported by a mHealth tool which allowed patients to introduce the number of hours of use per day and problems with the therapy. Advice was automatically delivered by the mobile tool in case a problem was reported. The control group received only usual care.

Results: Self-efficacy did not show differences after the intervention (mean[SD]=3.4[0.6] vs 3.4[0.5], *p*=.514). No changes were observed neither in adherence to therapy nor quality of life. Overall, the mHealth tool showed good usability score, 78; high acceptance rate, 7.5/10; user friendliness, 8.2/10; and, the ability to use the app without assistance displayed a mean score of 8.5/10. Patients' perception of continuity of care and person-cantered care showed high scores.

Conclusions: The mHealth tool did not improve patients' self-management. Acceptability of the app might indicate potential for enhanced communication among stakeholders. The study contributed to identify key elements required for a mHealth tool to provide effective support to collaborative work.

Trial Registration: NCT03932175 (clinicaltrials.gov, April 30, 2019)
Keywords: Behavioural change, eHealth, Non-invasive ventilation, Mobile Health, Chronic Diseases

4.1.4 Protocol IIIA - Continuum of care between specialized and community-based services.

As described above, the study is still under the data analytics phase. Completion of results is expected within the first trimester of 2020.

4.1.5 Protocol IIIB - Evaluation of the Connecare platform in primary care

The CONNECARE platform and its main components were assessed for all study protocols done in Barcelona throughout the project lifetime. The technological report can be found in D6.4 "Results from Case Study 3" (see also **ANNEXES I and II**). However, a specific study was undertaken to test the last version of CONNECARE, customized for Lleida, in 20 clinically stable patients studied in a primary setting, as reported in detail in the current **ANNEX IV**.

4.1.6 Protocol IIIC - Evaluation of Health-Circuit

The outcomes of the technological assessment are reported in **ANNEX V**.

Summary results of CS1 in Barcelona

Integrated care services – Completion of ongoing tasks associated with CS1 in Barcelona will provide the following results in terms of digitally enabled integrated care services:

1. **Hospital avoidance (HH) and early discharge (ED)** (Protocol IA) showed value generation, as compared to usual care, in a real world setting. The service clearly generated healthcare efficiencies both at provider and at health system levels. Ongoing activity, undertaken in collaboration with other providers, policy makers and the single-public payer (CatSalut) can contribute to enhanced standardization of the service at regional level. Moreover, the analysis of the service implementation using CFIR provides the basis for defining strategies for transferability to other sites. Finally, the proposed KPIs may contribute to long-term monitoring of quality of the service after large-scale adoption.
2. **Risk assessment for patients under HH/ED** (Protocol IB). The machine learning approach described in the document provides a good basis to assess likelihood of success of the service for evaluation of candidates at entry. The predictive modelling proposed can be also useful to customize transitional care services according to patient's risk. The ongoing work at HCB will serve to implement clinical decision support tools embedded into the service workflow aiming at dynamically improving prediction and care. The approach is also useful for other services, such as perioperative care.
3. **Home-based NIV** (Protocol II) - The manuscript accepted in JMIR despite generating negative results in terms of self-efficacy, provides valuable information on technological requirements of this type of service wherein a twofold aim is envisaged, that is: (i) enhancing patients'

empowerment and adherence to therapy, and (ii) facilitating productive interactions among various stakeholders (specialist, primary care professionals, industry and patient/carer) involved in the service workflow. It is of note that both aspects are shared by a number of healthcare services. Finally, a major lesson learnt is that assessment of usability/acceptability by patients and professional is needed but it is clearly not enough in order to assess an adequacy of digital support, as elaborated in WP7.

4. **Community-based services** (Protocol IIIA) **–** This still ongoing study will provide highly valuable information for generating recommendations to improve both vertical and horizontal integration.

Technological support – Despite a positive recognition of the conceptual approach adopted by the project, the analysis of the CONNECARE platform did not identify potential for its integration into the hospital information system (HIS) at HCB, nor for scalability of some of the components. Separate assessments of the three main technological components: SACM, SMS and the recommender system were recognized as showing potential in a research scenario, but major limitations for evolving to products, except for the case of the SMS. A summary analysis of the main components of the CONNECARE platform follows below.

SACM – Three main messages are conveyed:

1) The SACM should be conceived as an integrative component of the HIS, displayed in the clinical workstation of the professionals. Alternatively, the ACM concept can be build-up into specific applications or within digital tools supporting collaborative work;
2) The SACM should be developed in such a way that the professional can first create/edit tasks and then select and/or combine them to conform care pathways adapted to the specificities of the patient; and,
3) Future developments of SACM need to take into account heterogeneities, and evolutionary changes, of health professionals working in real world settings. Consequently, their contribution into the co-design process is mandatory.

SMS – It shows great potential to be a source of future specific products, if the current SMS can have a backend other than the SACM and if such backend takes into account the need for interoperability with existing health information systems or with other digital tools supporting collaborative work. This was the approach taken by Barcelona in Protocol IIIC and in Case Studies 2 (D6.3 “Results from Case Study 2”) and 3 (D6.4 “Results from Case Study 3”).

Recommender tool - The conceptual approach, as well as the specific design generated throughout the project lifetime, are highly valuable contribution. Relevant challenges identified in Protocol II and in D6.4 “Results from Case Study 3” will be further developed in WP7.

4.2 Lleida

4.2.1 Recruitment results

At the end of July 2019, the recruitment of patients for Implementation Study 1 was completed. From July 2018 to July 2019, a total of 112 patients were found to be eligible according to the EMRs. Of them, 60 patients could not be recruited: 42 patients did not pass the technological test and 18 patients did not agree to participate in the study. On the other hand, 52 patients were recruited. An overview of the recruitment of CONNECARE patients is provided in Figure 3. Up to 48 CONNECARE patients in Implementation Study 1 completed the 3-month post-discharge follow up and were discharged from the program. The losses of follow-up corresponded to 2 drop-outs and 2 deaths. Similarly, up to 35 control patients were recruited, of whom 28 completed the follow-up. The recruitment chart is provided in Figure 4. The main cause for the low number of recruited controls (the initial target was 50), was the need to maximize the recruitment of CONNECARE patients, thus slowing down the recruitment of controls. In this sense, it is key to note that the reluctance of aged patients spread across a large territory (over 4300 km^2) to travel to the hospitals located in the city of Lleida for the completion of the different phases of the study resulted in the need for home visits to conclude the patients' participation in the study and complete all the discharge forms.

Figure 3 - Overview of patient participation and recruitment.

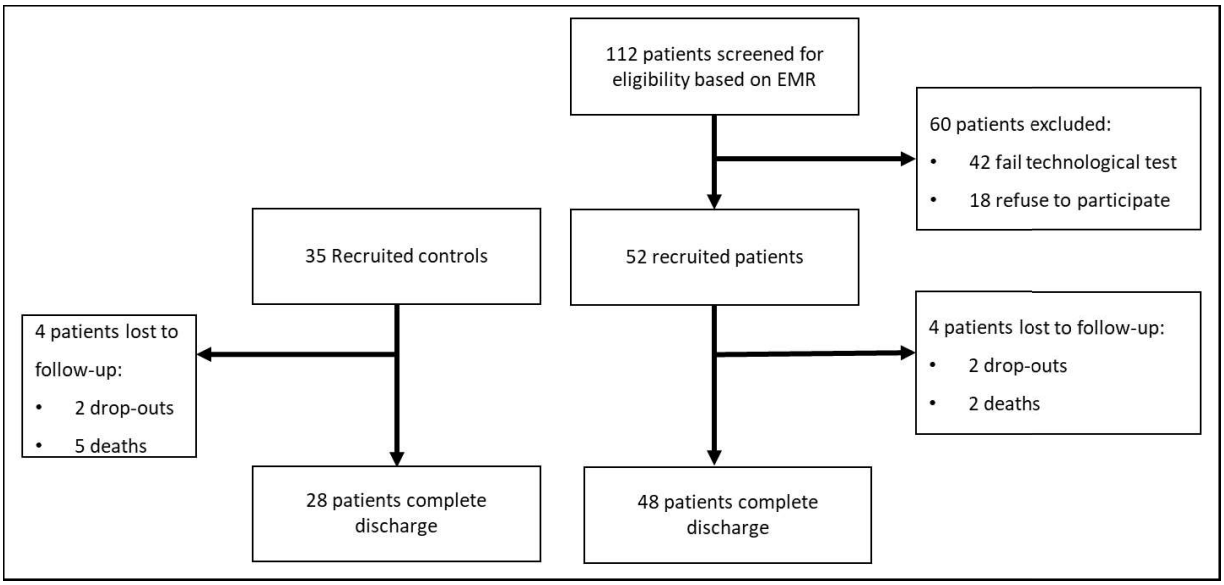


Figure 4 - Study recruitment chart.

4.2.2 Main reasons for failure to recruit and for patient drop out

The main reasons of failure to recruit were:

- The patient was discharged to a nursing home.
- The patient or the family were not interested in participating because they anticipated difficulties to be compliant with the process of monitoring clinical variables.
- The patient had an outdated smartphone in which it was not possible to install the SMS system.
- The patient had an IOS smartphone at the time were the SMS did not support IOS.
- The patients and/or caregivers used smartphone exclusively for phone calls and messages and they were not been keen on learning how to use apps (SMS).
- The patient did not want to overwhelm the caregiver with additional work, especially when this role is held by a family member.

The main reasons for patient drop-out were:

- The caregiver or the patient were not willing to comply with the program, regardless of being appropriately informed during the recruitment.
- After a short stay at home after discharge the patient decided to go to stay in a nursing home because the degree of care that he needed couldn't be supplied by the family or his degree of dependence became more than he or her family expected.
- The patient reconsidered the decision of participating few days after hospital discharge.

4.2.3 Patient assessment of implementation of the integrated care service and model

Patient rating of the Integrated Care Service and model

Person Centred Coordinated Care Experiences Questionnaire (P3CEQ)

At discharge, patients were asked to assess the patient-centeredness of the CONNECARE system by means of the P3CEQ. This questionnaire consists of six questions, with a scale of 0 – 3, (0 - Not at all, 3 - Always). The mean (SD) P3CEQ, from a total maximum score of 18, was 16.4 (2.3) for CONNECARE patients and 16.6 (3.0) for control patients. This rates the patient-centeredness of the CONNECARE system as excellent, but not different to the experienced among controls. Detailed results on P3CEQ can be found on **Annex VI**, Table 4.

Items G1-G5 from the Nijmegen Continuity Questionnaire (NCQ)

At discharge, patients were asked to assess the perceived continuity of care from hospital to primary care of the CONNECARE system by means of items G1-G5 from the NCQ. The mean (SD) score of G1-G5 NCQ was 4.2 (0.9) from a total maximum score of 5. This, rates the perceived continuity of care of the CONNECARE system as very good. Detailed results on NCQ can be found on **Annex VI**, Table 5.

4.2.4 Issues reported in the Implementation Log – Organization and Process Issues

Organization and process issues

- Communications enabled via SACM/SMS are part of CONNECARE's core features. However, the feature was not implemented on day one but in a subsequent update. While waiting for the messaging feature professionals had to contact patients using standard phone calls and had no option for sharing images.
- The recruitment of patients into the CONNECARE system was slower than expected mainly because of the limitations on patients'/carers' technological abilities and outdated technological equipment (smartphones with non-supported android versions and limited internal memory).

Description of the processes that worked well and successfully

- A wide range of medical problems and health care doubts were solved through the message system with chronic complex patients.
- Regarding critical changes in monitored variables. Those with the referred symptoms, were assessed in a shared way with the patient or the carer. As a consequence, changes in the medication agreed with the primary care team have been carried out. Those actions avoided visits to primary care and emergency rooms.
- A new collaborative relationship with the primary care teams has been established. A significant number of times coordinated actions between primary care team and hospital team have been carried out after hospital discharge.

- Through the messages system, an education of patient and the carer regarding how to control the chronic disease has been carried out. Moreover, many times, shared taking of decisions about the management of the disease has been made with the patient and carer. As a result, the aim of achieving the empowerment of the control of the disease by caregivers and patients has been achieved many times.
- A new degree of wellbeing of the health care users through a new relation with patients and carers that feel supported is achieved.

Description of the processes that did not work

- The current CONNECARE model in Lleida did not have the possibility providing a 24h/day service to patients (mostly because of involved professionals having well-defined working hours and not being available 24h/day), this caused that some preventive actions that could have been effective could not been implemented by the professionals. This issue suggests the need of involving either professionals in the night/shifts or introducing the system to doctors on call.
- The caregivers and patients needed a significant time to learn how the apps and system worked and adapt to the features they actually ended using the most.
- Despite the broad range of possibilities for monitoring and communication that allows the system. The use by the patients is restricted based on their skills or preferences. Therefore, a personalized indication of the technical resources has been needed most of the time.

4.2.5 Patient engagement and actual usage of the ICT tools and devices

Using the Pedometer (Fitbit)

Use of the Fitbit was measured by the number of days that the Fitbit of each patient transmitted to the SMS app. The mean (SD) number of prescribed Fitbit use was 87 (27) days, and the mean (SD) number of active Fitbit usage days was 69.5 (29.1). Clearly, the majority of the patients were compliant in their use of the Fitbit, with 72% of patients using the Fitbit for more than 60 days and 34% of patients using it every day during the post discharge follow-up period. No significant differences between men and women were found. However, age was associated to lower number of Fitbit transmitted days. Detailed results on Fitbit use can be found on **Annex VI**, Table 1.

Using the messaging function of the SMS app

The mean (SD) number of messages sent by the patients was 29 (30). All patients sent at least 1 message and up to 74% of patients sent more than 10 messages. Women tended to use this feature more. It must be noted that the messaging function was not implemented from the beginning of the project, and this limited the engagement of the very first participants in the use of this feature. Once implemented, the patients perceived the feature as very useful and used it a lot. Detailed results on the use of the messaging function can be found on **Annex VI**, Table 2.

Responding to questionnaires

CONNECARE patients participating in Implementation Study 1 were asked to answer through the SMS about their heart failure or COPD status when the professionals consider it necessary. Among COPD patients, the median (p25-p75) number of questionnaires successfully submitted out of all requested questionnaires was 10% (1% - 22%). Among heart failure patients, the median (p25-p75) number of questionnaires successfully submitted out of all requested questionnaires was 1% (0% - 2%). This shows that most patients replied to requested questionnaires at least once, but were reluctant to answer the same questionnaire on a regular basis. Our hypothesis is that there was a burn-out effect most provably because patients did not perceive added value in filling the questionnaires.

Monitoring blood pressure

Patients were asked to measure their blood pressure (BP) frequently and at different times of the day in accordance with their medical status. The report for BP using the SMS app, was done either manually (by typing the results after using a standard BP cuff) or automatically (by using an electronic device linked with the SMS app). The mean (SD) percentage of measures reported out of times prescribed was 40% (18%). Thus, most patients were willing to monitor BP on a daily basis but no more than once a day.

Monitoring heart rate

Patients were asked to record their heart rate (HR) frequently and at different times of the day in accordance with their medical status. The report for HR using the SMS app, was done either manually (by typing the results into the SMS) or automatically (by using the variable recorded by blood pressure monitoring (Withings/Nokia) that provided this information in beats / minute (b.p.m.)). The mean (SD) percentage of measures reported out of times prescribed was 40% (18%). Thus, most patients were willing to monitor HR on a daily basis but no more than once a day.

Monitoring SpO_2 with a digital pulse-oximeter

Patients were asked to record their SpO_2 frequently and at different times of the day in accordance with their medical status. The report for SpO_2 using the SMS app, was done automatically by using an electronic device linked with the SMS app. The mean (SD) percentage of measures reported out of times prescribed was 31% (15%). Thus, most patients were willing to monitor SpO_2 on an almost daily basis but no more than once a day.

Monitoring weight with a digital scale

Patients were asked to record their weight frequently and at different times of the day in accordance with their medical status. The report for weight using the SMS app, was done automatically by using an electronic device linked with the SMS app. The mean (SD) percentage of measures reported out of times prescribed was 62% (38%). Thus, most patients were willing to monitor weight on a daily basis but no more than once a day.

Detailed results on the use of monitoring devices can be found on **Annex VI**.

4.2.6 Patient satisfaction with the technology

Satisfaction with the CONNECARE system – Likert scales and Net Promoter Score (NPS)

At discharge, patients were asked to assess their experience with the CONNECARE system (including the SMS app and linked devices). The overall satisfaction with the CONNECARE system was outstanding, with scores in overall satisfaction, easiness of use, and ability to use without help having medians of 10/10 or 9/10. The answer to the question "How likely is it that you recommend the CONNECARE system to a family member or friend?" was used to calculate the NPS. Subtracting the percentage of Detractors from the percentage of Promoters. The NPS ranges between −100 and +100, a positive score is considered good, a NPS of +50 is generally deemed excellent, and anything over +70 is exceptional. The NPS score was +67% in patients using SMS app + Fitbit and +67% in patients using only SMS app. These rates are excellent, and close to reaching the exceptional threshold (+70%). Detailed results on the Likert scales and NPS can be found in Annex VI, Tables 6-8.

Satisfaction with the CONNECARE system – System Usability Scale (SUS)

At discharge, patients were asked to assess the usability of the CONNECARE system (including the SMS app and linked devices) by means of the SUS. Based on research, a SUS score above a 68 would be considered above average and anything below 68 is below average. The mean (SD) SUS was 79.1 (14.4), with 79% of patients scoring ≥ 68, which rates the product as excellent. Detailed results on the Likert scales and SUS can be found on **Annex VI**, Table 9.

Satisfaction with the CONNECARE system- Changes Over Time During the Pilot

The Implementation of the CONNECARE system in the Implementation Study pilots was an integral part of the final PDSA cycle and the co-design approach with the users that has been central to the CONNECARE project. Many changes, refinements and improvements were made to the system during the course of the pilot. In line with this, Lleida analysed changes in patient/carer satisfaction throughout the pilot according to recruitment date of the patients. There is a clear trend of increasing satisfaction and usability ratings over time. In Lleida, for CS1- overall satisfaction increased from 9-9.2, easiness of use rating increased from 7.3 to 8.8, ability to use without help increased from 7.3 to 8.7 The NPS score increased from 67% to 71% and the SUS Score increased from 67.5 to 80.6. This is depicted in Figure 5.

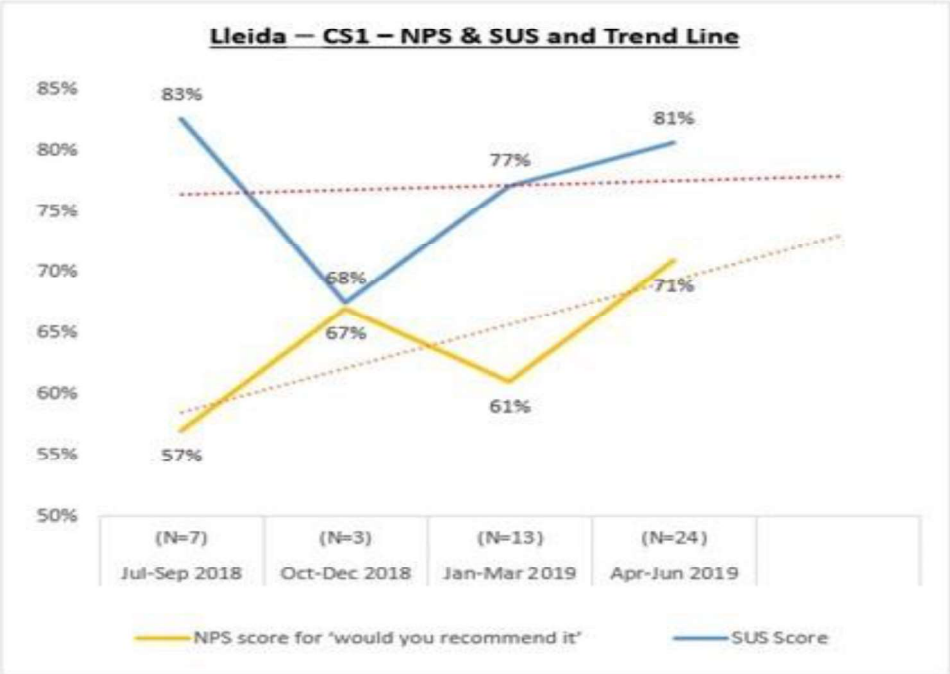


Figure 5 - Overview of NPS and SUS scores.

4.2.7 Staff satisfaction with the technology

A total of 30 professionals involved in CS1 and/or CS2 were asked to assess the SACM platform using Likert scales, NPS and SUS between April and May 2019: 1 hospital case-manager, 3 hospital physicians, 1 hospital surgeon, 1 hospital anaesthesiologist, 3 primary care case-managers, 12 primary care physicians, and 9 primary care nurses. As opposite to patients, the overall satisfaction with the CONNECARE system was poor, with scores in Overall satisfaction, easiness of use, and ability to use without help having medians of 6/10 or 6.5/10. The NPS score was -25%, and most provably reflecting the difficulties experienced in using a tool being under development and not fully integrated with existing systems. Similarly, the SUS score was average, with a mean (SD) of 62.7 (19.7) and 45% of staff scoring ≥ 68. Detailed results on the staff satisfaction with the technology can be found in **Annex VI**, Tables 10-12.

4.2.8 Issues with the digital tools recorded in the implementation log

SACM & SMS usability problems

- Most of the day to day problems reported by the case manager were related to patients' accessibility issues (password recovery) and missing data (human or technological errors on the input of data that resulted in missing data, data recorded with errors, or duplicated data or tasks). This fostered the addition of correction features to be used by either the patient or professionals.

Furthermore, it implies the need for a permanent user support team while the CONNECARE system is implemented and ongoing.

- Another set of issues had a direct relationship with usability and user friendliness of the system, and leaded to improvements on the front end of the SACM and/or SMS (i.e., improvements in the graphical visualization of repeated measurements over time). These issues were solved throughout the refinement and fine-tuning phase of the project.

Technical problems with SACM & SMS

- Most of the technical issues reported in the implementation log were bugs that needed to be reported, prioritized and solved on a regular basis. These bugs included tasks being tagged as completed at the time of prescription; issues with decimal values introduced to the SACM/SMS; messages not reaching all the involved professionals; desynchronization between the SACM and SMS when changing prescriptions, team members or other key aspects of a given patient care plan; issues in the time registry of when a given action was performed; etc. All these issues were solved promptly but generated some occasional discomfort with the system among its users. This implies the need for a permanent technological support team while the CONNECARE system is implemented and ongoing.

Integration with other Information Systems

- The degree of integration with the hospital and primary care electronic medical records (SAP and eCAP, respectively) was very low. This reduced the overall potential of the CONNECARE system and halted the use of past recorded episodes of the patient as an automated assist to professionals in terms of risk assessment.

4.2.9 Intervention effectiveness – Patient outcomes and use of resources

Intervention effectiveness - Health and wellbeing questionnaires (SF-12)

The intervention effectiveness was measured by the comparison of a health-related quality of life measure, the SF-12 questionnaire, at baseline and after the 3-month intervention period, both in CONNECARE patients and in controls. The intervention generated significant changes in the physical dimension of SF-12 (mean (SD) change: +3.7 (8.4); p-value=0.004) and the total SF-12 score (mean (SD) change: +5.8 (12.8); p-value=0.003). No significant changes were seen among the control patients. However, crude or adjusted (sex, age, and Charlson) linear regression models did not find statistically significant differences in the changes experimented by patients in the CONNECARE program or control patients, most likely because of the lack of statistical power, as a total net difference of +5 points gained in SF-12 was found when comparing CONNECARE patients to controls. Detailed results on the effectiveness as measured by the SF-12 can be found on **Annex VI**, Table 13.

Intervention effectiveness - Service utilization during the follow-up

The number of unplanned hospital or primary care visits, as well as hospital admissions, either related or unrelated to the main chronic disease of the patients were recorded during the 3-month follow-up. Being in the CONNECARE program significantly reduced the total number of unplanned visits (mean (SD) among controls: 2.31 (2.92); mean (SD) among CONNECARE: 1.04 (1.12); adjusted p-value=0.006). Regarding hospital admissions, although being lower in the CONNECARE arm, the differences were not statistically significant (mean (SD) among controls: 0.54 (0.78); mean (SD) among CONNECARE: 0.36 (0.56); adjusted p-value=0.261). Most likely, the small sample size and low number of admissions precluded statistical significance. In CS1, five mortalities were registered during the study among control patients and two among patients in the CONNECARE program, which could suggest a reduction in mortality associated to the CONNECARE program. Overall, the main benefit of the CONNECARE system in terms of service utilization was the avoidance of unplanned visits. Detailed results on the effectiveness as measured by service utilization can be found on **Annex VI**, Table 14.

4.2.10 Costs – benefit analyses

Intervention costs

Estimating the overall cost per patient of implementing the CONNECARE program is not trivial. For the purpose of the current study, a hospital-based nurse case-manger was recruited for the duration of the study (Jul 2018 – Oct 2019), with a total cost per month of 3,500€. During the whole study period, she recruited and managed 91 patients in the CONNECARE program (52 CS1 + 39 CS2), taking responsibilities in the management of the patients as well as providing technical support and assistance, collecting research-related data and participating in the overall development of the CONNECARE H2020 project. Therefore, in a real-life non-research scenario, it is estimated that a single hospital-based nurse case-manger could manage up to 500 simultaneous patients, resulting in a cost of 7€ per patient and month. During the study, the rest of involved medical staff either in the hospital or in the primary care assumed any potential increase in workload related to the use of the CONNECARE platform at no additional cost. In this sense, it must be noticed that, in one hand, a fully implemented CONNECARE program would imply a higher number of CONNECARE patients and thus an increase in workload; on the other hand, a fully mature and integrated platform would be much less requiring for involved professionals. In any case, the re-structuration of staff's time to include the new tasks would be fully assumed by the health system and no additional personnel would be required, thus no additional cost would be generated. The cost of licensing and running the CONNECARE platform as well as the costs to maintain, evolve and support it cannot be easily stablished. In this sense, the costs of other health services like Home-based oxygen therapy, where a supplier covers the role of providing devices, licenses and technical support, have been used to generate a per year per patient estimation of 200€. Therefore, a total cost of 23.67€ /patient and month has been estimated as direct costs of the CONNECARE program for the purpose of the current analyses. Given that the duration of the intervention was 3 months, the final costs of the CONNECARE program was 71.01€.

Additionally, 2 sensitivity scenarios were also analysed were CONNECARE program costs were incremented by +50% and +100%. No indirect costs were considered.

Cost of unplanned visits and hospital admissions

According to the official data of 2013 (CVE-DOGC-A-13051031-2013), the overall cost of unplanned medical visits in the health region of Lleida is 62€. The cost of hospital admissions is 555€ per day. The average total cost of unplanned visits during the 3-month study period was 143.49€ among control patients and 64.48€ among CONNECARE patients. Similarly, the cost of hospital admissions was 2,537.14€ and 1,986.90€, respectively. Therefore, patients in the CONNECARE program generated an average saving of 629.25€.

Overall costs

When considering both the cost of the CONNECARE program and the cost of unplanned visits and hospital admissions, patients in the CONNECARE program generated an average saving of 5,58.24€. When considering scenarios with +50% and +100% CONNECARE program costs the CONNECARE program still generated savings: 522.73€ and 487.23€, respectively.

Cost-effectiveness

The cost-effectiveness of the CONNECARE program was assessed by means of the incremental cost-effectiveness ratio (ICER). Effectiveness was measured by the comparison of the change in SF-12 total score, at baseline and after the 3-month intervention period. Costs were measured considering overall costs in the 3 CONNECARE program scenarios (100%, 150%, and 200%). All three scenarios reported a negative ICER, thus demonstrating a negative incremental cost associated with 1 additional point gain in SF12 (100% CONNECARE program costs: -112.10; 150% CONNECARE program costs: -104.97; and, 200% CONNECARE program costs: -97.84). This means that the CONNECARE program was more cost-effective than standard care, even when considering scenarios with increased costs of the program.

Detailed results on the costs and cost-effectiveness can be found on **Annex VI**, Tables 15 and 16.

4.3 Israel

4.3.1 Recruitment results

From July 2018 until the end of September 2019, there was a total of 4,566 hospitalized Maccabi members aged 60 +, 561 patients (12%), were found to be potentially eligible according to the medical record. Of them: 215 patients (38%) were found unsuitable after a conversation with the patient or with a nurse on the ward, 82 patients (15%) said explicitly that they were not interested, and 54 patients (10%) were recruited.

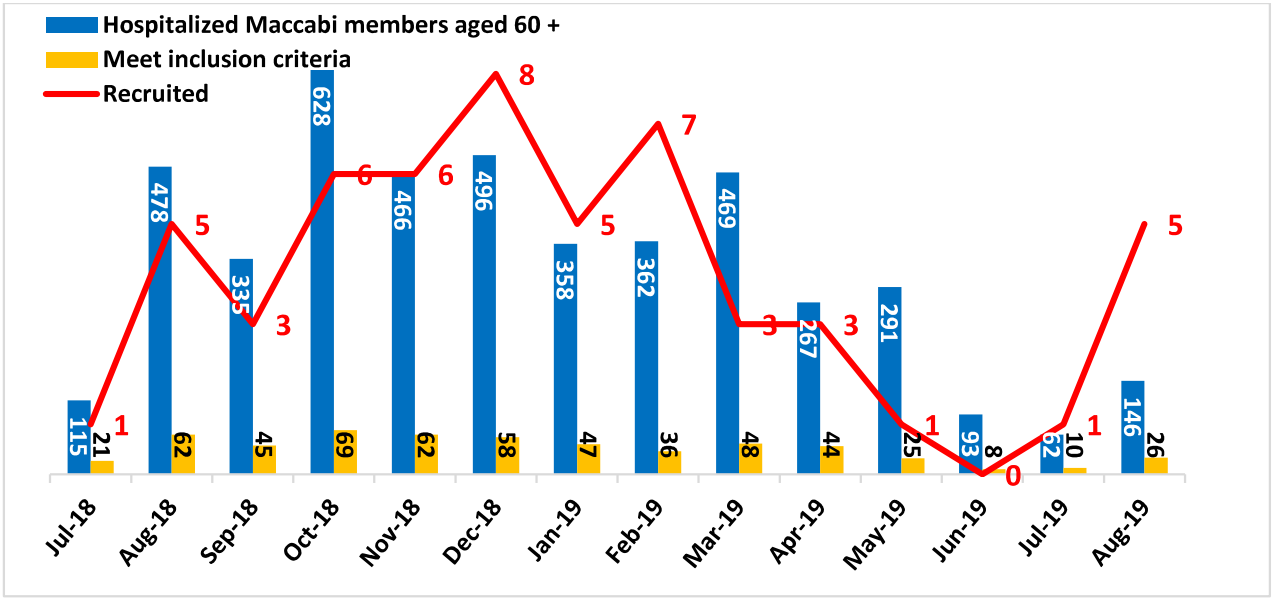
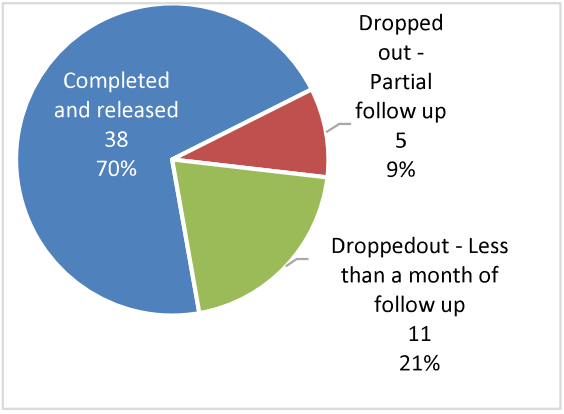


Figure 6 - Overview of recruitment rates and patient drop-out.



As of the end of September 2019, of the 54 patients recruited, 38 patients (70%) completed the three months follow-up and were discharged from the project after completing the feedback questionnaires (Figure 6). Some patients have even continued the follow up for another month at their request. Sixteen patients (30%) dropped out of the project prior to completing the entire course of three months follow-up. Five of these received partial follow up (more than a month but less than 3 months) and 11 patients dropped out of the study after less than a month of follow-up. The group of patients who chose to leave the study early were not different from the whole group, in age or sex distribution. However, the average Charlson Comorbidity Index score was significantly higher - 5 for the dropout group compared to 4 for the other patients. The flowchart of patient recruitment is depicted in Figure 7.

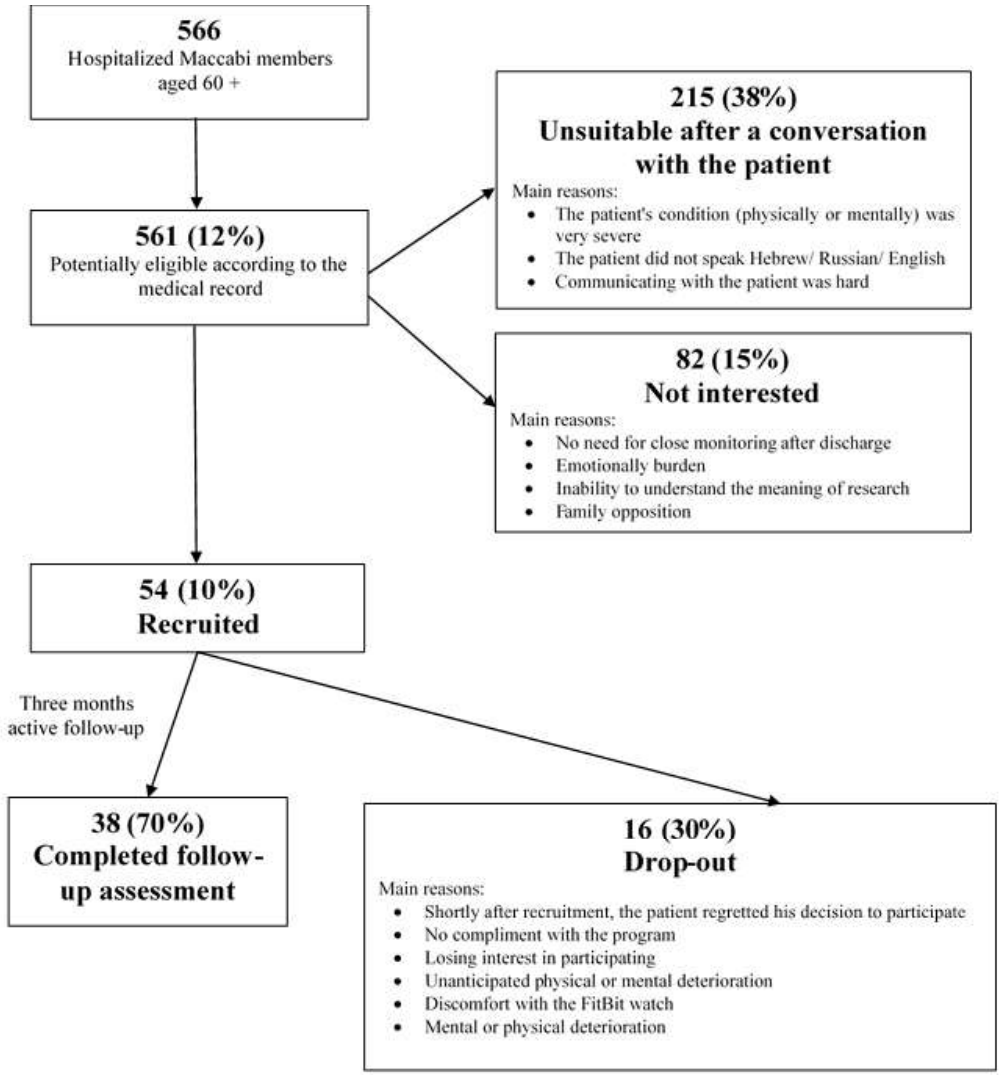


Figure 7 - Study flowchart.

Between July 2018 and August2019, 54 patients were recruited. 28 (52%) males and 26 females ranging from ages 59-79 with an average age of 68.4 and median of 68.5. Average LACE score is 9.55 (median 10). Most of the patients were living with a spouse (72%), defined themselves as having middle socioeconomic status (80%), and had university education (57%).

At the end of September 2019, 38 patients in Implementation Study 1 completed the 3 month post-discharge follow up and were discharged from the program, and two patients were in follow-up for more than a month. The following results are therefore based on the data reported for these 40 patients. Not included are 14 patients who dropped out after less than a month of their recruitment date.

4.3.2 Main reasons for failure to recruit and patient drop out

Some of the main reasons for failure to recruit were:

- The patient was discharged from the hospital before the Maccabi's nurses had an opportunity to see him/her.
- The patient's condition (physically or mentally) was very severe and therefore1 was not appropriate for the study.
- The patient was scheduled for discharge to a nursing home for an extended period of time.
- The patient was not interested in participating in the study. Sometimes patients explained why they were not interested, for example:
    - The patient felt that he had no need for close monitoring after discharge and therefore would not benefit from participating in the program.
    - The patient was unable to understand the meaning of research and the need to sign a consent form, and refused to sign anything.
    - The patient was emotionally burdened by the unexpected hospitalisation.
    - The patient was dissatisfied with the service at the hospital or with Maccabi and was unwilling to cooperate.
    - The patient was interested in participating but his children objected.

Some of the main reasons for patient drop-out were:

- Shortly after recruitment, the patient regretted his decision to participate (sometimes because of family opposition).
- Some patients did not cooperate with the program.
- Unanticipated physical or mental deterioration post-discharge.
- Discomfort with the Fitbit watch.

4.3.3 Patient assessment of implementation of the integrated care service and model

In order to assess the patient's perceptions about patient-centeredness during the project, patients were asked to fill the Person Centred Coordinated Care Experiences Questionnaire (P3CEQ). This questionnaire consists of six questions, with a scale of 0 – 3, (0 - Not at all, 3 - Always). The median (p25-p75) P3CEQ was 14 (10.0-16.0) from a total maximum score of 18, which rates the patient-centeredness of the CONNECARE system as good.

Table 2 - Overview of the results of the P3CEQ questionnaire.

0 - Not at all 3 - Always	% of patients answered "Always"
F1. Did you discuss what was most important for YOU in managing your own health and wellbeing?	40%
F2. Were you involved as much as you wanted to be in decisions about your care?	49%
F3. Were you considered as a 'whole person' rather than just a disease/condition in relation to your care?	66%

F4. Did your care-team / providers involve your family/friends/carers as much as you wanted them to be in decisions about your care?	43%
F5. Have you had enough support from your care team / providers to help YOU to manage your own health and wellbeing?	69%
F6. To what extent do you receive useful information at the time you need it to help you manage your health and wellbeing?	71%

A total of 71% of the patients felt that they received useful information at the time they needed it to help manage their health and wellbeing (Table 2). 69% of the patients felt that they had enough support from the project's staff to help manage their health and wellbeing. 66% of the patients felt that were considered as a 'whole person' rather than just a disease/condition. 49% of the patients felt that they were involved as much as they wanted to be in decisions about their care. Only 40% of the patients felt that the project's staff involve their family/friends/carers enough, and that they discussed what was most important for them with the project's staff.

The results described here are relatively high, suggesting the perceived patient-centeredness in the CONNECARE system for the patients completing the whole post discharge follow-up period, as very good. However, the two questions with the low score regarding family/friends/carers involvement and the patient's own important issues, should be taken into consideration, since both issues were part of the CONNECRE patient's empowerment agenda.

These results are supported by patients comments in the open questions at the end of the satisfaction questionnaire:

- "The team that did my follow up and cared for me was very nice and always willing to help"
- "The team was very pleasant and professional"
- "The research team gave me a sense of security, compassion, warmth and support"
- "It was a good feeling that I was being monitored and could address any problem"
- " The project is very important, because it enables close post-discharge monitoring, I had a sense of control and a sense that there is a team that helps me"
- "A very important project, should make it mandatory for older patients"
- "Increased self-discipline"
- "The nurses' response via the app was very important, gave the feeling that there was someone to turn to"
- "The follow up period post-discharge should be extended to 6 months"

In order to assess the patient's perceptions about the continuity of care during the project, patients were asked to fill items G1-G4 from the Nijmegen Continuity Questionnaire (NCQ), 33 patients responded. This questionnaire consists of five questions, with a scale of 1 – 5, (1-Strongly agree, 5- Strongly disagree). The median (p25-p75) score of G1-G4 NCQ was 12.0 (10.0-13.0) from a total maximum score of 0-20 (20 presenting the worst continuity).

Table 3 - Overview of the results of the NCQ questionnaire.

1- Strongly agree 5- Strongly disagree	% of patients answered "Agree" or "Strongly agree"
G1. My care providers transfer information very well to one-another	88%
G2. My care providers work together very well	82%
G3. My care providers are very well connected	73%
G4. My care providers always know what one-another is doing	67%
G5. I have to wait too long to obtain a service/appointment	18%

The results show patients' high satisfaction with their treatment and continuity of care among different physicians and caregivers during the study period (Table 3). 73%-88% of the patients perceived that their care providers transfer information to one-another very well, that their care providers work together very well, and perceive their care providers as very well connected. 67% of the patients perceived that their care providers always know what one-another is doing. On the last question, regarding waiting too long to obtain a service/appointment, only 18% thought they had to wait too long for an appointment

The results described here are relatively high, suggesting the perceived continuity of care of the CONNECARE system for the patients completing the whole post discharge follow-up period, as very good. The main hypothesis for this result is the availability and high level of service of Maccabi's case manager nurses, and also the addition of a secretary to help patients to deal with bureaucracy and coordination.

These results are also exemplified by patients' comments in the open questions at the end of the satisfaction questionnaire:

- "There was good communication between my neurologist and my family doctor, so I didn't need a case manager nurse"
- "Received help in a very short time to set an appointment for occupational therapy"
- "The response of the nurses through the application was very important, there was a feeling that there is someone to turn to"
- "Project staff helped me understand the hospital discharge summary and make appointments for post-discharge care"
- "The reminders about appointments were very important to me"

4.3.4 Issues reported in the Implementation Log – Organization and Process Issues

The issues reported in the organization and processes section reflect specific problems encountered by the nurse case managers and the research team that were generally addressed and resolved during the course of project.

- Most of the day to day problems reported by the case managers under Organization and process issues were related to workflow problems and patient adherence.

- Regarding workflow, tips for better recruitment were reported, like reducing the minimal age of recruitment, and taking into account during recruitment the patients' ability to respond to the study and the treatment plan for 3-4 months, i.e., not just recruiting anyone who might agree.
- Regarding patient adherence, some positive patient comments were reported, but mainly patient's usability problems were reported such as forgetting the app's password, inconvenience with using the Fitbit, etc.
- Other reports were about problems in collaboration among members of the study's staff and changes in the study protocol.
- Difficulties encountered in coordinating with hospital staff (such as nurses on the wards) were addressed by meetings with the head nurses resulting in significant improvement

4.3.5 Evaluation of the implementation process

Description of the processes that worked well and successfully

- Making right decisions in choosing the case manager nurses - Recruitment of two half-time nurses instead of one full-time nurse, so both of them could work together and back each other up, also recruitment of Russian speaking nurses was found to be very important due to the size of the Russian-speaking population in Ashdod.
- In order to add value for patients to participate in the study, a part-time medical secretary from Maccabi Healthcare Services was added to the project team to assist patients in scheduling appointments for specialists and imaging tests in the community and reduce bureaucracy. The addition of the secretary helped in the process of recruiting patients, and assisted the nurses in integration and coordination when needed.
- Enabling multiple options for the patients to meet the nurses/physiotherapists for recruitment, re-training on the app and Fitbit use and in cases where there was a problem with the Fitbit or the App. Maccabi's NCMs were given the option of home visits with patients, (which was not in the original protocol), this option was used extensively by the nurses to the high satisfaction of the patients. In addition, hospital's parking tickets were purchased and distrusted to patients on a need basis.
- Engaging more active involvement of the family physician. When the nurses encountered a suitable patient for the study who expressed interest in the study but had doubts, the nurses turned to the personal secretary of the patient's family physician and the family physician encouraged the patient to participate in the study.
- Strengthening the communication between the staff, after several cases of errors and problems with information transmission by creating a joint WhatsApp group for all the staff to communicate in a fast and real time way, and by creating weekly routines, mainly by using the Outlook

reminders, to remind the staff regarding scheduled time of patients' surgery, when to visit patients in the hospital or patients discharge from the study.

- During recruitment, presenting the study to the patient as innovative project, that by participating he will help us learn what is good and what requires improvement in technology. This presentation was very helpful in recruiting patients.
- Distribution of step-by-step clear printed guide with screenshots on the use of the application and the Fitbit watch, at the first meeting with the nurses.
- Purchasing tablets for the nurses so that they could recruit anywhere, anytime
- Purchasing tablets for patients whose mobile phone did not support the app

Description of the processes that did not work:

- The nurses chosen for the role of Case Manager had high interpersonal abilities, but low technical abilities which limited their ability to support the patients who experienced technical problems
- The recruitment of patients at the hospital during hospitalization resulted in gaps in information about the study and use of the technology. Recruitment at the patient's home a few days after discharge was preferable
- The cooperation of the patient's family physician was not ideal, the family physicians were informed of the patient's participation in the study, but a deeper relationship and integration was only created in a few cases
- Integrating hospital managers and clinical staff (head nurses, department heads ...) into the project was challenging, largely due to the fact hospital staff was focused on the day to day challenges of putting routine procedures in place in a new hospital with a new staff
- The SACM system was a standalone system, all data needed to share was double entered - once into the SACM and a second via organizational emails or the Maccabi EMR
- The Nurse Case managers were initially managed by a senior nurse. During the course of the project, management of the case managers was shifted to a physician, the medical director of the integration unit. This resulted in a lack of close nursing supervision and affected the Case Managers' performance.
- Although the application has a chat option for messaging between the nurses and the patients, it was not available to the patients recruited at the beginning of the project. Many patients found it difficult to use this feature. For these patients the nurses instituted a weekly phone call with each patient.

4.3.6 Patient engagement and actual usage of the ICT tools and devices

This section reports the overall findings for use of and satisfaction with the CONNECARE digital tools. The detailed tables and statistical analyses can be found in **Annex VII**.

Using the Pedometer (Fitbit)

Use of the Fitbit was measured by the number of days that the Fitbit of each patient transmitted to the SMS app during the 3 month post discharge monitoring period, as well as the number of steps reported by the device over the same period. The average number of days reported for all 3 months of follow up was 24 days per month – per patient. Between 73%-75% of the patients transmitted steps more than 21 days per month. Even more encouraging, the average daily number of steps increased from 4509 in month 1, to 6277 in month 3. In Month 3 67% of the patients were walking more than 5000 steps daily. Clearly, the majority of the patients were compliant in their use of the Fitbit, and the increase in the number of daily steps is indicative that they also derived a positive benefit in terms of increased physical activity. This is supported by findings that will be reported in the next section on reported improved physical health by patients after the intervention compared to prior to the intervention. Men and women did not differ significantly with respect to percentage of days reporting use of the Fitbit or average number of daily steps. Age did not significantly predict the percentage of days reporting use of the Fitbit, However, there was a significant contribution of age with respect to average daily steps. Older people reported significantly less daily steps than younger people. It is important to note that 20 patients continued to report steps after being discharged from the program with more than an average of over 6000 number of steps daily.

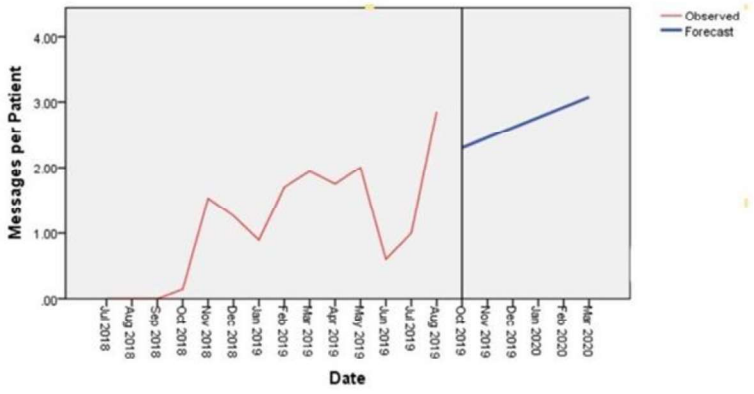


Figure 8- Overview of the messaging per patient.

Using the messaging function of the SMS app

The average number of messages sent by all 40 patients was 4.98, with 20 patients sending between 3-10 messages and only 4 patients sending more than 10 messages. However, a time-series analysis revealed an overall increase in the number of messages per patient sent over the intervention period. We speculate that the reason for the low uptake of messaging is that the messaging function only became available after many of the patients were already in post discharge follow up and they had already become accustomed to communicating with the Nurse Case Managers by phone. Consequently, there was less use of the messaging function than anticipated for this group of patients. When analysing the messaging

function use according to patient's recruitment month, we can see a significant increase in the use of the patients recruited later (Figure 8).
There was no effect on the use of messaging by sex or by age.

Responding to questionnaires

Patients in Israel were asked to fill in the EQ5D questionnaire weekly on the SMS app, in order to follow their self-reported quality of life during the follow up period. Despite reminders, only two patients (8%) responded and not frequently. Patients apparently did not perceive added value in filling in the questionnaire.

Monitoring blood pressure

Patients were asked to measure their blood pressure (BP) in accordance with instructions from their clinicians. 28 of the 40 patients in implementation study 1 were instructed to measure their blood pressure. Of those instructed to measure their blood pressure daily, 23% reported their blood pressure daily whereas the reporting of blood pressure for those instructed to measure twice or once a week was very low. It should be noted that there was no automatic transmission to the app from a blood pressure cuff so that all blood pressure reports needed to be entered manually by the patient into the app. It is likely that blood pressure was actually measured more often than it was reported.

4.3.6 Patient and staff satisfaction with the technology

At discharge, patients were asked to assess their experience with the CONNECARE system, including the SMS app and the Fitbit watch, using the Net Promoter Score (NPS) tool, consisting of four questions, each of which with a Likert scale score of 0 – 10, (0 = poor, 10 = good). Thirty-three patients responded (Table 4).

Table 4 - Overview of patient satisfaction.

Likert scale score (0 = poor TO 10 = good)	SMS App		Fitbit	
	median	p25-p75	median	p25-p75
1. Overall satisfaction	6.0	3.25-9.75	10	7-10
2. Easiness of use	7.0	4.25-9	10	7.5-10
3. Ability to be used without help	7.0	4.25-10	10	8-10
4. Would you recommend it?	5.50	0-10	10	7.5-10

Overall satisfaction with the Fitbit was very high, whereas satisfaction with the SMS was moderate. The answer to the question “How likely is it that you will recommend the CONNECARE system to a family member or friend?” was used to calculate the NPS score (Tables 5 + 6). The NPS ranges between −100 and +100, a positive score is considered good.

Table 5 - NPS – SMS scores.

Score 'would you recommend it'	# patients	% patients
0-6 (detractors)	18	56%
7-8 (passives)	2	6%
9-10 (promotors)	12	36%

Table 6 - NPS – Fitbit scores.

Score 'would you recommend it'	# patients	% patients
0-6 (detractors)	7	21%
7-8 (passives)	4	12%
9-10 (promotors)	22	67%

The NPS score was +46% for the Fitbit which rates it as good, and -20% for the SMS which is a low rating Another tool to evaluate and assess the usability of the CONNECARE app, was by the System usability Scale (SUS) tool, consisting of eight questions, each of which with a Likert scale score of 1 – 5, (1.0 = strongly disagree , 5.0 = strongly agree). The median (p25-p75) SUS score was 59.4 (45.0-77.5), which rates the product below average of the SUS, and as poor but not awful. However, 12 patients (35%) gave the SMS a score of above 68 which is above average.

Overall, we can see that the patients rated the Fitbit watch as easy to use and would recommend it to their friends. However, the CONNECARE app was evaluated by the patients as less easy and less attractive. These results are reflected patients' comments in the open questions at the end of the satisfaction questionnaire:

- "Using the Fitbit was convenient and clear, I did not use the SMS app because I was busy caring for my health, and did not have time to get guidance on using it, even though the nurses contacted me several times"
- "The Fitbit was clear to use, but the SMS app was not so clear to me"
- "If the SMS app was part of the Maccabi Online website, it would have been more effective for me"
- "Very pleased with the Fitbit and reminders in the SMS app, it encouraged me to exercise and helped my self-discipline"
- "It was very difficult to use the SMS app and I was assisted by my husband and son, but despite repeated instructions, I did not succeed"
- "In fact, I did not use the SMS app except for reporting on daily blood pressure measurements"
- "Using the app was difficult, perhaps the nurses explained how to use it, but I forgot everything"
- "The application is very important, the idea is good to actively follow patients, but it was hard for me to use because of my age"

Essentially, the comments provide an explanation and a better understanding of the quantitative results of the actual use of both the Fitbit and the SMS App. The Fitbit was simple and easy to use and required

very little effort on the part of the patient. They could also view the number of steps they walked on the watch itself without going into the app. The SMS app required much more effort, logging in and entering the various functions in order to use them. Nonetheless, it is important to remember that the development of the CONNECARE SMS was a work in progress that continued to evolve throughout the course of the implementation study based on feedback from patients and staff. Therefore, a time series analysis was done to address the level of satisfaction with both the Fitbit and the SMS by month of patient recruitment. Satisfaction with the fitbit was high regardless of when patients entered the study in terms of overall satisfaction,NPS and SUS. However, there was a real difference in satisfaction with the SMS between patients who entered early and patients who entered later when the technology was more mature. Overall satisfaction increased from 4.3 to 6.5, ease of use increased from 4.1 to 7.1, ability to use without help increased from 3.6 to 8.3, and the response to "would you recommend it?" increased from 3.4 to 7.0. The SUS Score increased from 56.07 to 60.36. This is depicted in Figure 9.

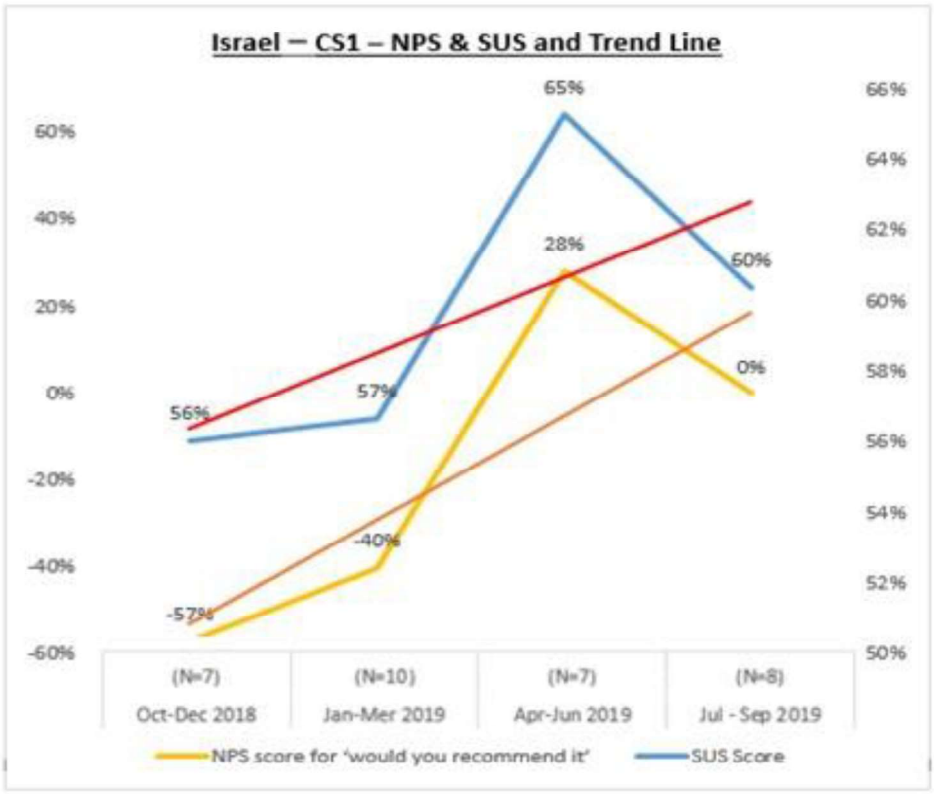


Figure 9 - Trends in Patient Satisfaction.

4.3.7 Staff satisfaction with ICT tools

The Nurse Case managers were asked to assess their experience with the CONNECARE system, including the SMS app, the Fitbit watch and the SACM using the Net Promoter Score (NPS) tool, consisting of four questions, each of which with a Likert scale score of 0 – 10, (0 = poor, 10 = good) (Table 7). The answer to the fourth question "How likely is it that you recommend the CONNECARE system to

a family member or friend?" was used to calculate the NPS by subtracting the percentage of Detractors from the percentage of Promoters. The NPS ranges between −100 and +100, a positive score is considered good.

Table 7 - Overview of the results of nurse case managers.

	Likert scale Average score (0 = poor to 10 = good)	March 2019 (n=3)	Sep 2019 (n=3)
SMS App	1. Overall satisfaction	3.0	4.7
	2. Easiness of use	2.3	5.0
	3. Ability to use without help	2.7	4.7
	4. Would you recommend it?	2.7	4.3
	NPS score for 'would you recommend it'	**-100%**	**-67%**
FITBIT	1. Overall satisfaction	7.7	8.3
	2. Easiness of use	7.3	8.3
	3. Ability to use without help	7.7	8.3
	4. Would you recommend it?	7.7	8.3
	NPS score for 'would you recommend it'	**0%**	**33%**
SACM	1. Overall satisfaction	4.0	5.7
	2. Easiness of use	3.0	5.0
	3. Ability to use without help	3.0	5.3
	4. Would you recommend it?	3.0	4.0
	NPS score for 'would you recommend it'	**-100%**	**-33%**

The staff assessed the digital tools twice – once in March – 9 months after project start and in September at the end of the project. The answer to all four questions for all of the technologies improved substantially between the two time periods. The NPS also improved, for all of the technologies, however, only the Fitbit received a positive score.

SUS score

The staff also rated the CONNECARE digital system using the System Usability Scale. Based on research, a SUS score above a 68 would be considered above average and anything below 68 is below

average. Although there was improvement between March and September, the average rating by the staff was below average and none of the staff members rated the system above 68 (Table 8).

Table 8 - Overview of SUS scores for staff members.

SUS total score - mean (SD)	March 2019 (n=3)	Sep 2019 (n=3)
SMS App	16.00 (6.08)	20.00 (6.08)
SACM	16.67 (5.03)	19.67 (5.86)

Staff engagement and assessment of project implementation

Staff engagement and their assessment of the CONNECARE project implementation was measured the ACT@SCALE which measures the level of agreement of staff members with statements about the project and its implementation.

Table 9 - Overview of results of the ACT@Scale questionnaire on staff engagement.

% answered "Agree" / "Very agree"	Nov 2018 (n=1)	March 2019 (n=3)	Sep 2019 (n=3)
1. I have a clear understanding of what this project is trying to achieve	100%	100%	100%
2. I feel I am able to influence the way in which the project is managed and delivered	100%	100%	100%
3. I was consulted about the implementation of the project	100%	67%	33%
4. I believe patients are benefiting from participating in this project	100%	67%	100%
5. The implementation of the project was well planned	0%	67%	0%
6. I was given appropriate training and education to support my role in the project	100%	100%	67%
7. My views about the project are gathered and acted upon	100%	67%	33%
8. I was actively involved in the development and implementation of the project	0%	67%	67%
9. I believe that the approach to integrated care used in the project is now part of 'normal' practice	100%	100%	67%
10. I have been supported to develop the skills and knowledge necessary to deliver the service	100%	67%	67%

11. My involvement in the implementation of this project has positively changed my views on integrated care	100%	100%	100%

% answered "Agree" / "Very agree"	Nov 2018 (n=1)	March 2019 (n=3)	Sep 2019 (n=3)
1. The contents and teaching methods are tailored to my needs	100%	67%	100%
2. All different categories of staff have the same access to training	100%	67%	33%
3. There was sufficient staff time available to support my training	100%	33%	33%
4. Frontline staff are quite involved in training or supporting (e.g. through mentorship) their colleagues in relation to the project	100%	67%	33%

Most of the staff felt they were actively involved and encouraged to provide feedback on the development of the CONNECARE integrated care model.

The team considered a number of factors in the integrated care model as most important:

- The multi-professional team communication efficiency, when all physicians are involved and updated on the patient situation and needs.
- Ongoing follow-up and monitoring on the patient tailored to the patient's need.
- First meeting with the patient and his/her family in the hospital, either during hospitalization and / or before surgery, or prior to discharge to the community.
- Active participation of the patient in improving his or her health.
- Raising awareness and education for physical activity.

As barriers to implementing the model, the team noted the following:

- Lack of cooperation from the Assuta staff in the inpatient wards and outpatient clinics.
- Technical difficulties for the patient in using the app.
- Lack of connection between the hospital and community.

The staff made the following suggestions for improving staff engagement:

- Stronger involvement of hospital management
- More work meetings with regular updates and feedback
- Direct contact with a technical assistance person who can respond quickly and efficiently to patients but also to staff when problems arise with any of the digital tools
- Designated working space that enables the entire project staff to sit together
- More comprehensive training for every team member on the app and the SACM
- Periodic sessions of the multi-professional team to briefly discuss each patient

4.3.8 Issues with the Digital Tools Recorded in the Implementation Log

SACM & SMS usability and technical problems

- The implementation logs tended to address organizational problems rather than technical problems as technical problems required immediate resolution
- There were many day-to-day urgent bugs and these were reported to the technical staff via email or phone and were not reported in the log. Usability problems that were reported in the log were those of low or medium priority.
- Most of the problems reported by the case manager in the implementation log were regarding the SMS installation process and specific problems in the use of the SACM.
- Issues raised in the implementation log were suggestions for improving the visibility and use of both the SMS and the SACM. For example:
    - Patients requested the ability to create their own tasks
    - Patients requested that the pop-up alerts make a sound and not just appear on the screen
    - The nurses proposed to change the graphs presenting the simple task's reports in the SACM.
    - The nurses proposed to change the order of graphs for physical activity in the SACM.

Other Digital Health Tools

- Most of the problems reported in this section of the implementation log were regarding the Fitbit and the Tablets given to patients
- Some were technical problems in using the devices, and some were more administrative problems, such as a patient who has lost his watch or charger.
- Most technical issues were related to connectivity problems between the Fitbit watch and the app.

4.3.9 Intervention effectiveness – Patient outcomes and use of resources

The following is a summary of the findings for intervention effectiveness in terms of perceived health and well-being by patients as well service utilization and costs, and cost-effectiveness and cost benefit. The detailed figures and statistical analysis can be found in the **Annex VII**.

Intervention Effectiveness –Health and Well-being

The effectiveness of the intervention as perceived by the patient was assessed by comparing the responses of patients to 6 questionnaires prior to the intervention and after the intervention. The assessment tools used were the Barthel Index (measures Activities of Daily Living), the Lawton Index (measures Instrumental Activities of Daily Living), the SF12, HADS, EQ-5D and Sweet 18. These questionnaires were administered by the Nurse Care managers rather than being filled out by the patients

themselves. Patients reported positive improvement on all measures, without exception but for several of the measures there was substantial improvement that was statistically significant. The score for physical functioning on the SF12 was an average of 6.60 before the intervention and 9.25 after the intervention, a statistically significant change with a p-value of <.001. Likewise, the EQ-5D average score for decrease in pain discomfort and increase in feeling of health improved from an average of 59.65 prior to the intervention to 71.97 following the intervention – also significant with a p-value of <.001. In addition there was a reduction of depression and a significant decrease in anxiety.

Service Utilization

Service utilization was measured by comparing the intervention group with the matched control group. The intervention and control group were matched using the following variables: sex, age group, type of hospitalization and/or procedure code, date of hospitalization, inclusion in disease registries and medical costs in the year prior to hospitalization. There was no difference between the groups in ER visits (which was low in both groups), but there was a difference during the intervention period in number of hospitalizations per capita. There was a higher number of GP visits and visits to specialists in the intervention group.

4.3.10 Costs – benefit analyses

Pharmacy costs were much lower in the intervention group than the control group both during and after the intervention. Most significantly, the overall cost per capita was significantly lower for the intervention group (1,992 Euros) than the control group (3,068 Euros), with a p-value of <.04, mostly attributable to significantly lower hospital-related costs in the intervention group than in the control group.

Cost effectiveness was assessed by comparing the total costs in the intervention group – including both costs for service utilization plus the additional cost of the intervention itself with the cost for utilization of services in the control group. Two outliers in the intervention group and one in the control group with excessively high costs were removed for purposes of the analysis. Both before and after the removal of the outliers the savings achieved in the intervention group was significant. Before the removal of the outliers during and one month after the intervention, the intervention group cost an average of 2,241 Euro per patient less than the control group. With the removal of the outliers, the difference increased to an average of 2,991 Euro per patient.

The significantly lower costs in the intervention group must also be viewed together with the positive benefits achieved by the intervention and in particular the patient reported improvement in physical function, decreased pain discomfort and overall feeling of health and well-being.

Summary of Patient outcomes in Israel for Implementation Study 1

Overall, the CONNECARE integrated care intervention for the chronically ill patients (60+) who had an unplanned hospitalization appears to have been significantly beneficial both in terms of health and well-being outcomes as well as cost-effectiveness of the intervention. Despite the relatively small sample size

patients perceived themselves to be significantly physically stronger and healthier after the intervention with reduced depression and anxiety and they had significantly lower healthcare service costs, even with the additional expense of the intervention factored in. The apparent conclusion is that digitally supported integrated care for this population is not only sustainable but also beneficial to patients' health and financially beneficial to the health care system.

4.4 Groningen

4.4.1 Recruitment results

A total of 130 patients were approached between March and July of 2019, of which 51 patients signed informed consent for participation in the study. Of the 51 patients recruited, 50% was female, the average age was 60 (IQR 31-82). Patients were diagnosed with either asthma (30%), COPD (65%) or asthma/COPD overlap syndrome (5%). Reasons to decline include high mental burden, no internet available or smartphone and continuous monitoring not being compatible with patients' day-to-day activities. Complete follow-up data up to six-month after study enrolment was collected for 25 patients, 16 patients are still enrolled. Ten patients dropped out of the study after enrolment, due to reason of high mental stress of daily measurement or lack of motivation to keep up with the study protocol. There main reason for delay in the start of patient recruitment was that the technology did not reach sufficient maturity for the case manager to feel confident that patients could work with it. Figure 10 shows the inclusion diagram.

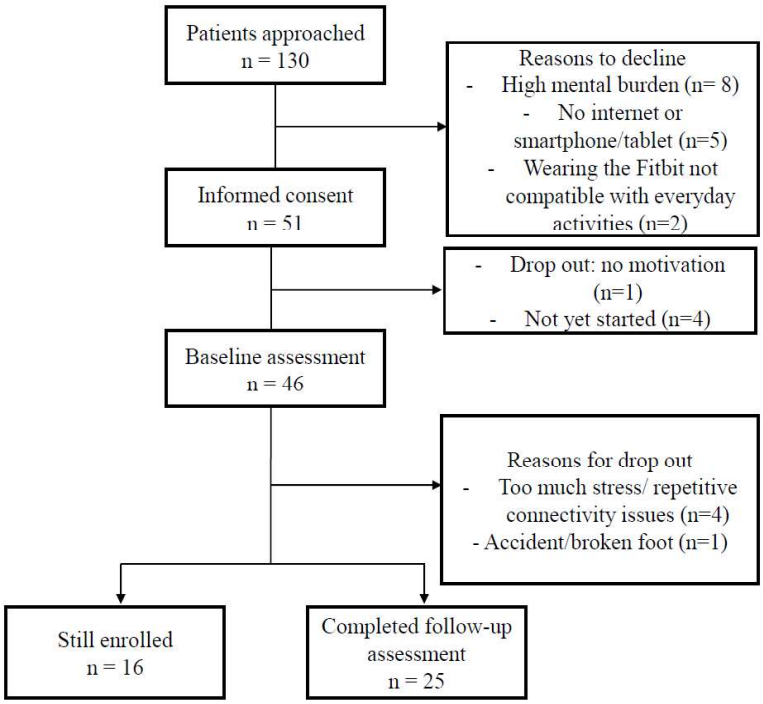


Figure 10 - Study flowchart

4.4.2 Main reasons for failure to recruit and patient drop out

Difficulties in patient recruitment had several causes:

- The case manager had to wait until the functionalities of the app reached sufficient maturity that she felt confident enough to start clinical testing.
- Initially we considered one recruitment site for patients, however this yielded not enough potential patients for inclusion. As a mitigating action two more recruitment sites were added.
- The first versions of the app and its functionalities were considered a burden for the patient, and too time consuming. This was found during the qualitative examinations and before inclusion of the patients.
- Patient expressed a 'what's in it for us' notion regarding the CONNECARE system.

4.4.3 Patient assessment of implementation of the integrated care service and model

On average, our patients are older and we were surprised to see that so many patients were enthusiastic about the CONNECARE ICT systems and connected devices. Although patients had some difficulties to work with the technology, most were willing to try and considered this concept as an important step forward. They think that integrated care services like CONNECARE can improve healthcare.

4.4.4 Issues reported in the implementation log – organizational and process issues

Organization and process issues

- The majority of the issues reported related to usability and connectivity issues using the SMS. All issues were recognized and solved locally or when necessary with support of the IT colleagues in the consortium.
- The recruitment of patients into the CONNECARE system was slower than anticipated. As mitigating action, the number of recruitment sites was increased, mainly by involving the Dutch Lung Foundation.

4.4.5 Evaluation of the implementation process.

Description of the processes that worked well and successfully

- Recruitment of patients using the Dutch Lung Foundation was very successful and increased the number of patients included in the study considerably.
- The SMS app is working well at the moment, as is the connection with the FitBit.
- The implementation of the CONNECARE app worked fine and patients are satisfied with the app.
- Additional support in terms of students recruited to support patient inclusion and data management improved management of all patients.
- Providing information via the SMS app on disease management and control was well received by patients.
- Using the CONNECARE system and connected devices on tablets instead of a smartphone.

Description of the processes that did not work

- The first versions of the SMS app were difficult to use by the patients, thereby start of patient inclusion was postponed
- In some cases, patients had to restart their mobile phone because the Bluetooth connection was lost.
- Using the system as a stand-alone resulted in double work for the case manager and other engaged professionals.
- The researcher visited the patients for the installation of the CONNECARE app and the Fitbit. If difficulties emerged during the installation the researcher could choose to give the patient a tablet. Most problems emerged because patients had a smart phone that was too old and the tablet offered by CONNECARE solved this issue.

4.4.6 Patient engagement and actual usage of the ICT tools and devices

Using the Pedometer (Fitbit)

All participants received the Fitbit along with support from the researcher with installing the device. Patients were compliant in their use of the Fitbit (**Annex VIII**, Table 1), however it should be noted that a portion of the included patients are still in the study and have not yet reached the 90 days follow-up.
The overview of average step count for all groups is presented in **Annex VIII**, Table 2. Asthma patients showed an increase in the numbers of steps, whereas the COPD patients showed a decrease. Based on the data available for analyses, a repeated measures analysis was performed in both the control and interventions as a function of time over the course of 9 weeks after study enrolment (**Annex VIII**, Figure 1). The results showed a non-significant difference between groups, primarily caused by a marked decrease in the mean daily step count of the control group. The course of step count for the intervention group remained stable over time.

Using the messaging function

A total of 42 patients used the message function to send information or questions to the researcher (**Annex VIII**, Table 3). 50% of the participants received messages (regarding the beneficial effects of physical activity) from the researcher.

Responding to questionnaires

The CARAT, SF12, CCQ, TIC-p and the IPQ-k have been sent to patients at baseline. Most patients have already received the follow-up questionnaires. All 36 patients completed these questionnaires at baseline, 3 participants answered the 3 months follow-up questionnaires. An overview of the responses to the questionnaires is presented in **Annex VIII**, Table 4).

4.4.7 Patient satisfaction with the technology

Satisfaction with the CONNECARE system – Likert scales and Net Promoter Score (NPS)

Patients were asked to assess their experience with the CONNECARE system, including the SMS app and connected devices (Annex VIII, Table 5). They were asked how probable it is that they would recommend the system to a friend or co-workers. The average NPS score was 8.2 and thereby reached the threshold of excellence (>70%).

Satisfaction with the CONNECARE system – Likert scales and Net Promoter Score (NPS)

Patients were asked to assess the usability of the CONNECARE system, including the SMS app and connected devices (**Annex VIII**, Table 6). Acceptability scoring ranged from 0 (lowest) to 10 (highest). The median SUS was 83, which rates the product in the threshold for excellence (>80). A detailed overview of response between both the control and the intervention groups is presented in **Annex VIII**, Figure 2.

4.4.8 Issues with the Digital Tools Recorded in the Implementation log

SACM & SMS usability problems

- Mainly usability and connectivity issues were mentioned by patients. We performed focus groups with mock-up versions of the SMS app to test the user friendliness and to make recommendations for improvements.
- Patients reported problems with the navigation in the SMS app. Especially the number of icons and font size was mentioned as being difficult.
- The SMS kept crashing without opening it. The problem was caused by the setting on an iPhone 6S: the option of using the app with mobile data was turned off. When the setting was turned on again the problem was solved.
- The email with password was not received, also not in the spam folder.
- There was an error while creating a professional account in the SACM.
- In older Android phones the CONNECARE application was not visible in the Play store.

Technical problems with SACM & SMS

- Most of the technical issues reported in the implementation log were bugs that needed to be reported, prioritized and solved on a regular basis. These bugs included tasks being tagged as completed at the time of prescription; issues with decimal values introduced to the SACM/SMS; messages not reaching all the involved professionals; desynchronization between the SACM and SMS when changing prescriptions, team members or other key aspects of a given patient care plan; issues in the time registry of when a given action was performed; etc. All these issues were solved promptly but generated some occasional discomfort with the system among its users. This implies the need for a permanent technological support team while the CONNECARE system is implemented and ongoing.

4.4.9 Intervention effectiveness – Patient outcomes and resource use

Based on the data available for analyses, change scores between baseline and 3-month assessment were calculated for the control (n=11) and intervention groups (n=13) for disease severity (CCQ survey) and for the control (n=8) and intervention groups (n=10) on health status (SF-12). Results are presented in **Annex VIII**, Table 7. Disease severity as measured by the total CCQ score showed a non-significant improvement in both groups, with the intervention groups improving in mental status. The SF-12 (subscale MSC) showed a non-significant improvement in the intervention group.

Data on resource use and care utilization was available up to 3 months after study inclusion. The mean length of hospital stay, hospitalisation and total number of days is presented in **Annex VIII**, Table 8. No significant differences were observed between the groups.

Annex VIII, Table 9 provides an overview of visit to the general practitioner (GP) for both groups. A non-significant decrease in the mean number of GP contacts was observed in the intervention group, whereas an increase was observed in the control group. The cumulative number of hospital days also reduced in the intervention group, whereas in the control group this remained stable. The number of specialist visits is presented in **Annex VIII**, Table 10.

4.4.10 Costs – benefit analyses

Direct and indirect costs of the intervention were all covered by the project budget allocated to us as clinical site. The majority of the costs made constituted hiring research personnel to act as case managers for both implementation studies. The costs-effectiveness analyses could not be completed due to a lack of complete data. Information collected in the TiC-P questionnaire, combined with data on healthcare use (as depicted above), illness and occupation with be used for analyses will form the costs element of the analyses, together with health outcome measures as a measure of effectiveness.

4.5 Summary for all sites

In general, the model of integrated care delivery supported by the CONNECARE systems was well perceived and implemented. Use of the SMS and connections with mobile devices providing remote monitoring and communication with the case manager was perceived as very positive by the patients. As such, the continuity of care delivered by the systems connecting hospital services with primary care extending to social services was successfully introduced. Patients rated the integrated care service as measured by the P3CEQ and the NCQ in all sites as good, suggesting a high perceived patient-centeredness of the CONNECARE system. Actual recruitment of patients was challenging at the start of the implementation studies, but increased by making adaptations to patient inclusion criteria, patient instruction protocols, recruitment sites and collaboration among professionals. Although recruitment rates were satisfactory, and drop-out rates low, still a considerable portion of eligible patients could not be included in the study. Reasons for exclusion are many but main reason include high mental burden and to some extent digital illiteracy.

With regard to the technology, compliance of patients with using the Fitbit was especially high, also up to 90 day follow up and in the case of Groningen 180 days. Compliance with the other connected devices such as blood pressure and heart rate proved more difficult and some patients had to rely on manually entering the information into the SMS app. As the messaging function and possibility to digitally send questionnaires became available relatively late in the project, actual usage of these functionalities was relatively low. In terms of IT integration in most sites the CONNECARE system was used as a stand-alone, as automated connections with primary and/or hospital information systems proved challenging. Still, progress has been made in this respect and features such as a digital copy of EMR health status was successfully integrated in the CONNECARE system. Important observations and lessons learned

were collected throughout the implementation process, relevant for the potential for scaling up of the CONNECARE IT system and connected devices. Clearly, the role of the case manager and involved professionals should be further developed, as to support integration into routine clinical care pathways. Results showed that training of case managers was feasible, but as their activities were predominantly financed out of project budgets, sustained implementation was not yet achieved. The interfaces and functionalities available for patients and professionals should receive continued attention as this promotes engagement and continued use of the systems. Also, continued support of local IT department is foreseen as technical issues such as connectivity problems and lack of integration into information systems are mentioned as large obstacles for sustained implementation.

With regard to the use of the SMS and the SACM, important usability issues were mentioned that could hinder sustained implementation. With regard to the SACM, full integration of its component in hospital information systems is necessary, with a pivotal role of care professionals in the co-design and implementation of the system. As such the functionalities should be integrated in care-as-usual processes, so as the professionals do not have to work in two separate systems simultaneously. For the SMS development of specific back-end technologies other than the SACM should be considered, an approach taken by Barcelona in protocol IIIC and case studies 2 (D6.3 “Results from Case Study 2”) and 3 (D6.4 “Results from Case Study 3”). Still, patient engagement with SMS and connected devices was high in all clinical sites, reflecting satisfactorily implementation of the concept.

It is important to note that, in the analysis done by Lleida and Israel, patient satisfaction and (in Israel) staff satisfaction increased over time as the technology matured. One of the main intents of the implementation pilots was co-design of the technology through actual use in a “real life: situation. This led to identification of bugs and technical problems, obstacles to usability and ease of use that were feedback to the technology developers and addressed by refining and improving the digital tools. This resulted in a significantly more mature product by the end of the implementation pilots.

Across clinical sites the CONNECARE, intervention, although tested in relative small groups, suggest significant improvement in patient health outcomes. Especially the domain of physical activity was improved among patient groups, as a results of the intervention. The costs and associated cost-effectiveness was assessed by the majority of the clinical sites. Compared to care-as-usual, the CONNECARE system seems to generate value for money, and cost-effectiveness analyses suggest extended dominance for the CONNECARE intervention. Importantly, the positive results are associated with improvement in patient health status such as physical activity, decreased pain discomfort and an overall feeling of health and well-being. Significant reductions in hospital admission and other care providers suggest that the CONNECARE system indeed has the potential to reduce healthcare costs by preventing care utilizations of patients. These results should be studied in other populations and larger groups in order to support further scaling up and implementation of CONNECARE-like systems in daily practice.

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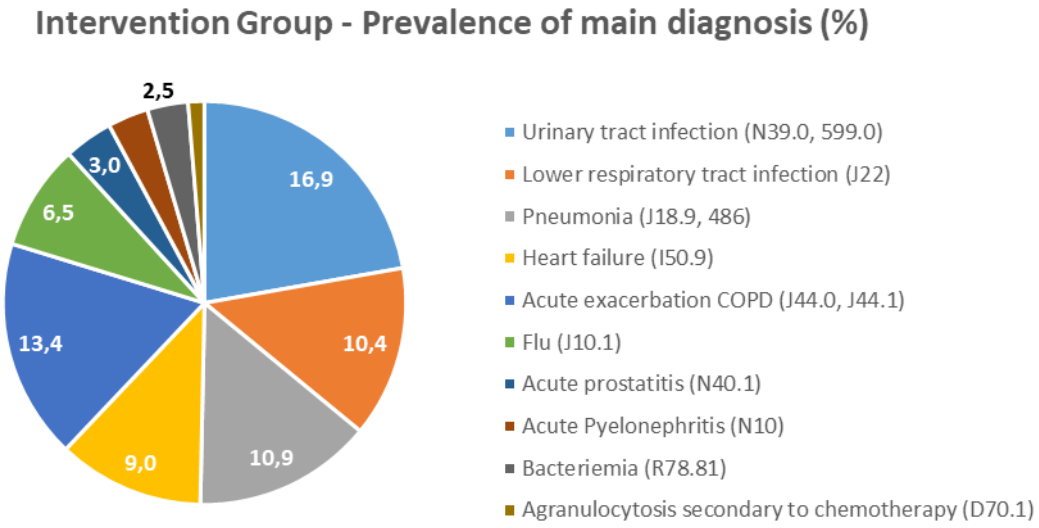
6.1. Barcelona

ANNEX I – Implementation study results of home hospitalization in AISBE (Protocol IA)

Table 1S. Baseline characteristics of the home hospitalization and the usual care groups for a subset of 200 patients and for home hospitalization of the entire study group (n=620).

Table 1 - Baseline Characteristics	Home Hospitalisation (n=201)	Usual Care (n=181)*	p value <0.05	Entire study group (n=620)	p value <0.05
SOCIO-DEMOGRAHICS					
Age (yrs), m(SD)	73.58 (13.3)	73.19 (14.86)		72.2 (16.09)	
Gender (male), n (%)	121 (60.2)	100 (55.25)		354 (57.19)	
USE OF HEALTH CARE RESOURCES					
Hospital resources in previous 12 m					
Rate of all-cause emergency room visit, mean(SD)	1.79 (1.27)	1.86 (1.32)		1.71 (1.14)	
Last ER visit (days) before admission, mean(SD)	94.27 (106.94)	119.59 (105.73)		95.08 (110.76)	
Rate of all-cause Hospital admissions, mean(SD)	**1.56 (0.92)**	**2.05 (1.49)**	**0.0375**	1.69 (1.13)	
Rate of planned admissions, mean(SD)	1.46 (0.73)	1.58 (0.85)		1.4 (0.7)	
Last visit (days) to outpatient clinic before admission, mean(SD)	85.98 (90.27)	79.27 (84.84)		79.34 (88.24)	
Last hospitalisation (days) before admission, mean(SD)	200.72 (106.1)	223.23 (111.33)		190.26 (108.14)	
Length of stay in days (total days per year), mean(total)	11.37 (614)	17.7 (991)		11.51 (2129)	
Intensive care unit stays, n(%)	9 (10.7)	12 (10.4)		27 (8.7)	
Outpatient visits, mean±SD	5.85 (6.83)	6.02 (6.52)		6.41 (7.46)	
Hospital resources in previous 7 days					
Outpatient visits, mean±SD	1.18 (0.6)	1.28 (0.57)		1.2 (0.55)	
MULTIMORBIDITY & SEVERITY					
GMA scoring	3.21 (0.69)	3.28 (0.72)		N/A	
"Complex Chronic Patient " (PCC), n(%)	55 (27.36)	48 (26.52)		154 (24.88)	
"Advanced chronic disease and life limited prognosis " (MACA), n(%)	4 (1.99)	10 (5.52)		26 (4.2)	
"Limitation of therapeutic effort" (LET), n(%)	**5 (2.49)**	**15 (8.29)**	**0.011**	17 (2.75)	

As displayed in **Table 1S**, the usual care group of 200 patients showed higher rate of hospitalizations in the previous year and higher percentage of patients classified as LET (limitation of therapeutic effort) than the home hospitalization group. But the two groups were similar in all other dimensions depicted in the table. It is of note that the intervention group of 200 patients is highly representative of the entire intervention group of 620 patients.



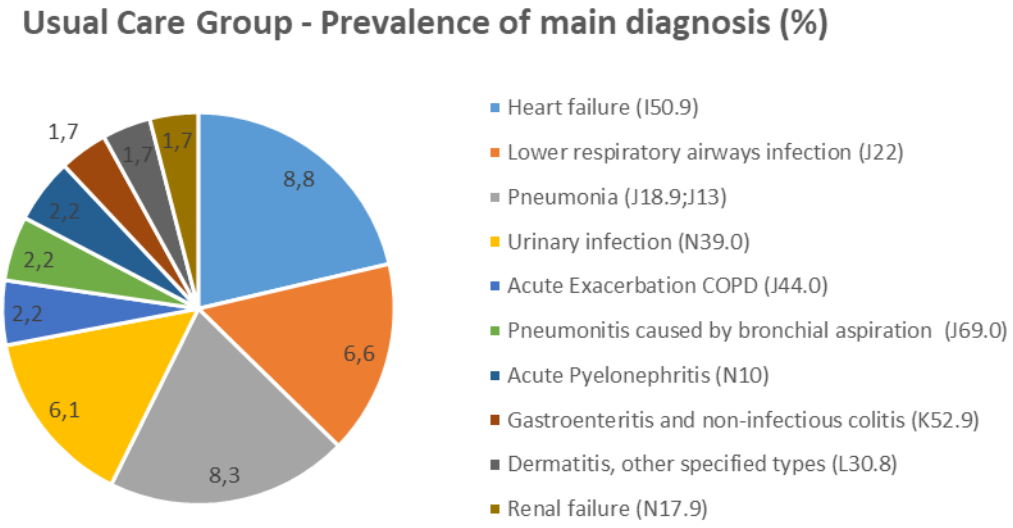


Figure 1S. Top ten main diagnosis of the intervention (upper panel) and control (lower panel) groups for a subset of 200 patients of the entire study group.

The HH group (n=200) showed significantly better health outcomes during the 30-day period post-discharge and displayed better patient reported outcomes than the control group. It is of note that health outcomes were similar between the subset of 200 HH patients and the 620 patients of the entire study group.

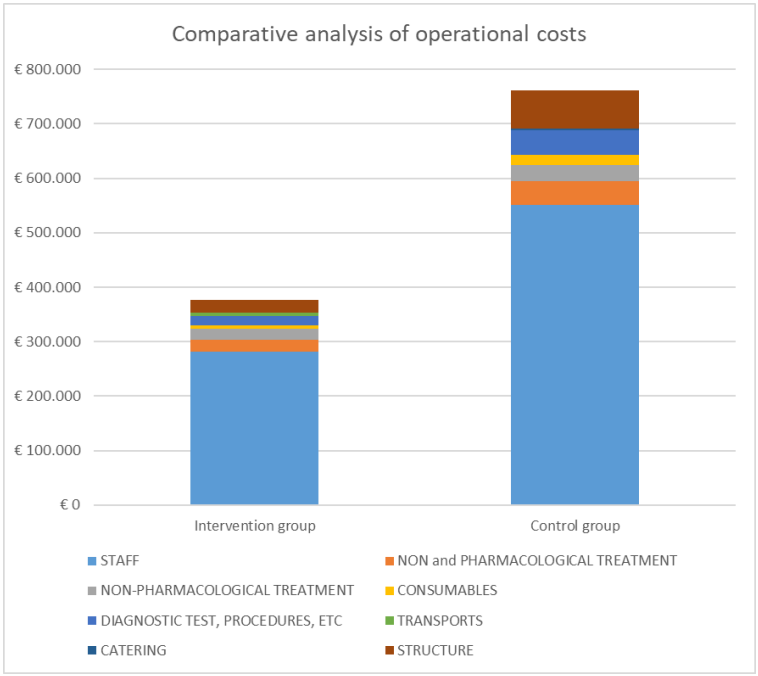


Figure 2S. Comparative analysis of operational costs for a subset of 200 patients of the entire study group.

As shown in **Figure 2S** below, the overall cost of home hospitalization was half than usual care for almost all items. However, the most striking differences were seen in two components: personnel and structure.

Table 2S. Main health and patient reported outcomes of the intervention (HH) and usual care groups (UC) for a subset of 200 patients of the entire study group and health care outcomes for all 620 patients of the study group.

Table 2 - Intervention Effect	Home Hospitalisation (n=201)	Usual Care (n=181)*	p value <0.05	Entire study group (n=620)	p value <0.05
nº discharge	201	181		620	
Total length of stay, days,m±SD	8.08 (4.4)	8.64 (7.37)		8.09 (4.79)	
Use of resources during HH					
Number of Physician visits, m±SD	0.98 (0.7)	N/A		0.94 (0.76)	
Number of nurse visits, m±SD	**7.94 (4.14)**	N/A		**7.87 (4.6)**	**0.00001**
Number phone call to the patient, m±SD	1.36 (0.89)	N/A		1.3 (0.8)	
All-cause Emergency Room visits, n(%)	3 (1.49)	N/A		11 (1.77)	
All-cause In-Hospital re-admissions, n(%)	6 (2.97)	N/A		28 (4.5)	
Mortality during episode, n (%)	0 (0)	0 (0)		0 (0)	
Outcomes at 30 days after discharge					
All-cause emergency Room visits, n(%)	**9 (4)**	**29 (13.3)**	**0.00016**	38 (5.8)	
All-cause Hospital admissions				52 (8.9)	
Hospital admissions, n(%)	**11 (5)**	**21 (11)**	**0.0308**	41 (6)	
Number of planned admission, n(%)	5 (2.5)	10 (5.5)		20 (3.1)	
Mortality, n (%)	2 (1)	2 (1.1)		7 (1.1)	
Patient reported outcomes after discharge					
Quality of Care Transitions (CTM-15)[1]	**87.16 (18.24)**	**57.33(23.23)**	**<0.000**	N/A	
Patient experience (IEXPAC)[2]	**5.10 (2.8)**	**3.78(3.22)**	**0.00002**	N/A	
Quality of life (EuroQol-5D)[3]	**0,80 (0,17)**	**0,75 (0,15)**	**0.0066**	N/A	

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Each item is scored from 0 to 10, as follows: Never 0 ; Almost never: 2.5 ; Sometimes: 5 ; Almost always: 7.5 ; Always: 10 .

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Index value from 0 to 1. The average of the country is taked into account for the final scire. The average scor for Spain is 0,914 (0,15) and for >85 yrs. is 0,625 (0,29).

Table 3S. Description of the implementation strategy following the CFIR approach [1].

CONSTRUCTS	**Implementation at HCB (2006-2015)**	**Expansion at health-district level, AIS-BE (2016-2018)**	**Key recommendations**
INTERVENTION CHARACTERISTICS			
Intervention Source	Internally developed	Internally developed	-Hospital at home as an integrated care service -Core components: 1) Hospital avoidance or early discharge; 2) Hospital-based professionals 3) Service workflow defined 4) Define target patients' profiles 5) Transitional care strategies -Adaptability of non-core components is required. -Continuous quantitative & qualitative build-in evaluation is needed
Evidence Strength & Quality	Results from internal research [2, 3]	Results from period 1[4]	
Relative Advantage	-Patients & caregivers: satisfaction -Hospital-based professionals: satisfaction, organizational & clinical results -Managers: health outcomes & cost containment	-Identical to period 1 + -Health-district care providers endorse scale-up of the program -Community-based professionals: mixed feelings *(acknowledge advantage, but competitive issues emerge)*	
Adaptability	Core components: i) Hospital-based teams; ii) Hospital avoidance or early discharge; iii) Workflow defined & patient profiles; iv) Structure to support the workflow Adaptable components: i) Any other aspect	Core components: -Identical to period 1 + -Appropriate training & QA program Adaptable components -Any other aspect	
Trialability	-Results from internal research [5-9] -A building-blocks strategy with stepwise progression of deployment with continuous evaluation [8]	-Idem, as reported in the current manuscript	
Complexity	High complexity process requiring coordination of: i) Clinical protocols; ii) Redefine tasks & roles; iii) Home-based logistics; iv) Digital support; v) Professionals' training ; vi) Information for patients; vi) Coordination among providers; vii) Reimbursement modalities	- Identical to period 1	
Design Quality & Packaging	-Key elements: i) Explanation of the intervention to patients; and, ii) Home-based logistics	- Identical to period 1	
Cost	-Implementation costs were covered by efficiencies generated without allocation of a specific budget for this purpose	-Expansion costs were covered by a new financial structure	

	-Operational costs were calculated following an analytical approach [3, 4] showing health-value generation	agreed with the single public payer -Operational costs reported in the current paper. Cost-effectiveness confirmed	
OUTER SETTING			
Patients' needs & resources	-Alignment with PRISM (Patient-centered care): i) patient choices & barriers taken into account and solved; ii) transitional care after discharge implemented; iii) Lean strategy minimizing costs; and, iv) patients' accessibility, satisfaction & opinions considered and taken as inputs to improve.	- Identical to period 1 + -Patient experience program at HCB [10]	-Patient-centered orientation should be a core trait -Networking across experiences enriches the programs -Site customization is required to minimize potential negative impacts of external factors
Cosmopolitanism	-Build-up as a functional integration of healthcare providers at district level (AIS-BE) [12] -Progress through continuous interactions among regional providers [11] -Leading role at EU level (four stars reference site EIP-AHA) [13, 14]	-Further progress both at local *(regional consensus on home hospitalization driven by the single-public payer)* and EU levels [15]	
Pier pressure	- Support from the single-public payer and internal managers - Moderate transient resistances from professionals from primary care and other internal clinical units -Expansion beyond HCB limited by reimbursement modalities to other health-district provider organizations	-Changes in reimbursement modalities facilitated expansion to other providers in the health district. -Previous resistances disappeared	
External Policy & Incentives	- Implementation was an internal decision with weak external support. - Program should be considered as a learning experience - EU funding provided additional financial support [16-18]	-Consolidation of the program at HCB fostered a specific mandate of the single-public payer to expand the program	
INNER SETTING			
Structure Characteristics	-Institutional traits favoring the driving role: i) dual mission (needs for tertiary care beds); ii) leading role of professionals in the management (efficiency is a must); iii) institutional choice towards continuum of care [19]; and, iv) digital transformation in place -The vertical organization in clinical institutes was a relative barrier	-Consolidation of Institutional traits -External support from the single-public payer	

Networks & Communications	-High professional engagement + rather mature digital tools	- Identical to period 1	
Culture	-Mix of type 1 (team culture) and type 3 (entrepreneurial culture) with high engagement of professionals	-Transfer of HCB's culture to the other AIS-BE's providers	
Implementation Climate	-Positive climate for entrepreneurship despite acknowledgment of some internal peer resistances -Tension for change was limited to champions supported by management -Initiative aligned with hospital values and rules. Change management required -The program was acknowledged as a high priority operation -No incentives & rewards were planned, but the role of champions was acknowledged - Goals & Feedback well defined accepted, evolving over time -High involvement of professionals in the development of new interventions to improve patient care	-Maturity of implementation at HCB + -External factors *(financial incentives)* fostered a positive climate for a health district extension of the service -Engagement of professionals from other providers was fostered by the prestige of the original team	-Bottom-up/Top-down interactions are needed for success -Key resources to generate and reinforce a positive climate change are needed
Readiness for implementation	-Readiness for implementation at regional level [8, 19] and at HCB level -High engagement of the leaders. Champion-driven initiative -Creation of a specific unit at HCB -Maturity of health information exchange platform	-Financial incentives facilitated expansion at health district level	
CHARACTERISTICS OF INDIVIDUALS			
Knowledge &Believes about the intervention	-Sustained positive perception of the intervention by both patients and professionals - Acknowledgement of enhanced health outcomes and positive impact on costs - Initial passive resistance of small sectors of professionals attenuated over time	-High level of acceptance at all levels -Refinement of transitional care & vertical integration is under debate.	-Continuous monitoring of satisfaction levels and consideration of feedback from patients and professionals is highly recommended [20]
Self-efficacy	- The service generates novel interactions between patients and professionals that foster self-efficacy	-Identical to period 1	
Individual stage of change	-Progressive achievement of active engagement of stakeholders throughout the deployment process	- Identical to period 1 +	

		-Interestingly, consolidation of new professionals' roles is prompting debates on organizational aspects	
Individual identification with organization	-A culture of individual identification with unique traits of the HCB's organization (health professionals' involvement in management) facilitated implementation	- Identical to period 1	
Other personal attributes	-Tolerance, motivation, innovativeness, and learning style have been reinforced during the implementation process	- Identical to period 1	
PROCESS			
Planning	-The deployment plan organized by blocks (specific patients' groups associated to patients' profiles of the clinical institutes at HCB) was designed and progressively implemented with adaptations considering feedbacks received from professionals and patients using different communication channels	- A multidisciplinary team used a PSDA (Plan-Do-Study-Act) methodology [17] during the period	-A building-blocks implementation strategy, with appropriate site customization prioritizing engagement, is required -Continuous evaluation of results [21, 22]
Engaging	-Implementation leaders (champions) triggered and conducted deployment with support, and direct interactions, with HCB's management -A specifically trained group of professionals with high degree of commitment and a transversal multidisciplinary approach contributed to consolidation	- Identical to period 1 + - As mentioned above, a debate on organizational aspects is currently open	
Executing	-Previous experience with two reported RCTs [2, 7] helped to set the basis of the deployment plan, which was executed accordingly. -Continuous monitoring and adaptability of the implementation process were key elements for successful adoption [4]	-Lessons learnt during the previous phase have defined the roots for the expansion phase beyond HCB	
Reflecting & Evaluating	-Continuous quantitative & qualitative assessments were done and reported [4] -Internal monthly meetings and periodic reporting to HCB's executive committee were scheduled and done	- Identical to period 1	

Legend: HCB: Hospital Clínic; AIS-BE: Area Integral de Salut Barcelona Esquerra

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Table 4S. Proposal of Key Performance Indicators for follow-up beyond deployment.

CATEGORIES	INDICATOR	INTENDED OUTCOME	MEASUREMENT	DATA SOURCE	TIME
STRUCTURE	**Coverage (Inclusions HH/ED:usual care ratio)**	Home-based hospitalization are aimed to reach 10% conventional hospital discharges with an expected 2% increase per year	**Denominator.**Total number of hospital discharges per year **Numerator.**Total number of home-based hospitalizations per year	CMBD	yearly basis
	Elements to be considered for running the service:				
	Trained professionals (patient-to-staff ratio depending upon target patients)				
	Accessibily (Call Center)				
	Logistics for home-based delivery of drugs, equipment and personnel				
	Financial structure of the service ensuring sustainability				
	Supporting information and communication technologies (ICT)				
	Educational and training program				
PROCESS	**Average bed occupancy**	95% occupancy	**Denominator.**Bed Days Available during the calendar year **Numerator.**Inpatient Days of HH/ED	CMBD	yearly basis
	Bed turnover rate	HH/ ED bed turnover rate: usual care hospital bed turnover rate, for the same DRG group= 1	**Denominator:** Total number of HH/ED discharges (including deaths) in a given time period **Numerator**: Total number of HH/ED beds during that time period	SAP-CMBD	yearly basis
	Average length of stay per DRG group (HH)	HH length of stay: usual care hospital length of stay ratio, for the same DRG group= 1	**Denominator.**Expected average usual care hospital length of stay per a given DRG. **Numerator.** Average HH length of stay per a given DRG	SAP	yearly basis
	Average length of stay per DRG group (ED)	ED length of stay: usual care hospital length of stay ratio, for the same DRG group= 1	**Denominator.** Average usual care hospital length of stay per a given DRG. **Numerator.** Average ED length of stay per a given DRG	SAP	yearly basis
	Quality Assurance (QA) Program (scoring 0-10)	Above 80%	**Denominator.** 10 **Numerator.** QA scoring x 100	Survey	yearly basis
	Items to be considered & scored (max 1 each)				
	1.Number of candidates excluded due to professionals' criteria				
	2.Comprehensive evaluation and action plan at entry				
	3. Adverse events, missing data and incidents				
	4.Rate of medication errors				
	5.Rate of incidents during the transfer from hospital to home				
	6.Rate of home visits during the first 24h of admission				
	7. Rate of nurse visits at home per day				
	8.Rate of Physisican visit at home				
	9Time response call (<5 minutes)				
	10.Rate of contacts to ensure transitional care at HH/ED discharge				
OUTCOMES	**PATIENTS - Intermediate outcomes**				
	% transfers back to hospital during HH/ED	No unplanned transfers back to conventional hospital admission	**Denominator.N**umber of episodes admitted to HH/ED **Numerator.** Number of unplanned transfers back to hospital during the episode x 100	SAP	yearly basis
	Mortality rate	No mortality during HH/ED	**Denominator. N**umber of patients managed in the HH/ED **Numerator**. Number of deaths during the episode of HH/Edx 100	SAP	yearly basis
	30-day emergency room visits' rate for related cause rate	HH/ED emergency room visits: conventional hospitalization ratio per DGR <=1	**Denominator.**Conventional hospitalization ER visits by a given DRG **Numerator.** HH/ED ER visits by a given DRG	SAP	yearly basis
	30-day unplanned hospital admissions' rate for related cause	HH/ED unplanned hospital re-admissions: Conventional hospitalization re-admissions ratio by a given DRG= <1	**Denominator.**Conventional hospitalization ER visits by a given DRG **Numerator.** HH/ED ER visits by a given DRG	SAP	yearly basis
	30-day total hospital re-admissions for related cause rate	HH/ED total hospital re-admissions: Conventional hospitalization re-admissions ratio by a given DRG= <1	**Denominator.**Conventional hospitalization ER visits by a given DRG **Numerator.** HH/ED ER visits by a given DRG	SAP	yearly basis
	PATIENTS - Final outcomes				
	Patient satisfaction	> 80% High level satisfaction with HH/ED	**Denominator.**Total number of HH/ED patients **Numerator.** Number of hihgly satisfied HH/ED patientsx100	survey	yearly basis
	Family satisfaction	> 80% High level satisfaction with HH/ED	**Denominator.**Total number of HH/ED patients **Numerator.** Number of hihgly satisfied HH/ED carersx100	survey	yearly basis
	% Complaint letters	No complaint letters	**Denominator.**Total number of HH/ED patients **Numerator.** Number of complaint letters x100	survey	yearly basis
	% Letters appreciation	> 20%	**Denominator.**Total number of HH/ED patients **Numerator.** Number of appreciation letters x100	survey	yearly basis
	30-day mortality rate	No deaths following a HH/ED episode of care	**Denominator.** Total number of HH/ED patients **Numerator**. Total number of HH/ED deaths	SAP	yearly basis
	HEALTH CARE PROVIDERS				
	Rate of professionals turnover	<10% turnover	**Denominator.** Number of personnel **Numerator**. Number of personnel changing workplacex 100	survey	yearly basis

ANNEX II - Health risk assessment for enhanced clinical decision support in patients under HH/ED (Protocol IB)

Predictive Modeling of 30-day Mortality and Readmission Risk from Multilevel Data: A Case Study on Patients Hospitalized at Home

Mireia Calvo[1], Isaac Cano[2], Núria Seijas[2], Emili Vela[3], Carme Hernández[2], Vicent Ribas[4], Felip Miralles[4], Josep Roca[2], and Raimon Jane[1,5,6]

[1]Institute for Bioengineering of Catalonia (IBEC), the Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2]Institut d'Investigacions Biomèdiques August Pi i Sunyer, Centro de Investigación Biomédica en red, Enfermedades Respiratorias, University of Barcelona, Barcelona, Spain
[3]CatSalut, Servei Català de la Salut, Barcelona, Spain
[4]Eurecat, Technology Center of Catalonia, Barcelona, Spain
[5]Universitat Politècnica de Catalunya (UPC)-Barcelona Tech, Barcelona, Spain
[6]Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Barcelona, Spain

Abstract

Home hospitalization (HH) is a healthcare alternative capable of providing high standards of care in the patient's home. A previous study on the HH program of Hospital Clinic of Barcelona over a 10-year period (2006-2015) clearly demonstrated its effectiveness and high level of user's acceptance. However, health-risk assessment is still needed so as to provide support for clinical decision made at patient admittance and discharge.

To this end, this paper proposes a machine-learning approach for the early-prediction of hospital readmission and death after HH. It is based on a multilevel solution since it relies on the hypothesis that health-risk assessment could be significantly improved by combining clinical, biological and population-based data.

Predictive models were evaluated on a real-world database including 1832 cases having been admitted to the HH program of Hospital Clinic of Barcelona from January 2012 to December 2015. The results show a prediction performance, captured by the Area Under the Curve (AUC), of 0.73 for the prediction of readmissions and of 0.90 for mortality risk. Moreover, this study provides directions for the translation of health-risk assessment models to daily clinical practice.

Introduction

Home hospitalization (HH) emerged in response to the growing demand for hospital care and the high costs associated with the diagnosis and treatment of acute and chronic decompensated diseases. This healthcare alternative is capable of providing high standards of care through a set of home-based medical and nursing services. Indeed, HH has demonstrated to lower healthcare-associated costs by shortening hospital stays and avoiding readmissions; and it has been presented as an opportunity to improve integrated care[1–3]. Moreover, HH has shown scalability potential for both acute and chronic

patients, strengthening care coordination between highly specialized hospital-based care and home-based services involving different levels of complexity.

An exhaustive assessment over a period of 10 years (2006-2015) on the deployment of HH at Hospital Clinic clearly demonstrated its safety and effectiveness, as well as a high level of user's acceptance and a great health value generation leading towards the sustainability of the service4 and the efficient transference of patients from hospital to the community5 after hospital discharge. However, the high heterogeneity of patient's clinical conditions is triggering the need for appropriately designed health-risk assessment strategies in order to give support to clinicians with respect to: i) the eligibility checking at the moment of admission to HH and ii) the proper allocation of transitional care services after HH discharge.

Recently reported works have already proposed machine-learning strategies for the early-prediction of 30-day readmission risk after hospital discharge in chronic obstructive pulmonary disease (COPD) patients6, as well as for the prediction of mortality risk after surgery7. Nevertheless, since HH patients can be extremely heterogeneous and mostly comorbid, this study proposes a novel approach capable of stratifying patients for whom there is no currently available score for their health-risk assessment.

To this end, this study reports a machine-learning approach for the prediction of 30-day mortality and readmission at HH discharge. It is based on the hypothesis that the application of holistic strategies for subject-specific risk prediction and stratification, that consider multilevel covariates influencing patients health, such as clinical, biological and population-based information, could increase the predictive accuracy and facilitate clinical decision-making based on sound estimates of individual prognosis8. More specifically, developed predictive models were evaluated on a real-world database including 1832 cases having been admitted to the HH program delivered by Hospital Clinic of Barcelona from January 2012 to December 2015. Therefore, this study evaluates the feasibility of the proposed approach as a clinical decision support system (CDSS) and its potential implementation in real-world settings.

Results

Table 1 summarizes the average classification performances, as well as their variabilities, when predicting the risk of 30-day readmission and mortality, both at the moment of HH admission (RM1 and RM2) and discharge (RM3 and RM4).

Regarding 30-day readmission risk at the moment of admission (RM1), the upper left panel in Figure 1 shows the importance of the 20 most relevant variables, for the hold-out combination providing the best AUC results (*AUC* = 0.73; *Se* = 0.68; *Sp* = 0.65; *Sc* = 0.67). Similarly, the lower left panel represents the importance of the 20 most relevant features, when predicting 30-day readmission risk at HH discharge (RM3), leading to the following best result: *AUC* = 0.73; *Se* = 0.71; *Sp* = 0.66; *Sc* = 0.68.

Table 1. Average results for implemented risk models.

	AUC	Sensitivity	Specificity	Score
Readmission risk at HH admission (RM1)	0.70 ±0.02	0.69 ±0.03	0.63 ±0.03	0.66 ±0.03
Readmission risk at HH discharge (RM3)	0.71 ±0.02	0.68 ±0.07	0.63 ±0.04	0.66 ±0.02
Mortality risk at HH admission (RM2)	0.86 ±0.03	0.80 ±0.13	0.73 ±0.05	0.77 ±0.06
Mortality risk at HH discharge (RM4)	0.90 ±0.03	0.85 ±0.15	0.78 ±0.05	0.82 ±0.07

Based on these results, although both clinical and biological data seem to provide relevant information for the prediction of 30-day readmission, it is to note the evident significance of the GMA index in predictive models. Moreover, the red cell distribution width (RDW) shows a significantly higher importance than the rest of features, for both RM1 and RM3 models. Other clinical variables such as the Charlson index, age or the body mass index (BMI) also showed elevated relative importance. In addition, when information during home hospitalization was taken into account in RM3, several variables gained importance, among which the number of days hospitalized at home (daysHH) stood out, showing a relative importance of almost 80%, with respect to GMA.

The importance of the 20 most relevant variables in case of 30-day mortality risk at the moment of admission (RM2), for the hold-out combination providing the best results, is shown in the upper right panel of Figure 1 (*AUC* = 0.89; *Se* = 1; *Sp* = 0.73; *Sc* = 0.86). Finally, the lower right panel represents variable importance for the best model predicting 30-day mortality risk at HH discharge (RM4): *AUC* = 0.94; *Se* = 1; *Sp* = 0.76; *Sc* = 0.88.

Variable importance for the prediction of 30-day mortality showed a similar behaviour when comparing models designed at admittance (RM2) and discharge (RM4). While in RM2 most variables showed a relative importance of less than 60% with respect to the most important feature, when the information acquired during home hospitalization was included (RM4), several variables gained significant importance. More specifically, 10 features demonstrated relative importances of more than 60%. In this case, although the GMA index remained an important variable, most of the predictive power was absorbed by other clinical variables, probably capturing similar information, such as the Barthel index, the mental state or the habit of walking regularly.

Discussion

According to obtained AUC and Score values, the results show reasonably high classification performances outperforming recent works on similar scenarios[6,9]; demonstrating the feasibility of the proposed machine-learning approach for the prediction of 30-day mortality and readmissions at HH discharge.

More specifically, the best results were obtained for mortality prediction, which might be related to the fact that more severe cases can be more easily identified from the information provided by collected features. Moreover, although better predictions were obtained at HH discharge (RM2 and RM4), risk models designed with only those features acquired at HH admittance (RM1 and RM3) already provided reasonably high performances. Thus, although data on HH stays could provide additional information, since most discriminant features seem to be already provided at admittance, the results highlight the importance of a proper health-risk assessment at the moment of hospital admission.

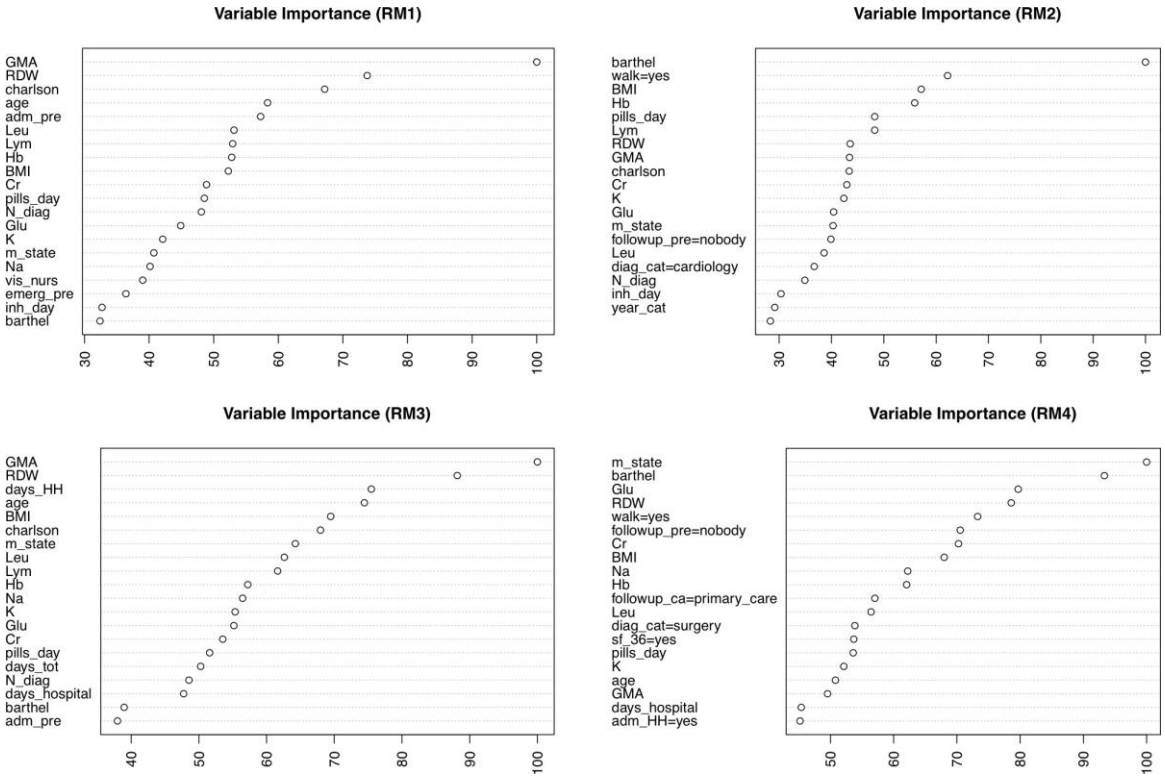

Figure 1. Relative importance of the 20 most relevant variables for each risk model.

However, a major limitation of data-driven approaches, such as the one proposed herein, is the fact that they can be considered as "black-box" solutions, difficult to interpret by clinicians. This machine-learning approach, though, is based on random forest models providing some interpretable information regarding variable importance and, thus, allowing to identify which features seem to be the most relevant for health-risk assessment in this particular home hospitalization scenario.

Thus, regarding variable importance results, although both clinical and biological data seem to provide relevant predictive information, it is to note the evident significancy of the GMA in 30-day readmission models, suggesting the inclusion of this population-based marker in order to improve health-risk assessment. In addition, red cell distribution width (RDW) turned to be a significant predictor of 30-day readmissions, which concurs with previous studies where a higher RDW was found to be a strong independent predictor of morbidity and mortality in heart failure[10]. The Charlson index, age, and BMI also showed remarkable importances and, when information on HH stays was taken into account, the duration of home hospitalization seemed to be a relevant marker of risk improving predictive performance.

Although previous features, including the GMA index, remained important variables for the prediction of 30-day mortality, most of the predictive power in these models was absorbed by other clinical variables capturing similar information, such as the Barthel index, the mental state or the habit of walking regularly.

Thus, this study proves the potential of the proposed machine-learning risk models for the prediction of readmissions and deaths after HH discharge in real-world settings. Since they are based on data regularly acquired in clinical practice, this work proposes a multilevel solution combining clinical, biological and, notably, population-based data, in order to design a clinical decision support system allowing to advance towards sustainable and patient-centered healthcare services. Although this study provides a first step to give support to clinicians in eligibility criteria at the moment of HH admission and in the proper allocation of transitional care services after HH discharge, future work will be focused on designing the

implementation of this approach in real-world settings so it can provide directions for the translation of health-risk assessment models to daily clinical practice.

Methods

Study design and participants

The clinical, biological and population-based data (64 variables) from 1950 patients having been admitted to the HH program delivered by the Integrated Care Unit at Hospital Clinic of Barcelona (Spain) were collected in the context of a retrospective study conducted from January 2012 to December 2015. The study protocol was approved by the Ethical Committee for Human Research at Hospital Clinic and all patients signed a written informed consent before participation. Nevertheless, the analyses conducted in this work were only based on those 1832 cases where readmissions and mortality were directly related to the main diagnosis of hospital admission.

Participants ages ranged between 16 and 105 (70.7±14.8) years old and 62% were males. In order to characterize different populations of risk, patients were classified as undergoing successful and unsuccessful HH stays based on their 30-day readmission and mortality after hospital discharge. From 1832 patients being firstly admitted to the HH program, 32 died and 177 got eventually readmitted to hospital due to complications of heterogeneous origin (unsuccessful groups). The remaining 1800 and 1655 respective patients were identified as the successful groups when analyzing mortality and readmission risks. Tables 2 and 3 summarize the baseline characteristics of both study groups, according to 30-day mortality and readmission, respectively.

Table 2. Clinical characteristics of successful and unsuccessful cases, based on their 30-day mortality after HH discharge.

	Successful (n=1800)	**Unsuccessful (n=32)**	***p*-value**
Age, *years old*	70.5 ± 14.9	78.0 ± 10.9	0.003
Male sex, *n (%)*	1124 (62.4%)	16 (50.0%)	0.209
Main diagnosis, *n (%)*			
Cardiology	186 (10.3%)	13 (40.6%)	<0.001
Respiratory	558 (31.0%)	4 (12.5%)	0.040
Oncology	140 (7.8%)	8 (25.0%)	0.001
Surgery	366 (20.3%)	0 (0.0%)	0.009
Acute	550 (30.6%)	7 (21.9%)	0.387

Values are mean ± standard deviation or number of observations (%).

Table 3. Clinical characteristics of successful and unsuccessful cases, based on their 30-day readmission after HH discharge.

	Successful (n=1655)	**Unsuccessful (n=177)**	***p*-value**
Age, *years old*	70.4 ± 15.1	73.3 ± 11.6	0.063
Male sex, *n (%)*	1021 (61.7%)	119 (67.2%)	0.173
Main diagnosis, *n (%)*			
Cardiology	169 (10.2%)	30 (16.9%)	0.009

Respiratory	510 (30.8%)	52 (29.4%)	0.758
Oncology	120 (7.3%)	28 (15.8%)	< 0.001
Surgery	343 (20.7%)	23 (13.0%)	0.019
Acute	513 (31.0%)	44 (24.9%)	0.109

Values are mean ± standard deviation or number of observations (%).

While age and the incidence of respiratory diseases seems to be higher in patients dying after 30 days, these variables show similar values between successful and unsuccessful groups based on 30-day readmissions. Moreover, the incidence of cardiovascular, oncological and surgical conditions was higher in both unsuccessful groups of patients.

Predictive analytics workflow

Figure 2 illustrates the global methodology proposed in order to identify patients at risk of readmission or death after HH discharge. It is based on a machine-learning approach built from the following three main steps, further explained in the following sections:

A. Feature extraction. The clinical, biological and population-based data acquired during HH stays were included as potential relevant features, composing a database of 64 features by 1832 cases.

B. Data preprocessing. In order to handle the impact of missing values, a robust method designed for mixed-type data imputation was applied to the whole dataset. Then, since some categorical variables presented a great amount of categories, some of them including few samples, we applied a re-discretization of such variables so as to avoid under-represented categories.

C. Classification. Data were 10-times divided in a training/testing subset (75% of randomly selected cases) and the remaining validation subset. In order to reduce the effect of class imbalance (successful cases were far superior in number), a random under-sampling strategy was applied to the training subset. Indeed, sampling and model training were only applied to these subsets, selected using a 10-times repeated 4-fold cross-validation. The remaining 25% of data were then used to quantify the classification performance of developed random forest models, eventually assessed as the average performance of all independent validations.

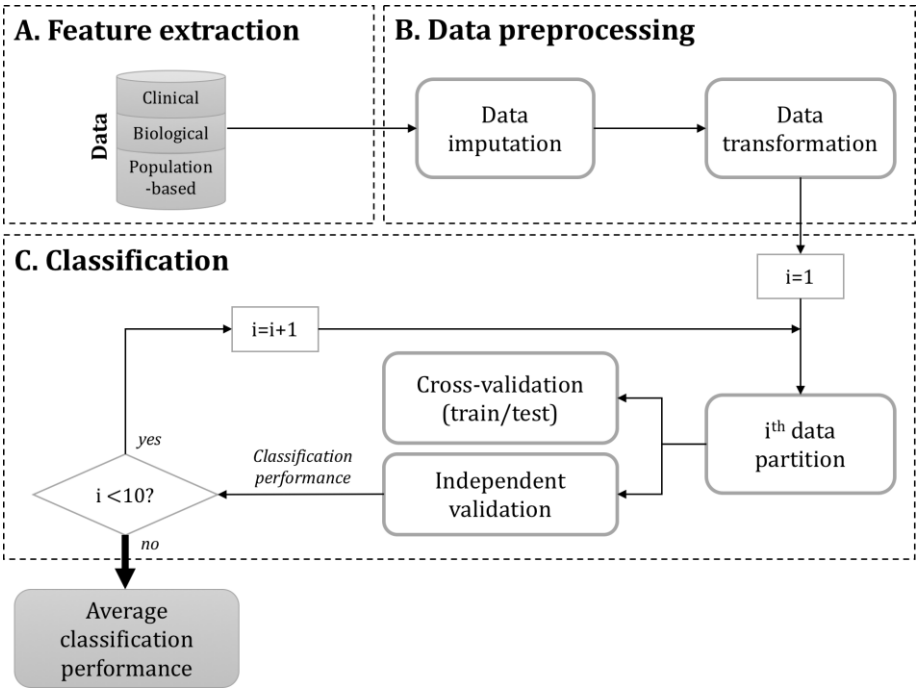

Figure 2. Predictive analytics workflow, composed of three main steps: A) Feature extraction, B) Data preprocessing and C) Classification.

This methodology was applied in four scenarios, leading to four different final models (RM1-RM4), represented in Figure 3. Each model was designed for the identification of patients undergoing unsuccessful stays, taking into account the two available outcomes in this study (30-day mortality and readmissions), as well as its two main objectives: i) while eligibility checking can only be based on those variables acquired at the moment of admission, ii) for the design of appropriate transitional care services, predictive models were built from the whole dataset, taking into account information collected before and during HH.

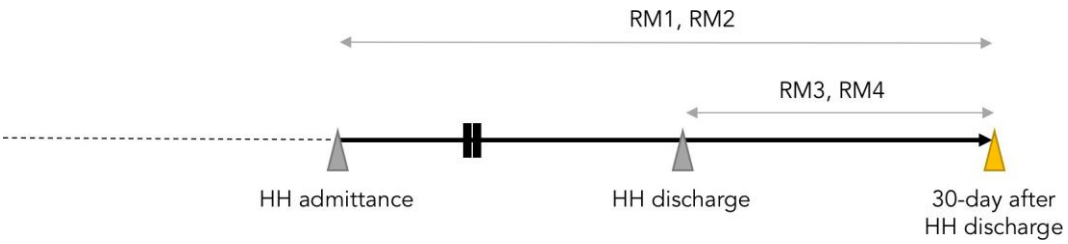

Figure 3. Implemented risk models. RM1 accounts for the model predicting 30-day readmission at the moment of admission; RM2 predicts 30-day mortality risk at admittance; RM3 and RM4 respectively refer to 30-day readmission and mortality prediction at HH discharge.

A. Feature extraction

Health-risk assessment was based on a multilevel solution relying on the hypothesis that subject-specific risk prediction and stratification could be significantly improved by considering multilevel covariates influencing patients' health, such as clinical, biological and population- based information.

On the one hand, 52 clinical variables regularly collected during HH stays, accounting for socio-demographic data, chronic conditions, patient's dependence and risk factors, treatments and use of healthcare resources, were analyzed. On the other hand, since blood test data have proven to provide significant prognostic information in many diseases[11–13], we hypothesized that those patients not being eligible for HH programs and/or requiring special transitional care services after HH discharge could be identified through routine blood tests, performed at the moment of admission. More specifically, after a previously reported statistical analysis performed on the same clinical series[9], the following 8 blood test variables were identified as the most relevant features for classification purposes: leukocyte count (Leu), percentage of lymphocytes (Lym), hemoglobin concentration (Hb), red cell distribution width (RDW), glucose (Glu), creatinine (Cr), sodium (Na) and potassium (K). More details on these features are provided as supplementary material (Table I).

Furthermore, in 2015, the Catalan Health System implemented an innovative population-based risk stratification tool named GMA, Adjusted Morbidity Groups[14, 15], complying with the following recommendations: (i) a population health approach (it uses the entire population of 7.5M inhabitants of Catalonia), (ii) publicly owned with no licensing constraints, based on (iii) open-source computational algorithms, and iv) mostly relying on statistical criteria, as opposed to other tools that include expert-based coefficients, thus facilitating quick transferability to other territories, as shown by the implementation of GMA in most of the regional healthcare systems in Spain. Based on this indicator, the following population-based features were included in the final dataset:

- *GMA cat*: Categorical variable classifying patients in 21 categories, based on the chronicity, complexity and number of physiological systems affected by their underlying diseases.
- *GMA*: Continuous variable capturing patients individual risk.
- *Pstrat*: Categorical variable classifying patients in four categories of risk (low, moderate, high and very high), based on the percentiles 50, 80, 95 and 99 of GMA grading for the general population.
- *Cstrat*: Categorical variable classifying patients in four categories of risk (low, moderate, high and very high), based on the percentiles 50, 80, 95 and 99 of GMA grading for this particular cohort.

B. Data preprocessing

Among the 64 selected features, 34 variables, represented in Figure 4, contained some missing data. Those features presenting more missings were *heparin* (45.5%), the number of applied techniques at home or *Ntecn home* (31.1%), the mental state or *m state* (31.0%) and the Body Mass Index or *BMI* (21.9%), while the other remaining thirty variables contained less than 7% of missing values. In order to reduce the impact of these missing data, a recently proposed method for data imputation, named missForest[16], was applied. Based on random forest algorithms, this non-parametric technique is capable of robustly predicting mixed-type missing values.

Moreover, since some categorical variables presented a great amount of under-represented categories, we applied a re-discretization phase so as to work with features of no more than 21 categories. Some of these re-discretized features were the *ABS* (Basic Health Area) and the *GMA cat*, in which some original categories were merged. Moreover, since diseases responsible for HH admission were labeled based on ICD9 codes, this information was translated into 9 main disease groups (*disease group*). More details on this translation are provided as supplementary material (Table II).

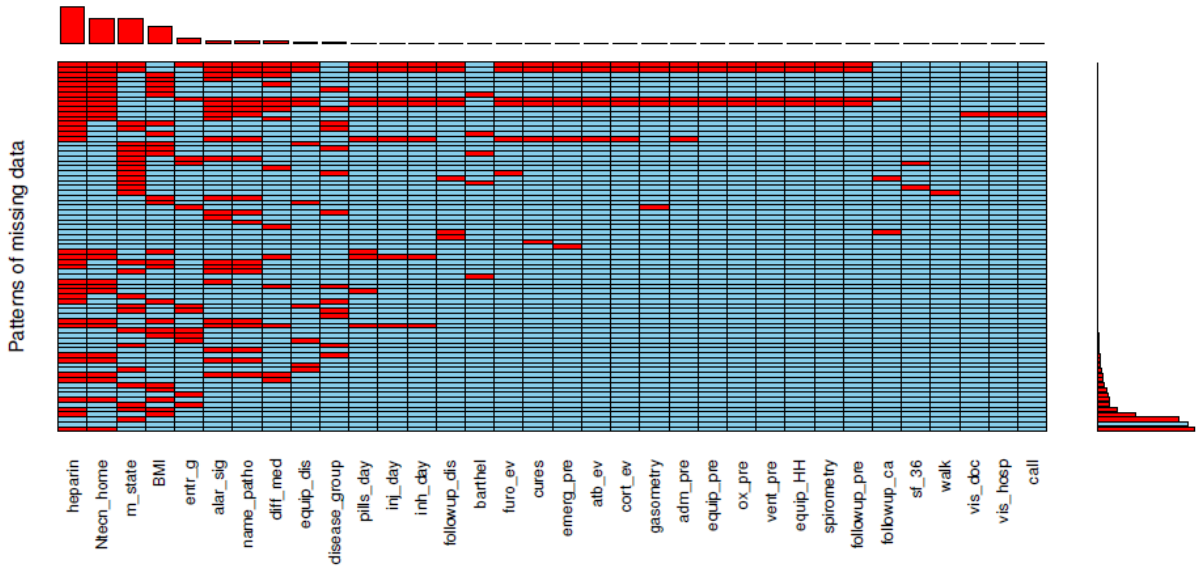

Figure 4. Patterns of missing values and their frequencies. Red squares refer to variables with missing values, while blue cells account for variables containing information in all samples.

C. Classification

For classification purposes, a stratified hold-out partitioning was applied so as to select 75% of data for training and testing (cross-validation) and the remaining 25% for independent validation. To estimate the mean performance variability of the resulting classifiers when applied to unseen data, independent validation was moreover run 10 times on differently divided subsets.

Regarding training and testing, they were applied following a 10-times 4-fold cross-validation in order to reduce classification error. This technique divides the entire training subset into 4 blocks where each classifier is firstly trained using 3 portions and then tested on the 4^{th} block. This is performed for the four different possible combinations of blocks for training/testing so the outputs of each solution are then averaged. Moreover, so as to obtain more realistic results, cross-validation was applied 10 times on differently divided subsets of data.

Moreover, since unsuccessful HH cases are rare and conventional machine-learning approaches are extremely sensitive to class imbalance, showing a strong bias towards the majority class (far superior in number), random under-sampling was independently applied on each training fold. According to a previous analysis where different sampling strategies designed to equal the number of samples coming from each target class were explored[9], the random selection of a subset of samples from the majority class turned to provide the best results in this particular scenario, based on random forest models.

Indeed, among several classifiers that were tested, random forest models generally provided the best performances. This ensemble learning method builds a forest of uncorrelated decision trees using a CART-like procedure, combined with randomized node optimization and bagging[17]. Moreover, it allows variable importance quantification using the out-of-bag error as an estimation of the generalization error. During the fitting process of a random forest, the out-of-bag error for each data point is recorded and averaged over the forest. Thus, to measure the importance of the j^{th} feature after training, the values of this j^{th} feature are permuted among the training data and the out-of-bag error is again computed on this perturbed dataset. The importance score for the j^{th} variable is computed by averaging the difference in out-of-bag errors before and after the permutation over all trees and the score is normalized by the standard deviation of these differences. As a result, features producing larger values for this score are ranked as more important.

Finally, model performance evaluation was based on the resulting confusion matrix, which specifies the number of true positives (*TP*), true negatives (*TN*), false positives (*FP*) and false negatives (*FN*), when comparing true and predicted labels and considering unsuccessful HH stays as positives. First, the AUC or area under the ROC (Receiver Operating Characteristic) curve was computed to quantify the classifier performance. Moreover, classical sensitivity ($Se = TP/(TP + FN)$) and specificity ($Sp = TN/(TN + FP)$) measures, associated with the optimal operating point in the ROC curve, were calculated to quantify the classifier capability of correctly detecting unsuccessful and successful cases, respectively. Finally, an alternative measure sometimes used as an evaluation metric for imbalanced datasets[18], defined as the average between sensitivity and specificity and herein named after score (*Sc*), was calculated.

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ANNEX III - Home-based NIV (Protocol II)

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

Erik Baltaxe[1,2], Cristina Embid[1,2], Eva Aumatell[1], Maria Martinez[1], Anael Barberan[1,2], Jack Kelly[3], John Eaglesham[3], Carmen Herranz[1,2], Josep Maria Montserrat[1,2], Josep Roca[1,2], Isaac Cano[1,2]

[1] Hospital Clinic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Universitat de Barcelona, Barcelona, Spain

[2] Center for Biomedical Research Network in Respiratory Diseases (CIBERES), Madrid, Spain

[3] Advanced Digital Institute (ADI), Salts Mill, United Kingdom

Short title: Behavioral intervention in NIV using mHealth

Corresponding authors and reprint requests:

Isaac Cano, PhD (iscano@clinic.cat)

Respiratory Medicine Department, Hospital Clínic de Barcelona

Villarroel 170, Barcelona, 08036, Catalonia, Spain;

T: +34 932·275·540 / F: +34 932·275·455

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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 mHealth can enhance patients' self-efficacy. It is also accepted that mHealth-supported services might enhance productive interactions among the stakeholders involved in home-based respiratory therapies.

Objectives: To measure changes in self-efficacy in patients with chronic respiratory failure due to diverse etiologies, during a follow-up period of three months after the intervention. Ancillary objectives were

assessment of usability and acceptability of the mHealth tool, as well as to learn on its potential contribution to enhance collaborative work among stakeholders.

Methods: A single blinded, single center, randomized controlled trial was performed on 67 adult patients with chronic respiratory failure undergoing home-based noninvasive ventilation, between February and June 2019. In the intervention group, a psychologist delivered a face-to-face motivational intervention. Follow-up was supported by a mHealth tool which allowed patients to introduce the number of hours of use per day and problems with the therapy. Advice was automatically delivered by the mobile tool in case a problem was reported. The control group received only usual care.

Results: Self-efficacy did not show differences after the intervention (mean[SD]=3.4[0.6] vs 3.4[0.5], *p*=.514). No changes were observed neither in adherence to therapy nor quality of life. Overall, the mHealth tool showed good usability score, 78; high acceptance rate, 7.5/10; user friendliness, 8.2/10; and, the ability to use the app without assistance displayed a mean score of 8.5/10. Patients' perception of continuity of care and person-centered care showed high scores.

Conclusions: The mHealth tool did not improve patients' self-management. Acceptability of the app might indicate potential for enhanced communication among stakeholders. The study contributed to identify key elements required for a mHealth tool to provide effective support to collaborative work.

Trial Registration: NCT03932175 (clinicaltrials.gov, April 30, 2019)

Keywords: Behavioral change, eHealth, Noninvasive ventilation, Mobile Health, Chronic Diseases

Introduction

In the fifties, the polio epidemics demonstrated the safety and efficacy of noninvasive ventilation (NIV) to decrease mortality [1]. Since then, this therapeutic approach at home has shown to reduce hospital admissions, has a favorable impact on health-related quality of life, improves sleep quality and reduces mortality in patients with chronic respiratory failure due to diverse etiologies [2–8]. These results have driven an 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], patients' adherence to home-based NIV has still potential to improve which should further enhance healthcare efficiencies of the intervention [13]. Monitoring and optimization of physiological settings can contribute to enhanced adherence by improving timely detection of problems such as mask leaks, patient-ventilator asynchronies, etc. [14]. However, improvement of behavioral aspects such as patient motivation and empowerment for self-management are also important factors to consider when addressing adherence to respiratory therapies.

The current report seeks to explore the transfer of previous positive experiences on behavioral interventions in

other fields (i.e. physical activity) [15,16] into home-based NIV. Specifically, we will address the concept of self-efficacy, defined as the individual's perceived capability to perform the particular behavior [17]. A person who does not believe in her or his own capacity to perform a 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 [17].

We propose the use of a motivational mHealth intervention to support changes in task self-efficacy, which can be framed by Bandura's model [18]. This model is based upon the concepts of health risk perceptions, health outcome expectancies and the patients' confidence to engage in a certain behavior. The model has been widely applied in studies of the adoption, initiation, and maintenance of health-promoting behaviors [19].

Besides task-self efficacy as a way to influence behavioral change, previous reports by Hernandez et al [20] and Cano et al [21] have identified two commonalities usually hindering effective implementation of complex respiratory therapies (i.e. long-term oxygen therapy, continuous positive airway pressure therapy, home NIV and home-based nebulizer therapy). Firstly, is the need for interaction and communication among several stakeholders, namely: health professionals at different healthcare tiers (primary care, specialized care, etc.), patients and carers, companies undertaking maintenance of the equipment, and others, which may greatly benefit from digital tools supporting collaborative work. Secondly, is the improvement in therapeutic adherence that should be achieved through patients' empowerment for self-management.

In this respect, we identify the role of information and communication technologies (ICT) as a promising scenario to generate efficiencies by enhancing coordination between stakeholders and contributing to improve health outcomes [22,23]. Nonetheless, it is acknowledged that the scenario is not still mature [24]. Mainly, because of lacking evidence in real-world scenarios for the capacity of ICT to escort behavioral changes in chronic complex patients. It is widely accepted that, despite current limitations, chronic complex patients are an ideal population where care coordination, patient and medical staff satisfaction alongside patient empowerment are of utmost importance to produce health benefits.

While the principal objective of the current study is to produce evidence on the capacity of a motivational mHealth intervention to increase patient empowerment for self-management and adherence to therapy, a key secondary aim of the research is to conduct a qualitative analysis, based on professionals' and patients' opinions, to learn how the mHealth tool should evolve to support collaborative work among stakeholders involved in respiratory therapies, beyond generation of high acceptability/satisfaction.

Methods

Study design

Randomized single-blinded, single center, controlled trial with two parallel arms (1:1 ratio). The intervention arm consisted of a motivational mHealth intervention, which included a face-to-face motivational interview by a psychologist (one of the authors, EA) and remote follow-up through the MyPathway® app tool, on top of usual care, whereas the control group received standard care only. MyPathway® [25] is a secure, digital communications channel connecting patients to clinicians and services. It is a browser and app-based application co-designed and tested by users to make it user-friendly for both patients and clinicians to use on phones, tablets and PCs. See Multimedia Appendix 1 for more details.

The randomization scheme was generated by using the Web site Randomization.com [26] by one of the researchers (EB), prior to patient enrolment. Blocks of 4 were used. Only after the participant signed the informed 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 them were blinded. Only the investigator in charge of data analysis was blinded.

Recruitment and data collection

Between February and March 2019, all the patients already being treated with NIV at the Noninvasive ventilation clinic at the Hospital Clinic in Barcelona were assessed for eligibility (n = 169). Inclusion criteria were defined as follows: all adult patients with hypercapnic ventilatory failure due to chest wall, neuromuscular, lung parenchyma and/ or airway disease already receiving treatment with NIV irrespective of treatment duration and having a mobile phone, tablet or personal computer that could support the use of MyPathway® application. The application could also be downloaded to the carers' phone in case the patient didn't have a smartphone. Patients with severe psychiatric and/or neurological diseases where excluded, as well as those hospitalized at time of assessment. 67 patients were finally included in the trial.

All the eligible patients were contacted by telephone in order 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, consent was signed. Afterwards, patient was allocated to the study group. Besides this baseline visit, a second and final visit was programed three months afterwards, also in the outpatient clinics. For the intervention group, follow-up was done remotely, by the nurse case manager (MM), using the MyPathway app® and its clinical portal. When deemed necessary, the nurse case manager visited the patient at home or a visit was programmed at the outpatient clinics. There was no active follow-up for the control group.

Study intervention

The motivational mHealth intervention was initiated by a psychologist who delivered a face-to-face motivational interview to assess patient's adherence profile and lifestyle habits. During follow-up, the MyPathway® app was used for bi-directional interaction between the study participants and the research team. It consisted on positive feedback or reinforcement messages in response to the number of hours of NIV use filled by the patient daily. Also, general advice on specific NIV clinical problems was given by the app according to patients' weekly input. Additional educational material on physical activity, diet and sleep hygiene could be accessed at any time from a dedicated link. See Multimedia Appendix 1 for look-and-feel screenshots and detailed explanation of functionalities.

Patients were given verbal and written explanation on how to use the app during the enrollment visit. 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 a username.

At time of enrollment semi-structured motivational interviews were conducted individually Participants were asked about the following topics: (i) Treatment adaptation experience, (ii) Lifestyle (physical activity and food habits) and (iii) Use of information and communication technologies. In each session, field notes were taken

anonymously, and no recordings were made. The intervention consisted of a 10 to 50-minutes face-to-face session at the hospital or at the participants' home, following the principles of collaborative and evocative motivational interview [27–30], favoring the participant's autonomy. The techniques used were open questions, active listening, empathy, returning reflected thoughts, exploring change in goals, summarizing and giving feedback. The qualitative analysis of the motivational interview, as well as the detailed description on mHealth's requirements for supporting collaborative work among stakeholders, will be reported elsewhere, using the COREQ checklist (see Multimedia Appendix 2).

A web-based clinical portal enabled the research team to monitor the NIV hours of use and clinical problems reported by the patients. As indicated above, a dedicated nurse (one of the authors, MM) took the role of case manager, with clinical and technical knowledge, in order to support collaborative work. She used the web-based portal to identify adherence problems and, accordingly, she contacted the participants via telephone or at home (for those with severe mobility problems) in order to enquire about potential problems, either clinical or technical and solve them.

Study outcomes

The primary outcome was a change in task self-efficacy towards NIV use. The self-efficacy variable was measured using the Self Efficacy in Sleep apnea (SEMSA) questionnaire. The SEMSA is a US-designed self-report questionnaire comprising 26 items rated from 1 to 4 on a 4-point Likert scale [31]. The arithmetic mean of the Likert rating for each participant is computed for the overall SEMSA score and for each of the three 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 [31].

Secondary outcomes included usability which was measured by the System Usability Scale [32]. Patient satisfaction was measured using the Net Promoter Score [33] alongside three custom made general satisfaction question using a Likert scale. As alluded to above, both patients' and professionals' requirements for mHealth support of collaborative work were relevant secondary outcomes. Also, mean hours of use per day were taken directly from the NIV machine memory card data download. Other variables that were obtained through data download from the NIV machine were: mask leaks (L/s), minute ventilation (L/min), tidal volume (mL) and back-up rate (breaths/min). Outcomes relating to patient experience [34] where continuity of care using the Nijmegen continuity of care questionnaire and the Person centered coordinated experience questionnaire as described by Leijten et al [35]. Patient experience questionnaires were measured only once at the end of the trial.

Tertiary outcomes included mortality, health-related quality of life (using the EuroQol 5D questionnaire [36,37] and sleepiness (using the Epworth Sleepiness Score).

Healthy-life style changes were indirectly measured by body weight changes.

Sample size data management and statistical analysis

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 31 subjects were necessary in the intervention group and 31 in the control group to recognize as statistically significant a difference greater than

or equal to 0.35 units in the SEMSA overall score. The common standard deviation was assumed to be 0.46 [38]. It was anticipated a drop-out rate of 10%.

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 REDCap electronic data capture tools hosted at Hospital Clínic of Barcelona [39,40]. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Data on NIV use and clinical problems with NIV was collected during the study period on-line as reported by the participants using MyPathway®

A descriptive analysis was carried out in which the results were expressed using the mean and standard deviation (SD). The statistical significance of the differences was assessed by the Student's t-test for the comparison of quantitative variables and a non-parametric test in case of non-normal distribution of the variable. The Chi-square test with Fisher's exact test was used in the comparison of qualitative variables. Intention-to-treat analysis was performed for the comparison of the two groups.

Ethics

Study approval was obtained from the Ethics Committee for Clinical Research of Hospital Clinic de Barcelona (HCB/2019/0510). Patients read, understood and accepted the informed consent which was signed before enrolment to the study.

Results

Study Population

A total of 169 patients were screened for eligibility. 50 patients did not meet inclusion criteria (32 did not have smartphone or tablet) and 23 declined participation. 67 patients were randomized between February and May 2019 (CONSORT flow diagram in Multimedia Appendix 3). Only one patient from the intervention group retired consent during the trial due to worsening of his clinical condition. Baseline demographic and clinical characteristics are shown in Table 1 and Multimedia Appendix 2.

Table 1. Baseline characteristics

	Intervention (n=33)	Control (n=34)
Age (mean, SD)	68.61 (15.8)	65 (14.7)
Male gender (n, %)	19 (57.6)	19 (57.6)
Weight (mean, SD)	86.4 (31.6)	78 (22.4)
Educational level (n, %)		
No scholarization	3 (9.1)	1 (2.9)
School education	12 (36.4)	13 (38.2)
Professional formation	17 (51.5)	19 (56)
Doctorate or equivalent	1 (3)	1 (2.9)

BMI	30.5 (7.1)	28.9 (7.4)
Smoking Status (n, %)		
Never	12 (36.4)	16 (48.5)
Past	18 (54.5)	16 (48.5)
Current	2 (6.1)	1 (3)
Pack/year (mean, SD)	55.5 (35.7)	52.5 (33)
Diagnostic group (n, %)		
Neuromuscular	4 (12)	8 (24)
Chest wall	11 (33)	10 (30)
Obesity-hypoventilation	5 (15)	5 15)
Airway obstructive disease	3 (9)	2 (6)
OSA – cOSA	10 (30)	8 (24)
Comorbidities		
Number/patient (mean)	2	1.8
Cancer (%)	3	3
Congestive heart disease (%)	33	27
Ischemic heart disease (%)	24	15
Diabetes (%)	27	36
Stroke (%)	9	9
Hypertension (%)	67	52
Dementia (%)	3	0
Other neurological disorders (%)	3	0
Depression / anxiety (%)	18	18
Dyslipidemia (%)	15	27
Time on NIV (months) (mean, SD)	81.55 (78.3)	54.64 (42.4)
AHI (mean, SD)	45.74 (28.8)	34.59 (31.6)
CT90 (%)(mean, SD)	46.88 (37.3)	43.88 (40.4)
Mean ventilatory parameters		
IPAP (cmH2O) (mean, SD)	16.3 (4.7)	14.1 (4.7)
EPAP (cmH2O) (mean, SD)	7 (2.8)	6.3 (2.1)
Leak (L/s) (mean, SD)	0.05 (0.2)	0.5 (0.09)
N° of hours use/day (mean, SD)	7.4 (2)	6.8 (3)

BMI: body mass index; OSA: obstructive sleep apnea; OSAc: central sleep apnea; AHI: apnea-hypopnea index; CT90: cumulative sleep time percentage with oxyhemoglobin saturation < 90%; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; Vmin: minute ventilation; NIV: noninvasive ventilation

Patient reported outcomes

For the primary outcome, there was no difference after intervention in the SEMSA score for self-efficacy (mean[SD]=3.4[0.6] vs 3.4[0.5], *p*=.514). For the perceived risks, outcome expectancies, Epworth Sleepiness Score and EuroQol 5Q-5D questionnaires, there wasn't any difference also (see Multimedia Appendix 2).

As for the patient experience questionnaires, neither the Nijmegen continuity of care questionnaire nor the Person centred coordinated experience questionnaire showed differences between groups (see Multimedia Appendix 2)

Clinical outcomes

Adherence (i.e. number of hours of use/d of NIV as recorded by the ventilators) showed no difference after intervention (mean[SD]=7.4[2] vs 7.7[2]). The only ventilatory parameter showing difference after three months in the intervention group was the minute ventilation (mean[SD]=7.0[2] vs 6.4[2.1], *p*=.031). The remaining ventilatory parameters and weight are shown in the Multimedia Appendix 2. None of the patients died during the trial.

mHealth tool use, usability and acceptability

The Net Promoter Score was -3 (31% promoters, 34% passives and 34% detractors). The three Likert-scale questions rated from 1 (very bad) to 10 (very good) the general impression the app (mean score of 7.5/10), its user friendliness (mean score of 8.2/10) and the ability to use the app without assistance (mean score of 8.5/10). In the System Usability Scale the mean score obtained was 78, which is considered as a good grading. Up to 42% of the participants used the link to the educational material and only 18% consulted the terms of use. The number of hours per day under NIV, reported using the mHealth tool, was 7.23 ±2.48. 44.9% of the patients reported use of NIV for more than 4 hour/day during 2/3 of study period. Likewise, the reported number of days using NIV for more than 4 hours in the entire intervention group was 35.67 ±23.63 (mean±SD).

Also, we found that 30% of the participants used the app through a family member or career. It is of note that the nurse case manager was able to solve 2/3 of the technical problems that arose during the first three weeks of the study. Additional information on the log book analysis results can be found in the Multimedia Appendix 2.

Discussion

Principal findings on patient reported outcomes

We report the results a motivational mHealth intervention based on a face-to-face interview and the use of a mHealth tool (MyPathway® app), during a follow-up period of three months, on patients with hypercapnic chronic respiratory failure under home-based long-term noninvasive ventilation. 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 the current study, the task-self efficacy mean score was already high at baseline (Table 1) and we did not find any significant effect on behavioral changes after the intervention. Several explanations can be proposed for these results. First, the intervention may need to be more intensive, for example, more than one face-to-face session [45]. Secondly, the patients participating in the study were all long-term users without significant sleep symptoms at time of enrollment (an average of 81.5 months of use with an Epworth Sleepiness Score lower than 10 on average). Therefore, we may hypothesize that they were already motivated and had previously done behavioral changes, as seen by the good average use of NIV (7.4 h/day) and high scores for task self-efficacy at baseline. Thirdly, we may argue that even though the NIV use was good in these long term users, the adherence was more a function of necessity or imposition (by family or physicians) than real feeling

of empowerment and self-management, and that most of these chronic patients have not even considered initiating behavioral changes [46,47], therefore any intervention at this stage won't be effective. This may be also reflected by the lack of interest in consulting the educational material of the app (less than 50% of the patients did so). Lastly, we should note that in the control group were more neuromuscular patients. The pathology should not affect the use of the app or the impact of the behavioral intervention. In this respect, the educational level is more an important factor [48,49], and both study groups were similar for that variable.

Usability, acceptability and requirements for supporting collaborative work

Notwithstanding the clinical results, it is important to note that the mHealth tool was well appreciated by the patients and their family/carers. Even though these are complex patients (two comorbidities on average) with many needs and burdensome treatment, all patients used the app on a regular basis, grading it as good in general, being user-friendly and easy to use without help. Moreover, the System Usability Scale resulted in a good score.

As stated in Methods, 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 even though in our case bilateral communication was done via telephone or Whatsapp®. We found lacking this function in our app, which according to our experience, should become an integral part of any app where case-management with technical skills is introduced. Such a communication functionality has to be cloud-based, GDPR compliant. Moreover, future developments should look towards an adaptive case management functionality. Also, this communication should be supported by intelligent bots in order to help guide the professionals though continuum care pathways and to 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 healthcare 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 workflows evaluation was highlighted [50]. Table 2 summarizes the key requirements of the mHealth tool to effectively support collaborative work among stakeholders involved in home-based respiratory therapies.

Table 2. Requirements to support collaborative work within the NIV service.

Feature	Description
Adaptive Case Management	Capacity to enable the case manager to combine pre-designed tasks, as well as to face new cases reusing structured experiences with previous cases. Over time, the case manager, or other authorized health professionals, should be able to timely adapt the work plan to specific patient's requirements, without any direct technological support.
Team collaboration	Cloud-based, GDPR-compliant, enterprise-proven team collaboration tools to allow patients and healthcare professionals to breakdown silos and collaborate seamlessly from any device (mobile phone, tablet or desktop) towards the health continuum care pathway.
Multimedia communication	Enterprise-grade, scalable and high-quality real-time communication among concurrent participants for file sharing, voice, video and screen-share sessions with an industry standard encryption.

Intelligent bots	Capacity to develop and integrate intelligent bots to guide professionals though continuum care pathways and to improve health risk assessment and service selection
Integration with hospital information systems	Use of an HL7 Fast Healthcare Interoperable Resource (FHIR) interoperability middleware to integrate with provider-specific hospital information systems.

In this respect, we measured two process outcomes [51] related to patient experience [34], i.e. continuity of care and person-centered care. Both parameters were very well valuated by all of our study population, which included not only patients, but also their family and carers in a third of cases in the intervention group. The importance of well-designed clinical workflows with embedded digital health tools may have impact not only on an NIV service, but also on other respiratory services as well. Commonalities include high-complexity patients with clinical and social needs from different stakeholders (physicians, providers, technicians, social workers, etc) and healthcare tiers (primary care, specialized care, etc). Hernandez et al showed how this complexity can hamper the effectiveness in the case of long-term oxygen therapy [20]. As mentioned, table 2 shows the proposed elements to overcome the barriers for 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 [52,53] and as such, they should be taken on account whenever evaluating a service in which there is considerable interplay between patients, the different healthcare tiers, social and technical services [54]. It has been shown [55] that for a mHealth tool to produce healthcare value it should be embedded in the clinical pathways of a well evaluated clinical service, and not as a standalone tool.

Strengths and limitations of the study

An important strength of our study is its potential to demonstrate the positive interaction and collaborative work among the nurse case manager, the patients and family members or carers of complex patients using digital health tools. A previous study [56] reported on the use of digital tools by family carers, emphasizing the importance of including this group of stakeholders, not only as users, but also in the co-design process. This stakeholders' involvement is also a step further to scale-up digital health tools within clinical workflows, which in our case were well valuated. We do acknowledge that by using an already existing app the co-design phase was skipped. Also we did not measure technological literacy in our older population (average age 69 years), but, according to Martinez-Alcala, et al, adults above 60 years, if highly motivated are capable of learning and acquiring digital literacy skills [57]. Therefore, we do not believe it was a barrier for our patients. Finally, a clear limitation of our study was the exclusion of new NIV patients, were the behavioral intervention may have had more impact. This warrants further study.

Conclusions

A motivational mHealth intervention did not show any effect on task self-efficacy, adherence with NIV or quality of life. Nonetheless, we showed the potential of the mHealth application to manage complex patients and foster collaborative work among stakeholders. Alongside a clinical service that was well graded in terms of continuity of care and person centered care, in which the needs of the relevant stakeholder 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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Conflict of Interest

The authors have no conflict of interest.

Abbreviations

NIV: Noninvasive ventilation

SEMSA: Self Efficacy in Sleep Apnea

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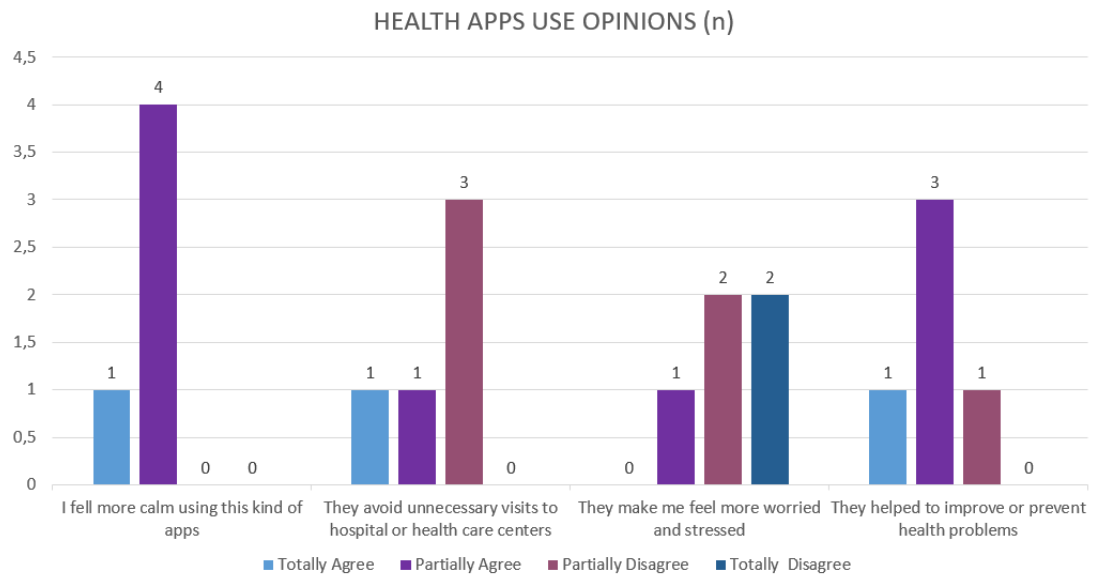
ANNEX IV – Assessment of the CONNECARE platform (Protocol IIIB)

Patient use of eHealth

All patients (n=19) have smartphone with internet connection. 89% (n= 17) of the patients have email address. Few of them (n=6) are using health devices such as pedometers, smart watches, etc.

5 out of 19 patients (26%) are familiar to health apps. They have been using those related to physical exercise, nutrition and health centre information. Additionally, all of them stated they would be willing to share the info coming from the app with their doctor or nurse. These 5 patients feel more comfortable when using this kind of apps, they perceived this could help to improve or even prevent health problems. However, most of them (n=4) also stated that the use of the app makes them feel more worried or stressed. Finally, 3 out of 5 perceived that the use of the app could not really avoid unnecessary visits to hospitals or health care centres.



Patient experience

The NPS score for patients is negative. However, since the median of overall satisfaction is 6, we could consider that patients had is slightly positive experience using Connecare.

Table 1. Rating of satisfaction with Connecare SMS by means of Net Promoter Score for patients.

Net Promoter Score (N = 19)		
Likert scale score (0 = poor TO 10 = good)	**1. Overall satisfaction**	**2. Would you recommend it?**
Skewness	-0.50	-0.09
Median	6	5
25th Pct	5	4
75th Pct	7	10
Score for 'would you recommend it'	N patients	% patients
0-6 (detractors)	11	57.8
7-8 (passives)	1	5.3
9-10 (promotors)	7	36.8
Net Promoter Score (Promoters-Detractors)		-21

A system or product that received SUS score of 68 and above is considered to have a good usability. Since the result of the Connecare experience is 42%, the usability perceived by patients is slightly poor.

Table 2 – System Usability Scale of the Connecare SMS for patients.

	n=19	
Mean (SD)	55.66 (30.19)	
Skewness	-0.63	
	N	**%**
Score above 68	8	42%

Patient usage

Lifevit for monitoring physical activity: During the follow up period, patients used the LiveVit an average of 11,2 days. 10 of the total patients (n=20) reported the steps done during more than 50% of the days.

Chat usage: Regarding the use of chat, 73.68% of the patients used chat to communicate with the case manager, so we could say that patients perceived the chat as a good communicative tool. During the

follow up period the average number of messages per patient sent through chat was 5.27, 3 patients sent more than 10 messages whereas others less than 5 or even 0.

Professionals' experience

During this pilot, only one case manager was using the Connecare SACM.

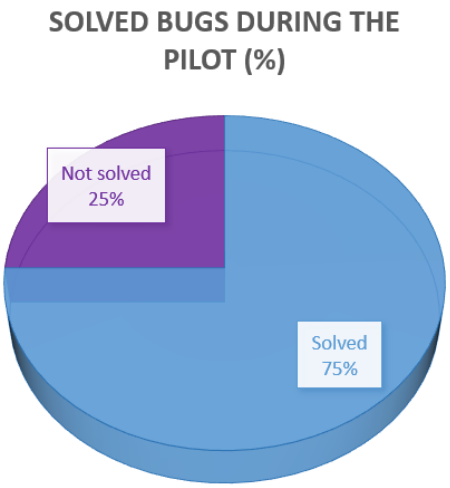
His NPS score was very low (1), that suggests that the professional involved would not recommend the Connecare SACM. Regarding usability, his SUS score was 42,5% which is under 68 and means that perceived usability was poor.

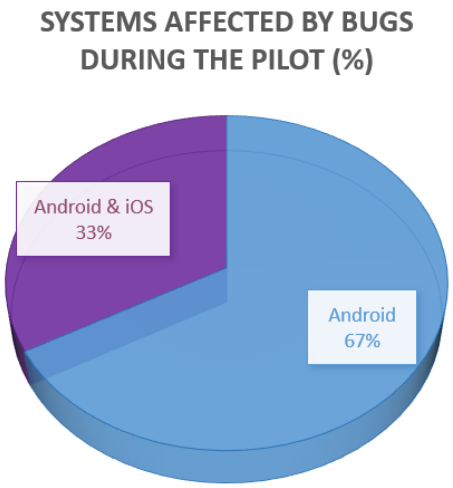
Professional usage

The case manager was in charge of including all patients in the Connecare SACM, evaluating their health status and personalizing a workplan for each of them. During the follow up period, the professional used the Connecare SACM to monitor the reported physical activity and to manage the communication with the patient through the chat. Part of thoses messages sent were directed to solve any kind of technical issues due to the Connecare SMS.

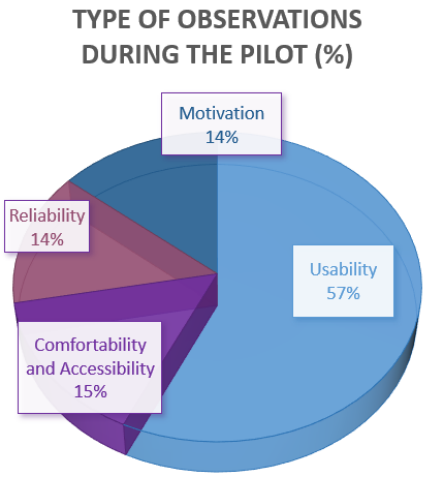
Implementation log

75% of the bugs reported during the pilot (N=4) were either solved an only one was in progress. Android devices were approximately reporting more bugs than iOS.





Most of the observations during the pilot were due to usability issues (57%). Reported observations regarding motivation, reliability and comfortability and accessibility reached around 14 and 15%.


TYPE OF OBSERVATIONS DURING THE PILOT (%)
Motivation 14%
Reliability 14%
Usability 57%
Comfortability and Accessibility 15%

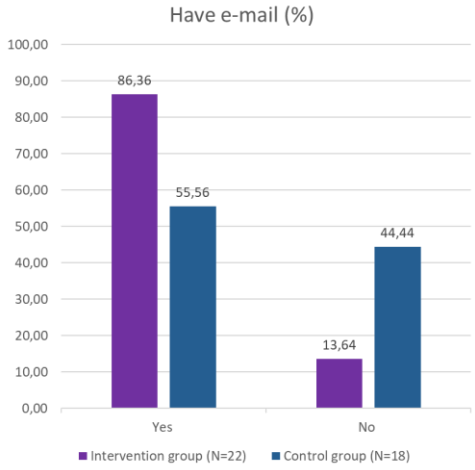
ANNEX V – Assessment of Health-Circuit (Protocol IIIC)

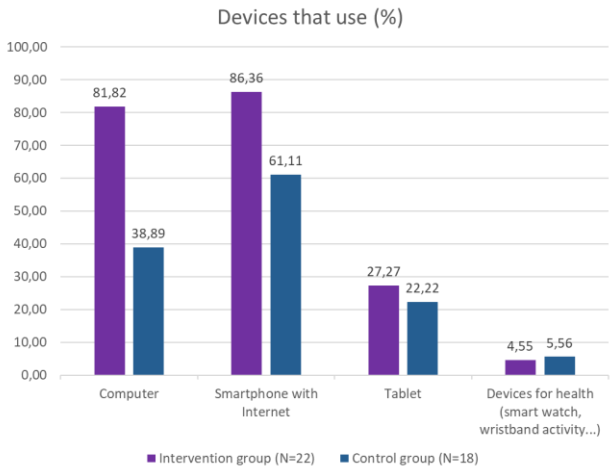
Patient use of eHealth

Most patients from the intervention group (77%) have access to an Android device of their own (64%). Moreover. most of them have access to e-mail (86%). considerably higher than patients in the control group (55%). In addition to the use of a smartphone with Internet connection (86% vs. 61%). patients from the intervention group have also a considerably higher use of a computer (81% vs. 38%).

Device	N	%
Android	17	77,27
IOS	5	22,73
Total	**22**	**100,00**

Owner of the Device	N	%
Patient	14	63,64
Couple	2	9,09
Children	6	27,27
Total	**22**	**100,00**





Patient experience

Although the NPS score is low (31%). the same number of passive and promoters suggests that in general most patients had a positive experience using Health Circuit but not enough to be active promoters. This is reinforced by the fact that median of overall satisfaction is 7.5 out of 10.

Table 1. Rating of satisfaction with Health-Circuit app by means of Net Promoter Score for patients.

Net Promoter Score (N = 16)		
Likert scale score (0 = poor TO 10 = good)	**1. Overall satisfaction**	**2. Would you recommend it?**
Skewness	-3.18	-1.20
Median	7.5	8
25th Pct	7	7
75th Pct	8	9.25
Score for		% patients

'would you recommend it'	N patients	
0-6 (detractors)	2	12.5
7-8 (passives)	7	43.75
9-10 (promotors)	7	43.8
Net Promoter Score (Promoters-Detractors)		31.3

A system or product that received SUS score of 68 and above is considered to have a good usability. Since the result of the Health Circuit experience is 31%, the usability perceived by patients is slightly poor.

Table 2. System Usability Scale of the Health-Circuit app for patients.

	n=16	
Mean (SD)	63.75 (14.66)	
Skewness	-1.55	
	N	**%**
Score above 68	5	31%

Patient usage

A total of 16 events have been generated and all of them have been resolved. The events were generated by 7 patients from 17 participants who completed the study from which 4 clinical consultations and 12 administrative doubts were risen. The number of interactions generated between patients and case managers was 20 for the events and 51 for the follow-up visits. The type of interactions was 8.

Professionals' use of eHealth

6 professionals participated in the study (4 doctors and 2 case managers). 75%(n=3) considers that global quality of the consultations in telemedicine was good. 2 of the doctors and 2 case managers stated the technical quality was good.

Regarding care quality, all doctors and one of the case managers stated they feel no difference between the quality care with telemedicine and the standard method. 50% of the doctors and 100% of the case managers considers telemedicine can improve health status of the patients. 75% of the doctors and 50% of the case managers have had some technical and organizational difficulties using telemedicine that could affect the care quality provided. However, 75% of the doctors and 100% of the case managers acknowledge they will continue using telemedicine up to now.

Professionals' experience

The NPS score for professionals is negative. However, since the median of overall satisfaction is 5. we could consider that professionals had a neutral experience using Health Circuit.

Table 3. Rating of satisfaction with Circuit by means of Net Promoter Score for professionals.

Net Promoter Score (N = 5)			
Likert scale score (0 = poor TO 10 = good)	**1. Overall satisfaction**	**2. Would you recommend it?**	
Skewness	-1.70	-1.58	
Median	5	5	
25th Pct	5	5	
75th Pct	6	7	
Score for 'would you recommend it'		N professionals	% Professionals
0-6 (detractors)		4	80.0
7-8 (passives)		1	20
9-10 (promotors)		0	0.0
Net Promoter Score (Promoters-Detractors)			-80.0

A system or product that received SUS score of 68 and above is considered to have a good usability. Since the result of the Health Circuit experience is 20%. the usability perceived by professionals is poor.

Table 4. System Usability Scale of the Circuit for professionals.

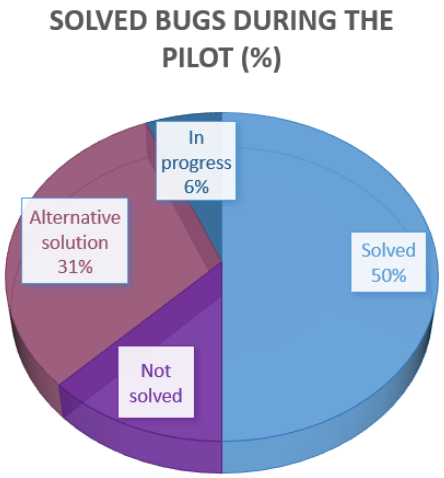
	n=5	
Mean (SD)	53.50 (17.46)	
Skewness	-0.02	
	N	**%**
Score above 68	1	20%

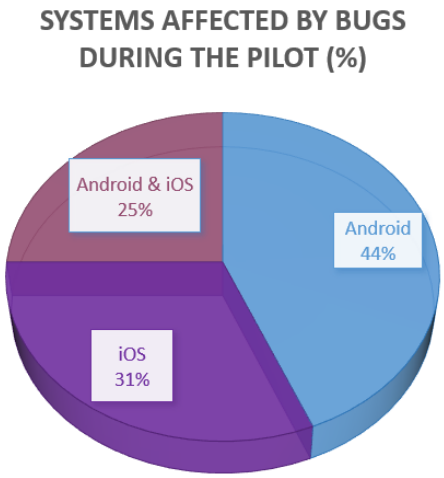
Professional usage

The number of professionals who have had to use the Circuit platform is 7 (5 family doctors and 2 case managers). They had to intervene in a total of 15 events.
The number of professionals per event has been maximum of 2. The case managers have intervened in all the events while the family doctors have participated in 8 of them.

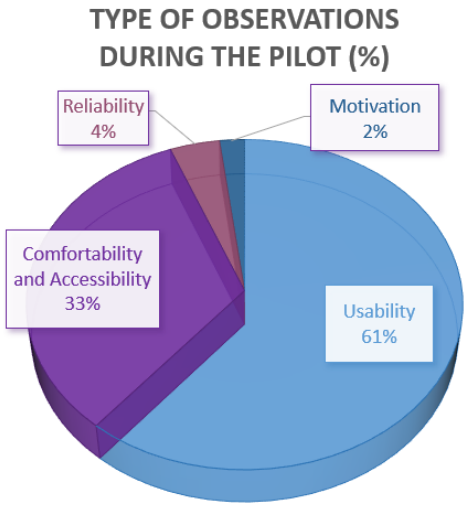
Implementation log

Most of the bugs reported during the pilot (N=16) were either solved or an alternative solution was given. Only 2% of the bugs would not be solved. Android devices were approximately reporting 25% more bugs than iOS.





Most of the observations during the pilot were due to usability (61.22%) and or comfortability and accessibility (32.65%) issues.



6.2. Lleida

ANNEX VI – Study results of Implementation study 1 in Lleida

CONNECARE – Lleida - All data analyses CS1

General description of the statistical analyses:

Statistical analyses were conducted using Stata (Ver. 12.1). Statistical level of significance was set to $\alpha = 0.05$.

Patients' usage of the ICT tools and devices

1A. Use of the Pedometer (Fitbit)

Table 1. Days Fitbit transmitted – CS1.

Days Fitbit transmitted	all	men	women
N	50	25	25
Mean (SD)	69.5 (29.1)	71.2 (24.5)	67.8 (33.5)
	N (%)	**N (%)**	**N (%)**
Less than 30 days	8 (16%)	2 (8%)	6 (24%)
30-59 days	6 (12%)	5 (20%)	1 (4%)
60-89 days	19 (38%)	10 (40%)	9 (36%)
90 days	17 (34%)	8 (32%)	9 (36%)

No significant differences between men and women were found in the mean number of days transmitted (T test p-value= 0.923).
Age was associated to lower number of transmitted days (Linear regression model adjusted by sex and Charlson p-value= 0.049).

1B. Use of the messaging function in the app

Table 2. Number of messages sent using the app – CS1.

	All	Men	Women
N	43	20	23
Mean (SD)	29.21 (30.0)	21.2 (13.5)	36.2 (38.0)
	N (%)	**N (%)**	**N (%)**
0 messages	0 (0%)	0 (0%)	0 (0%)
1-2 messages	3 (7%)	1 (5%)	2 (9%)
3-5 messages	3 (7%)	1 (5%)	2 (9%)
6-10 messages	5 (12%)	3 (15%)	2 (9%)

> 10 messages	32 (74%)	15 (75%)	17 (74%)

A Negative binomial regression model including age, sex and Charlson showed that being a woman was associated to a higher number of messages (p-value= 0.063) while no association for age was found (p-value= 0.608).

1C. Response to questionnaires in the SMS app

Patients in CS1 could be asked to answer questionnaires concerning their main chronic disease. Among COPD patients, the median (p25-p75) number of questionnaires successfully submitted out of all requested questionnaires was 10% (1% - 22%). Among heart failure patients, the median (p25-p75) number of questionnaires successfully submitted out of all requested questionnaires was 1% (0% - 2%). This shows that most patients replied to requested questionnaires at least once, but were reluctant on answering the same questionnaire on a regular basis.

1D. Use of monitoring devices

Table 3. Percentage of measures reported out of times prescribed.

Use of monitoring devices – CS1		
Prescribed measure	**N**	**Mean (SD)**
Weight	34	62% (38%)
Blood pressure	52	40% (18%)
Heart rate	52	40% (18%)
SpO_2	52	31% (15%)

Overall patients in CS1 were willing to report all the requested measures on a daily basis. However, when measures were prescribed more than once a day, patients tended to do it just once a day.

Patient's Experience

2A. Person- centered coordinated care experience questionnaire(P3CEQ)

Table 4. Answers to P3CEQ – CS1.

	Controls (n=28)	CONNECARE (n=48)	
P3CEQ questions	**% answering "always"**		**p-value***
1. Did you discuss what was most important for YOU in managing your own health and wellbeing?	82%	73%	0.205
2. Were you involved as much as you wanted to be in decisions about your care?	82%	73%	0.382
3. Were you considered as a 'whole person' rather than just a disease/condition in relation to your care?	86%	85%	0.384
4. Did your care-team / providers involve your family/friends/carers as much as you wanted them to be in decisions about your care?	82%	73%	0.621
5. Have you had enough support from your care team / providers to help YOU to manage your own health and wellbeing?	78%	83%	0.823
6. To what extent do you receive useful information at the time you need it to help you manage your health and wellbeing?	89%	73%	0.055
P3CEQ total score: mean (SD)	16.6 (3.0)	16.4 (2.3)	0.714

* Chi^2 test (considering all the response options) or T test as appropriate.

2B. Nijmegen Continuity Questionnaire (NCQ)

Table 5. Answers to NCQ.

Nijmegen Continuity Questionnaire (NCQ) – CS1 (n=28)	
NCQ G1-G5 statements	**N (%) answering "Agree" or "Strongly agree" ***
G1. My care providers transfer information very well to one-another	24 (86%)
G2. My care providers work together very well	22 (85%)
G3. My care providers are very well connected	21 (88%)
G4. My care providers always know what one-another is doing	20 (83%)
G5. I have to wait too long to obtain a service/appointment	34 (72%)
NCQ total G1-G4 score: mean (SD)	4.2 (0.9)

* Excluding patients answering N/A.

2C. Patients satisfaction with the technology – NPS

Table 6. Rating of satisfaction in patients using SMS app + Fitbit – CS1.

SMS app + FITBIT NPS (N=42)				
Likert scale score (0 = poor TO 10 = good)	**1. Overall satisfaction**	**2. Easiness of use**	**3. Ability to be used without help**	**4. Would you recommend it?**
Median (p25-p75)	10 (8-10)	9 (8-10)	9 (8-10)	10 (8-10)

Table 7. Rating of satisfaction in patients using SMS app – CS1.

SMS App NPS (N=48)				
Likert scale score (0 = poor TO 10 = good)	**. Overall satisfaction**	**2. Easiness of use**	**3. Ability to be used without help**	**4. Would you recommend it?**
Median (p25-p75)	10 (8-10)	9 (8-10)	9 (8-10)	10 (8-10)

The NPS:

The answer to the question "How likely is it that you recommend the CONNECARE system to a family member or friend?" was used to calculate the NPS. Subtracting the percentage of Detractors from the percentage of Promoters. The NPS ranges between −100 and +100, a positive score is considered good, a NPS of +50 is generally deemed excellent, and anything over +70 is exceptional.

Table 8. NPS score in CS1.

CS1 - NPS SCORE				
	SMS + Fitbit		**SMS**	
Score for 'would you recommend it'	N patients	% patients	N patients	% patients
0-6 (detractors)	3	7%	3	6%
7-8 (passives)	8	19%	10	21%
9-10 (promotors)	31	74%	35	73%

The NPS score was +67% in patients using SMS app + Fitbit and +67% in patients using only SMS app. These rates are excellent, and close to reaching the exceptional threshold (+70%).

2D. Patients satisfaction with the technology – SUS

Based on research, a SUS score above a 68 would be considered above average and anything below 68 is below average.

Table 9. SUS score in CS1.

SUS total score for the SMS App in CS1	
N	**48**
Mean (SD)	79.12 (14.44)
Score ≥68, n (%)	38 (79%)

Staff's Experience

A total of 30 professionals involved in CS1 and/or CS2 were asked to assess the SACM platform between April and May 2019: 1 hospital case-manager, 3 hospital physicians, 1 hospital surgeon, 1 hospital anesthesiologist, 3 primary care case-managers, 12 primary care physicians, and 9 primary care nurses.

3A. Staff satisfaction with the technology – NPS

Table 10. Rating of satisfaction in staff using the SACM – CS1.

Professionals using SACM (N=20)				
Likert scale score (0=poor to 10=good)	**Overall satisfaction**	**Easiness of use**	**Ability to be used without help**	**Would you recommend it?**
Median (p25-p75)	6 (5-8.5)	6.5 (5-8)	6.5 (5-9)	6.5 (5.5-8.5)

Table 11. NPS score in staff using the SACM.

NPS SCORE		
Score for 'would you recommend it'	N staff	% staff
0-6 (detractors)	10	50%
7-8 (passives)	5	25%
9-10 (promotors)	5	25%

The SACM NPS score was -25% among professionals involved in CS1. This rate is poor and reflect the difficulties experienced in using a tool under development and not fully integrated with existing systems.

3B. Staff satisfaction with the technology – SUS

Table 12. SUS score in staff using the SACM.

SUS total score for the SACM App	
N	**22**
Mean (SD)	62.7 (19.7)
Score ≥68, n (%)	10 45%)

Intervention effectiveness - Health & wellbeing questionnaires (SF-12)

Table 13. Changes in the SF-12 from baseline to discharge – CS1.

CS1				
CONNECARE patients				
	Baseline (N = 52)	**Discharge (N = 48)**	**Change (N = 48)**	
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**p-value***
SF-12 - Physical	28.2 (7.6)	32.7 (9.4)	+3.7 (8.4)	0.004
SF-12 - Mental	51.7 (10.4)	53.9 (11.5)	+2.0 (11.2)	0.214
SF-12 - Total	79.9 (12.3)	86.6 (16.3)	+5.8 (12.8)	0.003

Control patients				
	Baseline (N = 35)	Discharge (N = 28)	Change (N = 28)	
	Mean (SD)	Mean (SD)	Mean (SD)	p-value*
SF-12 - Physical	30.6 (8.2)	31.6 (9.0)	+2.0 (7.5)	0.159
SF-12 - Mental	45.9 (13.4)	45.8 (15.5)	-1.2 (11.9)	0.591
SF-12 - Total	76.5 (13.4)	77.4 (20.5)	+0.8 (14.7)	0.772

* Paired T test comparing baseline to discharge.

In CS1, the intervention generated significant changes in the physical dimension of SF-12 and the total SF-12 score. No significant changes were seen among the control patients. However, crude or adjusted (sex, age, and Charlson) linear regression models did not find statistically significant differences in the changes experimented by patients in the CONNECARE program or control patients.

Intervention's effectiveness - Service utilization during the follow-up

Table 14. Total use of health services during the study – CS1.

Total use of health services during the study – CS1				
	Control (N = 35)	CONNECARE (N = 50)	Model 1	Model 2
	Mean (SD)	Mean (SD)	p-value	p-value
N unplanned visits	2.31 (2.92)	1.04 (1.12)	0.003	0.006
N unplanned visits related to main chronic disease	0.91 (1.25)	0.40 (0.57)	0.010	0.021
N hospital admissions	0.54 (0.78)	0.36 (0.56)	0.212	0.261
N hospital admissions related to main chronic disease	0.43 (0.74)	0.20 (0.45)	0.079	0.124

Model 1: Negative binomial regression model, crude. Model 2: Negative binomial regression model, adjusted by age, sex, and Charlson.

Being in the CONNECARE program significantly reduced the total number of unplanned visits and unplanned visits related to the main chronic disease (CS1). Similarly, being in the CONNECARE program reduced the total number of hospital admissions and hospital admissions related to the main chronic disease (CS1), although the

small sample size and low number of admissions precluded statistical significance. In CS1, five deceases were registered during the study among control patients and two among patients in the CONNECARE program, which could suggest a reduction in mortality associated to the CONNECARE program.

Intervention's costs & Cost-effectiveness

6A. Cost of the CONNECARE program

Estimating the overall cost per patient of implementing the CONNECARE program is not trivial. For the purpose of the current study, a hospital-based nurse case-manger was recruited for the duration of the study (Jul 2018 – Oct 2019), with a total cost per month of 3500€. During the whole study period, she recruited and managed 91 patients in the CONNECARE program (52 CS1 + 39 CS2), taking responsibilities in the management of the patients as well as providing technical support and assistance, collecting research-related data and participating in the overall development of the CONNECARE H2020 project. Therefore, in a real-life non-research scenario, it is estimated that a single hospital-based nurse case-manger could manage up to 500 simultaneous patients, resulting in a cost of 7€ per patient and month. During the study, the rest of involved medical staff either in the hospital or in the primary care assumed any potential increase in workload related to the use of the CONNECARE platform at no additional cost. In this sense, it must be noticed that, in one hand, a fully implemented CONNECARE program would imply a higher number of CONNECARE patients and thus an increase in workload; on the other hand, a fully mature and integrated platform would be much less requiring for involved professionals. In any case, the re-structuration of staff's time to include the new tasks would be fully assumed by the health system and no additional personnel would be required, thus no additional cost would be generated. The cost of licensing and running the CONNECARE platform as well as the costs to maintain, evolve and support it cannot be easily stablished. In this sense, the costs of other health services like Home-based oxygen therapy, where a supplier covers the role of providing devices, licenses and technical support, have been used to generate a per year per patient estimation of 200€. Therefore, a total cost of 23.67€ /patient and month has been estimated as direct costs of the CONNECARE program for the purpose of the current analyses. Given that the duration of the intervention was 3 months, the final costs of the CONNECARE program was 71.01€. Additionally, 2 sensitivity scenarios were also analyzed were CONNECARE program costs were incremented by +50% and +100%. No indirect costs were considered.

6B. Cost of unplanned visits and hospital admissions

According to the official data of 2013 (CVE-DOGC-A-13051031-2013), the overall cost of unplanned medical visits in the health region of Lleida is 62€. Similarly, the cost of hospital admissions is 555€ per day. No indirect costs were considered.

6C. Cost and cost-effectiveness analyses

Table 15. CS1 within trial costs (average cost per patient) and cost-effectiveness, considering all unplanned visits and hospital admissions.

CS1 costs and cost-effectiveness, considering all unplanned visits and hospital admissions (all costs in €).				
	Standard Care (n=28)	**CONNECARE (n=48)**	**Difference**	**ICER**
Unplanned visits*	143.49	64.48	-79.01	
Hospital admissions*	2537.14	1986.90	-550.24	
TOTAL medical costs per patient	2680.63	2051.38	-629.25	
		1st scenario		
CONNECARE program	0	71.01	+71.01	
TOTAL costs per patient	2680.63	2122.39	-558.24	-112.10
		2nd scenario (+50% CONNECARE program cost)		
CONNECARE program	0	106.52	+106.52	
TOTAL costs per patient	2680.63	2157.90	-522.73	-104.97
		3rd scenario (+100% CONNECARE program cost)		
CONNECARE program	0	142.02	+142.02	
TOTAL costs per patient	2680.63	2193.40	-487.23	-97.84

ICER, incremental cost-effectiveness ratio: Incremental cost associated with 1 additional point gain in SF12
* Costs based on the Catalan Institute of Health (CVE-DOGC-A-13051031-2013).

Table 16. CS1 within trial costs (average cost per patient) and cost-effectiveness, considering all unplanned visits and hospital admissions related to the main chronic disease.

CS1 costs and cost-effectiveness, considering all unplanned visits and hospital admissions related to the surgery procedure (all costs in €).				
	Standard Care (n=28)	**CONNECARE (n=48)**	**Difference**	**ICER**
Unplanned visits related to the main chronic disease *	56.69	24.80	-31.89	
Hospital admissions related to the main chronic disease *	2267.57	1043.40	-1224.17	
TOTAL medical costs per patient	2324.26	1068.20	-1256.06	
	1st scenario			
CONNECARE program	0	71.01	+71.01	
TOTAL costs per patient	2324.26	1139.21	-1185.05	-237,96
	2nd scenario (+50% CONNECARE program cost)			
CONNECARE program	0	106.52	+106.52	
TOTAL costs per patient	2324.26	1174.72	-1149.54	-230.83
	3rd scenario (+100% CONNECARE program cost)			
CONNECARE program	0	142.02	-1114.04	
TOTAL costs per patient	2324.26	1210.22	-	-223.70

ICER, incremental cost-effectiveness ratio: Incremental cost associated with 1 additional point gain in SF12
* Costs based on the Catalan Institute of Health (CVE-DOGC-A-13051031-2013).

6.3. Israel

ANNEX VII – Study results of Implementation study 1 in Israel.

CONNECARE – Israel - All data analyses CS1

Patients' usage of the ICT tools and devices

1A. Using the Pedometer (Fitbit)

Table 1. Days Fitbit transmitted by period – CS1.

Days Fitbit transmitted	Week 1-4		week 5-8		week 9-12		week 13-16		Week 17-20		Week 21-24	
N	43		41		41		41		40		39	
Mean (SD)	27.07 (3.24)		27.10 (2.51)		24.71 (5.30)		23.39 (8.19)		26.15 (5.32)		22.26 (7.86)	
Skewness (Se)	-4.48 (0.37)		-3.13 (0.41)		-1.58 (0.47)		-1.88 (0.37)		-3.45 (0.41)		-1.31 (0.47)	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
less than 10 days	0	**0.0**	0	**0.0**	0	**0.0**	5	**12.2**	2	**5.0**	4	**10.3**
10-20 days	2	**4.7**	2	**4.9**	6	**14.6**	4	**9.8**	1	**2.5**	8	**20.5**
21 days and above	41	**95.3**	39	**95.1**	35	**85.4**	32	**78.0**	37	**92.5**	27	**69.2**

Table 2. Average daily number of steps by period – CS1.

Average daily number of steps (out of the valid transitions > 0)	Week 1-4		week 5-8		week 9-12		week 13-16		Week 17-20		Week 21-24	
N	43		41		41		41		40		39	
Mean (SD)	7,252 (4,819)		7,364 (4,068)		7,132 (4,030)		7,266 (4,269)		6,858 (4,326)		7,225 (4,699)	
Skewness (Se)	1.70		1.42		1.55		1.40		1.49		1.52	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
less than 2000 steps	1	**2.3**	1	**2.4**	1	**2.4**	1	**2.4**	2	**5**	2	**5.1**
2,000-5,000 steps	10	**23.3**	13	**31.7**	12	**29.3**	13	**31.7**	15	**37.5**	15	**38.5**

5,001-10,000 steps	24	**55.8**	19	**46.3**	22	**53.7**	18	**43.9**	15	**37.5**	14	**35.9**
more than 10,000 steps	8	**18.6**	8	**19.5**	6	**14.6**	7	**17.1**	7	**17.5**	7	**17.9**

Twenty patients in CS1 reported steps beyond the time of leaving the study, with 6,014 average daily number of steps. The number of patients is declining, because patients dropped out of the project over time, only 24 patients in CS1 and 20 patients in CS2 remained three months following the discharge from a hospital.

Statistical analyses on all period data

General description of the statistical analyses:
Statistical analyses were conducted using SPSS (Ver. 24.0). Statistical level of significance was set to $\alpha = .05$ (family-wise). For significant effects, multiple comparisons were conducted applying Bonferroni's adjustment for significance level (family-wise $\alpha = .05$).

Research Question 1: Do the percentage of days reporting usage of Fitbit (=total number of days reporting out of the total number of days in intervention) and the average number daily steps reported differ for men and women?

Statistical Analyses: Two multivariate one-way analyses of covariance (MANCOVA) were conducted separately for the CS1 and CS2 samples, with percentage of days reporting usage of Fitbit and average number of daily steps reported as the dependent variables, and sex as the independent variable. Participants age and Charlson scores were entered as covariates. **The analyses revealed no effect of sex, for both the CS1 and CS2 samples**. For CS1: multivariate F (2, 35) = 0.23, Wilk's Lambda = .99, *p-value* = .80. For CS2: multivariate F (2, 21) = 0.08, Wilk's Lambda = .99, *p-value* = .92. Univariate analyses revealed that men and women did not differ significantly with respect to percentage of days reporting usage of Fitbit, for both the CS1 (M_{men} = .67, M_{women} = .72, *p-value* = .66) and CS2 (M_{men} = .54 , M_{women} = .51, *p-value* = .70) samples, as also was the case for the univariate tests for the average number of daily steps reported, for both the CS1 (M_{men} = 4,821, M_{women} = 5,109, *p-value* = .79) and CS2 (M_{men} = 4,465 , M_{women} = 4,746, *p-value* = .73) samples.

Research Question 2: Does age affect the percentage of days reporting usage of Fitbit and the average number of daily steps reported?

Statistical Analyses: Four multiple linear hierarchical regressions predicting percentage of days reporting usage of Fitbit and the average daily steps reported were conducted, separately for the CS1 and CS2 samples. Predictors entered in step 1 were: Sex and Charlson scores, In Step 2: Age. **Results indicated that age did not significantly predict the percentage of days reporting usage of Fitbit**, beyond sex and the Charlson score, for both the CS1 sample (R^2*change* = .03, Beta = -.19, *p-value*=.30) and the CS2 sample (R^2*change* = .08, Beta = .39, *p-value* = .15). **However, with respect to the average daily steps reported, for the CS1 sample, there was a significance contribution of age (R^2*change* = .13, Beta = -.38, *p-value*=.02) indicating that older patients reported significantly less daily steps than younger ones.** However, **the age effect was not significant for the CS2**

sample, (R^2*change* = .02, Beta = -.18, *p-value*=.55) although the tendency was similar to the one emerging for the CS1 sample.

Research Question 3: **Do the percentage of days reporting usage of Fitbit (=total number of days reporting/total number of days in intervention) and the average number of daily steps reported change along intervention period?**

Statistical Analyses: Four two-way mixed-design analyses of co-variance (ANCOVAs) were conducted for percentage of days reporting usage of Fitbit and average number of daily steps reported as dependent variables, separately for the CS1 and CS2 samples. The repeated measure factor was months (1,2,3) for the CS1 sample and period (pre-hab, months 1,2,3) for the CS2 sample, and age-group (<>median of 69) was the between-subjects factor in all the analyses. **For both the CS1 and CS2 samples, there was no significant change in the percentage of days reporting usage of Fitbit**. For CS1, *F* (2, 21) = 1.68, Wilk's Lambda = .86, *p-value* = .21. For CS2, *F* (3, 15) = 1.26, Wilk's Lambda = .82, *p-value* = .37. **However, for both samples there was an increase in the average daily number of steps reported:** For CS1, *F* (2, 21) = 6.04, Wilk's Lambda = .64, *p-value* = .008, η2=.37. Multiple comparisons with Bonferroni's adjustment to significance level revealed an increase in the average daily steps from the first month (M=5,195) to the second (M = 6,055), adjusted *p-value*= .023, and to the third month (M = 6,477), adjusted *p-value*= .007. **Change in daily number of steps was found significant also in the CS2 sample:** *F* (3, 15) = 5.40, Wilk's Lambda = .48, *p-value* = .01, η2=.52. In this sample, there was an expected **decrease** in the number of daily steps from the PreHab period (M = 7, 011) to the first month after intervention (M = 3, 953), adjusted *p-value*= .004, but an **increase from the first month to the third one** (M = 5,692, adjusted *p-value*= .006. **The age-group factor was not significant in both samples** (*p* = .52 and *p* = .10, for CS1 and CS2, respectively) as were the **Time X Agegroup interactions** (*p* = .25 and *p* = .83, for CS1 and CS2: respectively), suggesting that the **increase in number of steps emerged for both younger and older patients.**

1B. Using the messaging function in the app

Table 3. Number of messages sent using the app – all period.

	CS1 updated	
N of messages	101	
Mean (SD)	2.35 (3.31)	
Skewness (Se)	2.67	
	N patients	**% patients**
0 messages	10	**23.3**
1-2 messages	22	**51.2**
3-5 messages	6	**14.0**

6-10 messages	3	**7.0**
> 10 messages	2	**4.7**

Statistical Analyses

Research Question 1: Does the number of messages sent differ for men and women?

Statistical Analyses: Two one-way analyses of covariance (ANCOVA's) were conducted separately for the CS1 and CS2 samples, with total number of messages sent by the patient as the dependent variables and sex as the independent variable. Participants age and Charlson scores were entered as covariates. **The analyses revealed a null effect of sex, for both the CS1 and CS2 samples**. For CS1: F (1,36) = 0.01, *p-value* = .97. For CS2: : F (1,29) = 0.08, *p-value* = .78.

Research Question 2: Does age affect the number of messages sent by each participant?

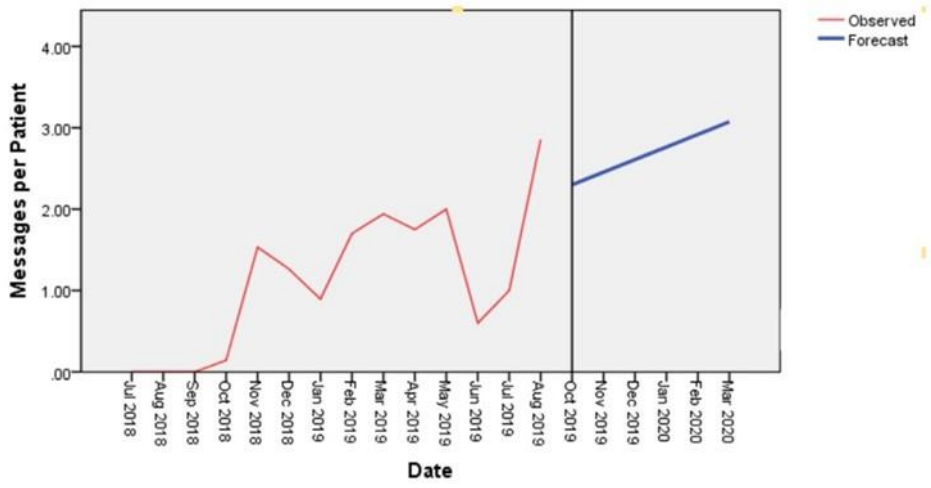
Statistical Analyses: Two multiple linear hierarchical regressions predicting the number of messages sent by each participant were conducted, separately for the CS1 and CS2 samples. Predictors entered in step 1 were: Sex and Charlson scores, In Step 2: Age. **Results indicated that age did not significantly predict the number of messages sent,** beyond sex and the Charlson score, for both the CS1 sample (R^2*change* = .008, Beta = -.10, *p-value*=.58) and the CS2 sample (R^2*change* = .001, Beta = -.03, *p-value* = .88).

Research Question 3: Does the use of messaging changes as study proceeds?

For that purpose, we first calculated for each study month: 1) the total number of patients participating in the study, and 2) the total number of messages sent (over all the participants). Then, for each month, we computed the ratio messages per patient.

Statistical Analysis: Two time-series analyses were computed for the CS1 and CS2 samples with the ratio messages:patient as the dependent variable and month as the independent one. The analyses also included predicted values for 5 months post study.

Figure 1. Observed and predicted number of messages per patient by study month – CS1 sample.



The time series analysis for the ratio messages:patient by study month for the CS1 sample revealed an overall increase in the number of messages per patient sent over the study period. There seems to be a down fold in June and July 2019 and a pick in August 2019. The high values of messages per patient predicted for the five months post study reveal an increase in messaging use.

1C. Responding to EQ5D questionnaires in the app

Due to a very low compliance, no analyses were performed for this measure.

In CS1 only 2 patients reported, and in CS2 8 patients reported 1-5 times, and 3 patients reported more than 5 times.

1D. Monitoring blood pressure or any other measurement

Table 4. Percentage of blood pressure measured reported out of times prescribed.

	CS1	
Prescription Type	**Mean (SD)**	**N**
Every day	23% (32%)	16
Twice a week	7% (8%)	8
Once a week	14% (25%)	4
Not prescribed	--	12

1E. Reporting performance of simple tasks

In CS1 only 8 patients reported on more than 20% of the tasks prescribed for them.

Patient's Experience

2A. Person-centred coordinated care experience questionnaire (P3CEQ)

SCALE: 0 - Not at all 3 - Always

Table 5. Results from the P3CEQ questionnaire.

	CS1
N	35
F1. Did you discuss what was most important for YOU in managing your own health and wellbeing?	40%

F2. Were you involved as much as you wanted to be in decisions about your care?	49%
F3. Were you considered as a 'whole person' rather than just a disease/condition in relation to your care?	66%
F4. Did your care-team / providers involve your family/friends/carers as much as you wanted them to be in decisions about your care?	43%
F5. Have you had enough support from your care team / providers to help YOU to manage your own health and wellbeing?	69%
F6. To what extent do you receive useful information at the time you need it to help you manage your health and wellbeing?	71%

% of patients answered "Agree" or "Strongly agree".

2B. Nijmegen Continuity Questionnaire (NCQ)

SCALE: 1 - Strongly agree 5- Strongly disagree

Table 6. Results from the NCQ questionnaire.

	CS1
N	33
G1. My care providers transfer information very well to one-another	88%
G2. My care providers work together very well	82%
G3. My care providers are very well connected	73%
G4. My care providers always know what one-another is doing	67%
G5. I have to wait too long to obtain a service/appointment	18%

% of patients answered "Agree" or "Strongly agree".

2C. Patients satisfaction with the technology – NPS

Since the ratings are strongly negatively skewed, central locations will be described using median instead of mean.

Table 7. Rating of satisfaction with Fitbit app NPS – CS1.

FITBIT NPS (N = 27)				
Likert scale score (0 = poor TO 10 = good)	**. Overall satisfaction**	**2. Easiness of use**	**3. Ability to be used without help**	**4. Would you recommend it?**
Skewness (Se)	-5.105	-5.120	-5.095	-4.909

Median	8	8	8	8
25th Pct	6	6	6	4
75th Pct	10	9	9	10

Table 8. Rating of satisfaction with SMS app NPS – CS1.

SMS App NPS (N = 32)				
Likert scale score (0 = poor TO 10 = good)	**1. Overall satisfaction**	**2. Easiness of use**	**3. Ability to be used without help**	**4. Would you recommend it?**
Skewness (Se)	-.46 (0.41)	-.70 (0.41)	-.81 (0.41)	-.11 (0.41)
Median	6.00	7.00	7.00	5.50
25th Pct	3.25	4.25	4.25	.00
75th Pct	9.75	9.00	10.00	10.00

2D. Patients satisfaction with the technology – SUS

Based on research, a SUS score above a 68 would be considered above average and anything below 68 is below average.

Table 9. Total SUS score with SMS app NPS – CS1.

SUS total score for the SMS App				
	CS1 3 months		**CS1 6 months**	
N	**31**		**26**	
Mean (SD)	79.76 (15.96)		74.13 (18.80)	
Skewness (Se)	-0.64		-0.37	
	N	**%**	**N**	**%**
Score above 68	**23**	**74%**	**15**	**75%**

Staff's Experience

Six staff members answered the questionnaire, three CM nurses and three physiotherapists.

The team was asked to answer the questionnaire anonymously three times during the study period - November 2018, March-May 2019 and at the end of the study.

3A. Staff satisfaction with the technology – NPS

Table 9. Results of NPS scores.

Likert scale score (0 = poor to 10 = good)	1. Overall satisfaction	2. Easiness of use	3. Ability to be used without help	4. Would you recommend it?
SMS App NPS (N = 9)				
Median	4.50	5.00	4.00	5.00
25th Pct	3.00	2.50	2.00	2.00
75th Pct	6.75	6.50	6.50	6.50
FITBIT NPS (N = 9)				
Median	8.00	8.00	8.00	7.00
25th Pct	7.00	6.00	6.00	6.00
75th Pct	9.00	8.00	8.00	8.00
SACM NPS (N = 9)				
Median	5.00	6.00	5.00	4.00
25th Pct	3.25	2.00	3.00	1.50
75th Pct	6.75	6.50	6.50	6.50

The answer to the question "How likely is it that you recommend the CONNECARE system to a family member or friend?" was used to calculate the NPS. Subtracting the percentage of Detractors from the percentage of Promoters. The NPS ranges between −100 and +100, a positive score is considered good.

Table 10. Results of NPS scores.

STAFF - NPS SCORE						
	Fitbit		SACM		SMS	
Score for 'would you recommend it'	N	%	N	%	N	%
0-6 (detractors)	3	33%	7	78%	7	78%
7-8 (passives)	5	56%	1	11%	1	11%
9-10 (promotors)	1	11%	1	11%	1	11%

Table 11. Results of NPS scores.

NPS score	Fitbit	SACM	SMS
CM nurses (N = 3)	+ 33	- 33	- 33
Physiotherapists (N = 6)	0	- 83	- 83
All (N = 9)	- 22	- 67	- 67

3B. Staff satisfaction with the technology – SUS.

Based on research, a SUS score above a 68 would be considered above average and anything below 68 is below average.

Table 12. Results of SUS scores.

SUS total score (N = 16)		
Mean (SD)	**SMS App**	**SACM**
ALL (N = 16)	20.2 (8.2)	20.6 (7.8)
CM nurses (N = 7)	17.4 (5.6)	17.7 (4.9)
Physiotherapists (N = 9)	22.3 (9.5)	22.8 (9.2)
* No respondent rated a final grade above 68		

3C. ACT@Scale - Staff engagement

Table 13. Results of the staff engagement questionnaire.

% answered "Agree" / "Very agree"	NCM N = 7	Physio N = 9
1. I have a clear understanding of what this project is trying to achieve	100%	89%
2. I feel I am able to influence the way in which the project is managed and delivered	100%	22%
3. I was consulted about the implementation of the project	57%	33%
4. I believe patients are benefiting from participating in this project	86%	100%
5. The implementation of the project was well planned	29%	22%
6. I was given appropriate training and education to support my role in the project	86%	56%
7. My views about the project are gathered and acted upon	57%	56%
8. I was actively involved in the development and implementation of the project	57%	11%
9. I believe that the approach to integrated care used in the project is now part of 'normal' practice	86%	44%
10. I have been supported to develop the skills and knowledge necessary to deliver the service	71%	22%

11. My involvement in the implementation of this project has positively changed my views on integrated care	14%	22%

Table 14. Results of the staff engagement questionnaire.

% answered "Agree" / "Very agree"	NCM N = 7	Physio N = 9
1. The contents and teaching methods are tailored to my needs	86%	56%
2. All different categories of staff have the same access to training	57%	67%
3. There was sufficient staff time available to support my training	43%	33%
4. Frontline staff are quite involved in training or supporting (e.g. through mentorship) their colleagues in relation to the project	57%	67%

Intervention effectiveness - Health & wellbeing questionnaires (only intervention Before VS After).

Table 15. Results of the health and well-being questionnaires.

CS1					
	Before (N = 40)		After (N = 32)		P-value (before-after)
	Mean	SD	Mean	SD	
Barthel	**96.50**	8.49	**97.19**	5.38	.49
Lawton	**20.80**	3.45	**21.84**	2.32	.13
SF-12 - Physical	**6.60**	**3.622**	**9.25**	**3.860**	**<.001**
SF-12 - Mental	**14.75**	4.640	**14.12**	4.871	.39
SF-12 - Total	**21.35**	6.971	**22.71**	7.903	.35
HADS-Anxiety	**3.15**	**2.741**	**2.76**	**2.686**	**.02**
HADS-Depression	**4.20**	3.495	**2.97**	2.949	.19
EQ-5D-5L – Q1-Q5	**1.69**	0.66	**1.52**	0.49	.08
EQ-5D-5L – Health Today	**59.65**	**19.55**	**71.97**	**17.72**	**< .001**
Sweet 16	**15.05**	1.224	**15.35**	.745	.84

Statistical Analyses:

Research Question 1: Did the questionnaires' total scores change following intervention?
Statistical analysis: One-way ANOVAs for repeated measures with total score as the dependent variables and time (before/after) as the independent variable were conducted for each of the total scores of the questionnaires. The analyses were conducted separately for the CS1 and CS2 samples. Results are presented in Table XY. As can be seen, from before to after intervention, **there was an improvement in the CS1 group in SF12-physical, anxiety (i.e., decrease) and feeling of general health, and in the CS2 group there was an improvement in anxiety (i.e., decrease) and feeling of general health.**

To test change in the individual items' ratings of the Barthel, Lawton, and EQ-5D-5L questionnaires, additional one-way ANOVAs for repeated measures were conducted for each individual item of these questionnaires. P-values are presented in tables XX-YY. **Regarding the Barthel items**, there was a significant **improvement only in BATHING in the CS1 group**. No changes emerged for this questionnaire's items in the CS2 group. **Regarding the Lawton items, there was an improve in housekeeping in the CS1 groups, and in shopping in the CS2 group**. Finally, regarding the **EQ-5D-5L** there was a significant **decrease in both CS1 and CS2 groups in in pain discomfort and an increase in feeling of health.**

Intervention effectiveness - Health & wellbeing questionnaires (only intervention Before VS After).

Table 16. Emergency department visits – no hospitalization.

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
One month before recruit/intervention	0.18	0.38	0.11	0.38	.40
During intervention	0.28	0.60	0.22	0.58	.61
One month after recruit/intervention	0.00	0.00	0.01	0.10	.52

Table 17. Number of hospitalizations per capita.

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
One month before recruit/intervention	0.05	0.22	0.26	0.73	.07
During intervention	0.38	0.81	0.56	1.10	.33
One month after recruit/intervention	0.00	0.00	0.10	0.47	.13

Table 18: Mortality (N).

	Intervention	Control	P-value ($\chi 2$)
N	**40**	**96**	
One month before recruit/intervention	0	0	--
During intervention	0	2	.36

One month after recruit/intervention	0	0	--

Table 19. Number of general practitioner visits per capita.

	Intervention		Control		P-value (t-test)
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
One month before recruit/intervention	**5.85**	**4.12**	**3.60**	**3.59**	**.002**
During intervention	7.30	4.67	5.18	5.43	.03
One month after recruit/intervention	1.30	1.47	1.00	1.18	.21

Table 20. Number of specialists visits per capita.

	Intervention		Control		P-value (t-test)
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
One month before recruit/intervention	2.78	2.81	1.56	2.12	.007
During intervention	3.28	2.76	1.96	2.38	.006
One month after recruit/intervention	0.73	1.11	0.44	0.74	.08

Table 21. Overall cost per capita (Euro).

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
Before recruit/intervention	699.48	1,847.79	1,012.99	2,912.99	.30
During intervention	1,987.01	3,133.77	3,060.26	5,142.08	**.04**
After recruit/intervention	951.95	2,584.16	1,492.73	4,923.38	.56

Table 22. Total hospital-related care cost (Euro).

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
Before recruit/intervention	406.49	1,689.61	701.04	2,175.32	0.21
During intervention	1,536.10	2,887.01	2,402.34	4,477.66	**0.06**
After recruit/intervention	552.21	2,312.47	700.26	2,957.40	0.8

Table 23. Total pharmacy cost (Euro).

	Intervention	Control	P-value
N	**40**	**96**	

	Mean	SD	Mean	SD	
Before recruit/intervention	89.09	130.65	92.99	122.60	0.78
During intervention	122.86	185.45	285.19	1,371.69	0.21
After recruit/intervention	117.14	125.71	408.05	1,796.88	0.37

Table 24. Total laboratory testing cost (Euro).

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
Before recruit/intervention	4.42	10.65	5.19	13.51	0.65
During intervention	5.97	13.25	6.49	11.95	0.78
After recruit/intervention	6.75	9.09	6.23	16.62	0.88

Table 25. Private institutes' visits cost (Euro).

	Intervention		Control		P-value
N	**40**		**96**		
	Mean	**SD**	**Mean**	**SD**	
Before recruit/intervention	11.69	40.78	32.47	188.83	0.26
During intervention	50.65	187.79	103.90	403.38	0.18
After recruit/intervention	14.03	61.56	18.18	44.68	0.7

Costs effectiveness of net expenses (in Euro)

For each patient in the intervention group, total cost during the intervention was calculated by adding the intervention cost itself (184 Euro) to the overall health costs from Maccabi database, which than was compared to the average cost of the matched patients from the control group.

Table 26. Overview of costs and neet expenses.

	Overall Expenses			Hospital Expenses		
N		**37**			**37**	
	Mean	**SD**	**P-value**	**Mean**	**SD**	**P-value**
During intervention	**-2640.5**	**7436.4**	**0.03**	**-2168.2**	**5742.7**	**0.023**
During + one month after intervention	**-2984.6**	**8812.8**	**0.04**	**-2273.6**	**5785.3**	**0.019**
One month after intervention	-297.3	3327.9	0.58	-105.4	2570.6	0.8

6.4. Groningen

ANNEX VIII – Study results of Implementation study 1 in Groningen

CONNECARE – Groningen - All data analyses CS1

General description of statistical analyses

All analyses were performed using IBM SPSS statistics version 24 (IBM Corporation, Armonk, NY). A statistical level of $p<0.05$ was considered statistically significant.

Patients' usage of the ICT tools and devices

1A. Use of the Pedometer (Fitbit)

Table 1. Compliance with use of the Fitbit.

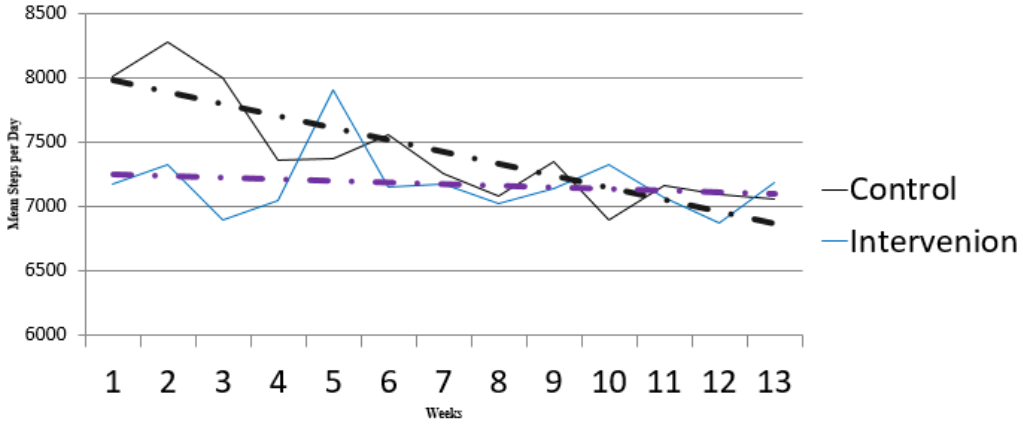
	Days Fitbit transmitted	# patients	% patients
Fitbit monitoring	less than 30 days	9	25.0%
	30-60 days	10	27.7%
	60-90 days	10	27.7%
	More than 90 days	7	19.4%

Table 2. Overview of the average step count.

	Control, mean (SD)	Intervention, mean (SD)	Total, mean (SD)
Total n (control) = 23, n (intervention) = 20	7419 (5410)	7145 (2443)	7291 (4248)
Asthma n (control) = 7, n (intervention) = 7	8005 (3318)	8283 (2885)	8123 (2990)
COPD n (control) = 15, n (intervention) = 12	7139 (6404)	6159 (1541)	6703 (4831)
ACO n (control) = 1, n (intervention) = 1	7520	11298	9409 (2672)

The average step count did not differ between groups, with a small overall decline observed in the intervention group.

Figure 1. Repeated measures analyses on the mean daily steps count.



1B. Use of the messaging function in the app.

Table 3. Use of the messaging function.

	# of messages	# patients	% of patients
Messaging function	No messages	30	72%
	1-3 messages	11	26%
	> 4 messages	1	2%

Of the patients who sent more than 4 messages, 3 sent more than 10 messages which denotes a frequent use of the SMS app for communicating with professionals. It must be considered that the messaging function was not implemented from the beginning of the project, and this limited the engagement of the very first participants in the use of this feature.

1C. Response to questionnaires in the SMS app.

Table 4. Overview of the responses to the questionnaires.

	Times prescribed	#answered questionnaires	# patients	% of patients
CARAT, SF12, CCQ, Tic-p, IPQ-k	Never	0	0	0
	At least once	0	6	12%
		1	30	60%
		2-3	14	28%
		>3	0	0%

Patient's Experience

2A. Patient satisfaction with technology - NPS.

Table 5. Overview of NPS scores.

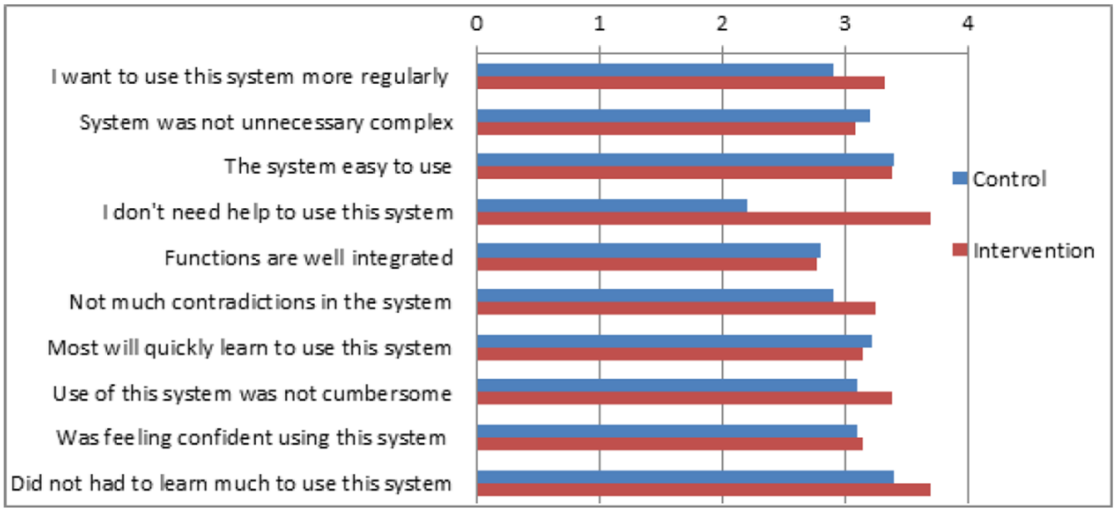
Control (n=10) Mean Score (Sd)	Control (n=10)	Intervention (n=13) Mean Score (SD)	Total (n=23) Mean Score (SD)	Between groups mean Score
	8.2 (1.2)	**8.2 (1.4)**	**8.2 (1.3)**	**.899**

2B. Patient satisfaction with technology - SUS.

Table 6. Overview of SUS scores.

Control (n=10) Mean Score (Sd)	Control (n=10)	Intervention (n=13) Mean Score (Sd)	Total (n=23) Mean Score (Sd)	Between groups Mean Score (Sd)
General Impression	**8.1 (1.2)**	**8.5 (1.1)**	**8.3 (1.1)**	**.466**
User Friendliness	**8.7 (0.9)**	**7.8 (2.0)**	**8.2 (1.7**	**.207**
Possibility for use without help	**7.9 (2.9)**	**8.6 (1.3)**	**8.3 (2.1)**	**.823**

Figure 2. Overview of responses to the SUS.



Scoring ranged from 0 (strongly disagree) to 4 (strongly agree)

Intervention effectiveness – Patient outcomes and resource use.

Table 7. Overview of patient reported outcomes.

	Change Score: 3 months - Baseline		
	Control (n=11)	Intervention (n=14)	
Variable	Mean (SD)	Mean (SD)	p-value
CCQ Total	-0.05 (.77) Improvement	-0.32 (.66) Improvement	.934
CCQ Symptoms	-0.07 (.70) Improvement	-0.17 (1.05) Improvement	.781
CCQ Mental state	0.18 (.87) Worsening	-0.18 (.70) Improvement	.263
CCQ Functional	0.30 (.94) Worsening	0.11 (.66) Worsening	.692
	Control (n=8)	Intervention (n=10)	
SF-12 MSC	-1.29 (5.63) Worsening	4.51 (7.60) Improvement	.091
SF-12 PSC	1.82 (6.30) Improvement	-1.19 (7.14) Worsening	.363

Table 8. Overview of hospital admissions up to 3 months after study inclusion.

Hospital admissions last 3 months	**Intervention**			**Control**		
	1 month N = 20	**3 months N = 19**	**6 months N = 15**	**1 months N = 25**	**3 months N = 18**	**6 months N = 12**
Mean length of stay (SD)	4.40 (14.11)	1.63 (6.0)	0.40 (1.55)	5.52 (14.36)	0.72 (2.42)	0 (0.0)
Skewness (Se)	4.167	4.126	3.873	2.453	3.753	-
Median (p25,p75)	0 (0, 0.75)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Total number of hospitalized persons (%)	5 (25%)	2 (11%)	1 (7%)	4 (16%)	2 (11%)	0 (0%)
Cumulative number of days in hospital	88	31	6	133	13	0

Table 9. Overview of GP visits.

GP visits	Intervention			Control		
	1 month N = 21	3 month N = 19	6 months N = 15	1 months N = 23	3 months N = 18	6 months N = 12
Mean number of contacts (SD)	2.81 (2.94)	1.79 (1.78)	1.40 (1.55)	1.22 (1.20)	1.33 (1.50)	2.00 (1.95)
Skewness (Se)	1.377	0.881	1.213	0.568	1.135	0.965
Median (p25,p75)	3 (0, 4)	1 (0, 3)	1 (0, 2)	1 (0, 2)	1 (0, 2)	1.5 (0.25, 3)
Total number of persons who visited GP (%)	15 (71%)	14 (74%)	10 (67%)	14 (61%)	11 (61%)	9 (75%)
Cumulative number of days in hospital	59	34	21	28	24	24

Table 10. Overview of specialists visits.

Specialists visits	Intervention		Control	
	3 month N = 18	6 months N = 15	3 months N = 19	6 months N = 12
Mean number of contacts (SD)	1.28 (1.45)	1.53 (3.02)	1.58 (3.61)	1.08 (1.31)
Skewness (Se)	1.155	2.097	3.913	1.270
Median (p25,p75)	1 (0, 2.25)	1 (0, 1)	1 (0, 2)	1 (0, 1.75)
Total number of persons who visited GP (%)	11 (61%)	5 (33%)	10 (53%)	7 (58%)
Cumulative number of days in hospital	23	33	30	13