Telemonitoring of chronic diseases: The Experience of Azienda Sanitaria Locale BR, Brindisi (IT) with heart failure, diabetes and chronic obstructive pulmonary disease

AReSS Puglia, Agenzia Regionale Strategica per la Salute ed il Sociale

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Limitations

This report is based on information available when the evidence searches were made and does not contain data on subsequent developments or improvements of the evaluated technology. The observations made on effectiveness, safety or cost-effectiveness of the technology evaluated in the report are to be considered current but may change as more evidence becomes available if an update of the document is commissioned.

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Declaration of Conflict of Interest

The authors declare that they will not receive either benefits or harms from the publication of this report. None of the authors have or have held shares, consultancies or family relationships with any of the producers of the technology assessed in this document.

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Acronyms and abbreviations

	Description
ADI	Assisitenza Domiciliare Integrata
AReSS	Strategic Agency for Health and Social Care (Agenzia Strategica Regionale per la Salute e il Sociale)
ASL-BR	Azienda Sanitaria Locale di Brindisi
CDC	US Centers for Disease Control and Prevention
COPD	chronic obstructive pulmonary disease
DBMS	Database Management System
DDCI	Drug Delivery Complexity Index
DGR	Act of the Regional Government (Delibera di Giunta Regionale)
DM	diabetes mellitus types 1 and 2
GP	General practitioner
HF	heart failure
http	HyperText Transfer Protocol
https	HyperText Transfer Protocol Secure
ICT	Information and Communication Technologies
LOSH	Length Of Stay
LOSUr	Length Of Stay for urgent hospitalization
MAST	Model for ASsessment of Telemedicine applications
PAI	Piano Assistenziale Individuale
PICO	P - problem/patient/population I - intervention C - comparison/control O - outcome
PTA	Community Care Centre (Presidio Territoriale di Assistenza)
RCT	Randomised Controlled Trial
RHSD	Regional Health System Database
SaMD	software which acts as a medical device
SQL	Structured Query Language
SSL	Secure Sockets Layer
TCP / IP	Transmission Control Protocol / Internet Protocol
TDE	Transparent Data Encryption
TLS	Transport Layer Security
TM	Telemedicine
VPN	Virtual Private Network
WHO	World Health Organization

1. Abstract (en)

1.1. Background

Telemedicine (TM) is the delivery of healthcare services at a distance using Information and Communication Technologies. Over the last decade, there have been numerous studies aimed at assessing the feasibility and effectiveness of telemedicine strategies.

1.2. Objectives

This study aims at identifying an evidence-base on the effectiveness of TM applications for patients with chronic obstructive pulmonary disease or diabetes or heart failure and at assessing the TM platform in use at the Local Health Authority Azienda Sanitaria Locale di Brindisi (ASL-BR) in the Italian Region Puglia. We used the Model for ASsessment of Telemedicine applications (MAST) as a guidance to report our study findings.

1.3. Search Methods

A systematic search was conducted in the PubMed database, extracting Systematic Reviews published in English, in the last five years and filtered by "humans".

1.4. Selection criteria

We selected only systematic reviews discussing telemedicine applications to support home care for chronically ill patients with heart failure and/or diabetes (Type I and II) and/or chronic obstructive pulmonary disease.

1.5. Main results

1.5.1. Published evidence

Heart Failure

TM intervention is more effective than usual care in decreasing all-cause mortality and HF-related mortality. In addition, a tendency toward reduced risk of HF-related hospitalization was observed. The all-cause mortality rate of the TM group was significantly lower than that of the usual care group among studies published in Europe, studies involving patients older than 65 years, and studies transmitting ≥3 biologic indicators.

Diabetes type I and II

TM achieved a statistically significant but modest reduction in glycated haemoglobin (HbA1C). The effect on HbA1C appeared clinically relevant and comparable to improvements associated with some oral antidiabetic agents, psychosocial interventions, or quality improvement strategies among patients with diabetes. However, the authors of the review did not find good evidence that telemedicine had positive effects on the risk of hypoglycaemia, quality of life or mortality. Some effects in improving glycaemic control were found also with interventions facilitating medication adjustments.

Chronic obstructive pulmonary disease

TM reduced emergency room visits and hospitalizations, improved the mental health quality of life, but did not make a difference in mortality, outpatient visits, or length of stay. TM was found to be more effective at preventing emergency room visits and hospitalizations in patients with severe respiratory failure or those who required home oxygen therapy and/or mechanical ventilation. Integrated interventions, including the delivery of coping skills or education online produced more significant improvement. TM significantly decreased emergency room visits and tended to decrease hospitalization rate in patients with severe chronic obstructive pulmonary disease.

1.5.2. Cost-Minimization Analysis of the TM platform in use at ASL-BR

The analysis had a quasi-experiment setting and consisted of a cost-minimization analysis between a treatment group with TM and two homogenous control groups of patients with the same characteristics in

terms of diagnosis, sex, age, and severity degree of pathology. Comparing the resources used in one year in the intervention group with the two control groups, we were able to identify an average saving per patient equal to €639.63. We also estimated the total additional cost per patient in one year due to the implementation of the organisational model designed by ASL-BR (€1,449.88), thus identifying a possible loss equal to €810.25/patient/year.

1.6. Limitations of the Cost-Minimization Analysis

The control groups were identified ex post and not through an ad hoc clinical protocol. This may have somehow influenced the identification of control groups and costs. Moreover, no clinical data are available from electronics records on the therapeutic efficacy of TM compared to usual care.

1.7. Conclusions

Compared with usual care, the addition of telemedicine can improve patients' outcomes, especially when the most appropriate organisational model is implemented. Moreover, the need to reduce staff and patient's exposure to sick people – e.g., during the COVID-19 pandemic – suggests fostering the adoptions of TM solutions. However, further studies such as large size randomised controlled trials with sub-groups by patient severity and intervention type, also collecting data on resources consumption allowing to properly investigate the economic domain, are needed to provide more evidence and inform the design of the most appropriate intervention(s) for the regional context in Puglia.

2. Abstract (it)

2.1. Background

La telemedicina (TM) è la fornitura di servizi sanitari a distanza utilizzando le tecnologie dell'informazione e della comunicazione (ICT). Nell'ultimo decennio sono stati effettuati numerosi studi volti a valutare la fattibilità e l'efficacia delle strategie di telemedicina.

1.2 Obiettivi

Questo studio ha lo scopo di identificare una base di conoscenze sull'efficacia delle applicazioni di TM per pazienti con broncopneumopatia cronica ostruttiva o diabete o insufficienza cardiaca e di valutare la piattaforma di TM in uso presso l'Azienda Sanitaria Locale di Brindisi (ASL-BR) nella Regione Puglia. Abbiamo utilizzato il modello per la valutazione delle applicazioni di telemedicina (MAST- Model for ASsessment of Telemedicine) come guida per riportare i risultati del nostro studio.

1.3 Metodi di ricerca

È stata condotta una ricerca sistematica nel database PubMed, estraendo le revisioni sistematiche pubblicate in lingua inglese, negli ultimi cinque anni e riguardanti la popolazione umana.

1.4 Criteri di selezione

Abbiamo selezionato solo revisioni sistematiche che trattano le applicazioni di telemedicina per supportare l'assistenza domiciliare per pazienti malati cronici con insufficienza cardiaca e / o diabete (tipo I e II) e / o broncopneumopatia cronica ostruttiva.

1.5 Principali risultati

1.5.1. Evidenze in letteratura

Insufficienza Cardiaca

L'intervento di TM è più efficace delle cure tradizionali nel ridurre la mortalità per tutte le cause e la mortalità correlata allo scompenso cardiaco. Inoltre è stata osservata una tendenza alla riduzione del rischio di ospedalizzazione correlata allo scompenso cardiaco. Il tasso di mortalità per tutte le cause del gruppo in TM è risultato significativamente inferiore a quello del gruppo di cure usuali tra gli studi pubblicati in Europa, gli studi che coinvolgono pazienti di età superiore ai 65 anni e gli studi che trasmettono ≥3 indicatori biologici.

Diabete di tipo I e II

La TM ha ottenuto riduzioni statisticamente significative ma modeste dell'emoglobina glicata (HbA1C). L'effetto su HbA1C è apparso clinicamente rilevante e paragonabile ai miglioramenti associati ad alcuni antidiabetici orali, interventi psicosociali o strategie di miglioramento della qualità tra i pazienti con diabete. Tuttavia, gli autori della revisione non hanno trovato prove robuste che la telemedicina avesse effettivi positivi sul rischio di ipoglicemia, qualità della vita o mortalità. Alcuni effetti nel migliorare il controllo glicemico sono stati riscontrati anche con interventi che facilitano l'aggiustamento terapeutico.

Broncopneumopatia cronico ostruttiva

La TM ha ridotto gli accessi al pronto soccorso ed i ricoveri, ha migliorato la qualità di vita in termini di salute mentale, ma non ha avuto effetto in termini di mortalità, visite ambulatoriali o durata della degenza. La TM è risultata più efficace nel prevenire gli accessi al pronto soccorso ed i ricoveri in pazienti con grave insufficienza respiratoria o che richiedevano ossigenoterapia domiciliare e/o ventilazione meccanica. Interventi integrati, compresi il trasferimento di strategie di adattamento o sessioni educative online, hanno prodotto miglioramenti più significativi. La TM ha ridotto significativamente gli accessi al pronto soccorso e ha portato a diminuire il tasso di ospedalizzazione nei pazienti con grave broncopneumopatia cronico ostruttiva.

1.5.2. Analisi di minimizzazione dei costi della piattaforma di TM in uso presso ASL-BR

L'analisi ha adottato un setting quasi-sperimentale ed è consistita in un'analisi di minimizzazione dei costi tra un gruppo di trattamento con TM e due gruppi di controllo omogenei di pazienti con le stesse caratteristiche in termini di diagnosi, sesso, età e grado di severità della patologia. Confrontando le risorse impiegate in un anno nel gruppo di intervento con i due gruppi di controllo, siamo riusciti ad individuare un risparmio medio per paziente pari a € 639,63. Abbiamo inoltre stimato il costo aggiuntivo totale per paziente in un anno dovuto all'implementazione del modello organizzativo progettato da ASL-BR (€ 1.449,88), individuando così una possibile perdita pari a € 810,25/paziente/anno.

1.6. Limitazioni della Analisi di Minimizzazione dei Costi

I gruppi di controllo sono stati individuati ex post e non attraverso un protocollo clinico ad hoc. Ciò potrebbe aver in qualche modo influenzato l'identificazione dei gruppi di controllo e dei costi. Inoltre, non sono disponibili dati clinici provenienti da cartelle cliniche sull'efficacia terapeutica della TM rispetto alle cure tradizionali.

1.7. Conclusioni

Rispetto alle cure tradizionali, l'aggiunta della telemedicina può migliorare gli esiti di salute dei pazienti, soprattutto quando viene implementato il modello organizzativo più appropriato. Inoltre, la necessità di ridurre l'esposizione del personale e del paziente a persone malate, ad esempio durante la pandemia da COVID-19, suggerisce di promuovere l'adozione di soluzioni di TM. Tuttavia, sono necessari ulteriori studi come studi controllati randomizzati di grandi dimensioni con sottogruppi per gravità di paziente e tipo di intervento, che raccolgano anche dati sul consumo di risorse, permettendo di indagare adeguatamente il dominio economico, ai fini di fornire maggiori evidenze e guidare la progettazione del più appropriato(i) intervento/i per il contesto regionale in Puglia.

3. Introduction

Telemedicine (**TM**), which literally means "healing at a distance" (from Latin ''medicus'' and Greek ''tele'') [Strehle, 2006], is the delivery of healthcare services at a distance using Information and Communication Technologies (**ICT**) [European Commission, 2008]. The World Health Organization (**WHO**) has adopted the following broad description: *the delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities* [WHO, 1998].

In Italy, telemedicine is defined as that "innovative approach to healthcare practice which allows the delivery of service at distance using digital devices, internet, software and telecommunications networks" [Conferenza permanente per i rapporti tra lo Stato, le Regioni e le Provincie Autonome di Trento e Bolzano, 2020].

Over the last decade, there have been numerous studies aimed at assessing the feasibility and effectiveness of telemedicine strategies. As the number of published TM studies began to increase, a plethora of systematic reviews on TM interventions of variable scope and quality, also began to emerge.

Hence, to create a base of evidence supporting the analysis in this report, we searched for the most updated systematic reviews discussing TM effectiveness for patients with chronic obstructive pulmonary disease or diabetes or heart failure and we assessed the TM platform in use at the Local Health Authority Azienda Sanitaria Locale di Brindisi (**ASL-BR**) in the Italian Region Puglia.

Moreover, the need to reduce staff and patient's exposure to sick people during the COVID-19 pandemic, suggested to improve the ability to monitor and treat patients at home fostering the adoptions of TM solutions; as a consequence, the need to address effective and sustainable TM organizational models becomes urgent.

To assess the TM application implemented by ASL-BR, we chose the Model for ASsessment of Telemedicine applications (**MAST**) [Kidholm, 2012], which was developed - using the EUnetHTA Core Model as a starting point - as a three-element model, including: (i) preceding considerations, (ii) multidisciplinary assessment, and (iii) transferability assessment. In the multidisciplinary assessment, the outcomes of TM applications comprise seven domains, i.e., Health problem and description of the application, Safety, Clinical effectiveness, Patient perspectives, Economic aspects, Organizational aspects, and Socio-cultural, ethical, and legal aspects.

4. Domain: Health problem and description of the health technology

This domain includes the description of the health problem of the patients expected to use the TM application and the description of the application being assessed. The content of this domain serves as a description of the background for the assessment.

4.1. Health problem

Three main long-term target conditions are considered in this report, heart failure (**HF**), diabetes mellitus types 1 and 2 (**DM**), and chronic obstructive pulmonary disease (**COPD**).

4.1.1. Definition of target condition/disease

Heart failure is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion [Bozkurt, 2021]. From a physiological point of view, HF can be defined as an inadequate cardiac output to meet metabolic demands or adequate cardiac output secondary to compensatory neurohormonal activation (generally manifesting as increased left ventricular filling pressure). HF has recently been classified into three subtypes, namely HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF) and HF mid-range ejection fraction (HFmrEF), according to the ejection fraction, natriuretic peptide levels and the presence of structural heart disease and diastolic dysfunction [Savarese, 2017].

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycaemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. DM type 1 (previously known as insulin-dependent, juvenile or childhood-onset) is characterized by deficient insulin production and requires daily administration of insulin. Neither the cause of DM type 1 nor the means to prevent it are known. DM type 2 (formerly called non-insulin-dependent, or adult-onset) results from the body's ineffective use of insulin. The majority of people with diabetes have DM type 2. This type of diabetes is largely the result of excess body weight and physical inactivity [WHO, 2020] Gestational diabetes is hyperglycaemia with blood glucose values above normal but below those diagnostic of diabetes. Gestational diabetes occurs during pregnancy. Women with gestational diabetes are at an increased risk of complications during pregnancy and at delivery. These women and possibly their children are also at increased risk of DM type 2 in the future. Finally, impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) are intermediate conditions in the transition between normality and diabetes. People with IGT or IFG are at high risk of progressing to DM type 2, although this is not inevitable.

Chronic obstructive pulmonary disease is a globally prevalent illness, characterised by chronic airway inflammation leading to slow progression of airflow limitation. The inflammatory nature of the disease leads to variable degrees of small airway obstruction and destruction of lung parenchyma. This disease is due primarily to tobacco smoke in high-income countries; tobacco smoking is also the primary cause of COPD in low-income countries, but air pollution and indoor biomass fuel consumption are more frequent causes compared to high-income countries [Oba, 2018].

4.1.2. Symptoms, consequences

People with **Heart failure** have numerous symptoms including dyspnoea, oedema, pain, depression, fatigue, sleep disturbance and anxiety. HF is characterised by a progressive deterioration in health status and marked by acute episodes of decompensated symptoms. HF patients have more unpredictable and less sequential stages than those with other chronic illnesses. This is because their health status may vary suddenly in just a few hours; this is something that happens frequently in their day-to-day lives. People with HF not only experience losses in physical function but must also live with a variety of changes in the emotional, cognitive, social, economic and spiritual domains, which can decline their quality of life. Similarly, they need to cope with complex treatment regimens and strict self-care behaviours. When living with this chronic irreversible syndrome, these patients must change their lifestyles, acquire self-care habits, and implement multiple adaptive and coping behaviours [Olano, 2016].

Diabetes symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes, and fatigue. These symptoms may occur suddenly. DM type 2 symptoms may be similar to those of DM type 1 but are often less marked. As a result, the disease may be diagnosed several years after onset, after complications have already arisen. Until recently, this type of diabetes was seen only in adults, but it is now also occurring increasingly frequently in children.

Chronic obstructive pulmonary disease is not one single disease, but an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow. The most common symptoms of COPD are breathlessness, or a 'need for air', excessive sputum production and a chronic cough [WHO, 2020].

4.1.3. Number of patients (epidemiology)

Heart failure has been defined as global pandemic, since it affects around 26 million people worldwide [Savarese, 2017].

Globally, an estimated 422 million adults were living with **diabetes** in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. This reflects an increase in associated risk factors such as being overweight or obese. Over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries [WHO, 2016].

In 2017, 544.9 million people (95% uncertainty interval [UI] 506.9–584.8) worldwide had a chronic respiratory disease, representing an increase of 39.8% compared with 1990, with **Chronic obstructive pulmonary disease** being the most prevalent disease-specific chronic respiratory disease worldwide, accounting for 55.1% of chronic respiratory disease prevalence among men and 54.8% among women globally [GBD, 2020].

Considering the context of the Puglia Region, the total number of patients and the prevalence are reported in Table 1 [DGR, 2018], where prevalence values have been calculated against the whole population in the AReSS Regional Health System Database "Banca Dati Assistito" (4,103,008).

Table 1. - number of patients and prevalence of the conditions in Puglia

	Population	**Prevalence**
Heart failure	225,056	5.5%
Diabetes	266,572	6.5%
Chronic obstructive pulmonary disease	173,754	4.2%
total	**665,382**	

4.1.4. Burden of disease, resource use

It has been observed [Stewart, 2001] observed that the overall population rate of expected life-years lost due to **heart failure** in men was 6.8 years/1000 and for women 5.1 years/1000. HF imposes a huge economic burden, estimated globally at $108 billion per annum [Cook, 2014], with total costs expected to increase by 127% between 2012 and 2030 [Savarese, 2017]. In developed countries 1-2% of all healthcare expenditures is devoted towards HF [Liao, 2008]. HF is the most common cause of readmission, and HF-related mortality has a similar or even higher incidence than cancer mortality [Yun, 2017]. The global economic burden of HF is estimated at $108 billons per annum, with $65 billons attributed to direct and $43 billons to indirect costs. Europe accounts for 6.83% of total global HF costs [Lesyuk, 2018]. In Italy, the direct cost per patient per year is approximately €11 864 (National Health Service perspective), of which 84.6% related to hospitalizations, 10.1% to medicines prescriptions and 5.3% to specialist examination/diagnostic procedures [Maggioni, 2016].

Diabetes caused 1.5 million deaths in 2012. Higher-than-optimal blood glucose caused an additional 2.2 million deaths, by increasing the risks of cardiovascular and other diseases. Forty-three percent of these 3.7 million deaths occur before the age of 70 years. The percentage of deaths attributable to high blood glucose or diabetes that occurs prior to age 70 is higher in low- and middle-income countries than in high-income

countries [WHO, 2016]. Estimates of healthcare expenditure due to diabetes in the adult population (aged 20-79 years) in the European Region in 2017 was 181 billion international dollars [EU SCIENCE HUB, 2020].

There were 3 914 196 (3 790 578 - 4 044 819) deaths due to chronic respiratory diseases in 2017 globally, an increase of 18.0% since 1990. **Chronic obstructive pulmonary disease** was the most common cause of chronic respiratory disease-attributable deaths, at 41.9 deaths per 100 000 individuals (5.7% of total all-cause deaths). Geographically, deaths attributable to chronic respiratory disease were most frequent in the south Asia super-region (81.2 deaths [75.4-86.3] per 100 000 individuals) in 2017, and least frequent in sub-Saharan Africa (15.5 deaths [14.4-17.0] per 100 000 Individuals). COPD was the most common cause of deaths attributable to chronic respiratory disease in each individual super-region [GBD, 2020]. Health-care costs for respiratory diseases are an increasing burden on the economies of all nations. Among the 28 EU Member States (at the date of the paper, 2011), the care of patients with chronic respiratory diseases costs annually about €380 billion, with COPD alone accounting for 141.4 billion euros at 2011 values (of which, 23.3 billion euros of direct costs, 25.1 billion euros of indirect costs, and 93 billion euros is the value of disability-adjusted life-years lost) [European Respiratory Society, 2020].

4.1.5. Current management of health condition

The current management of the three conditions includes self-management and medications, outpatient visits, diagnostic and therapeutic procedures, hospitalizations, usually organised in specific paths.

However, the TM application discussed in this report is not aimed at substituting any of the current practices, in fact it has to be considered as an additional intervention of remote monitoring supporting usual practice in order to prevent worst outcomes and higher costs.

4.1.6. Existing quality standards

In Puglia, the regional Strategic Agency for Health and Social Care (Agenzia Strategica Regionale per la Salute e il Sociale, **AReSS**), is in charge to provide the governance for implementing regional TM initiatives, thus favouring models and tools harmonisation as well as interoperability and exploitation of data. AReSS has also to define and monitor standards for TM services [DGR, 2020].

4.1.7. Relations to other conditions or treatments

The use of TM to support usual practice in managing home patients, with the same model adopted at ASL-BR, or a similar one, can be easily adapted to patients with more than one of conditions considered in this report as well as to patients with other chronic and non-chronic conditions that can be assisted at home.

4.1.8. Change in patient segments

Once the service has been deployed and regularly running and, once clearer evidence on TM effectiveness has been made available, it will be possible to expand the target population including more long-term conditions, e.g., asthma and cancer.

Moreover, it has been clearly highlighted by the experts of the US Centers for Disease Control and Prevention (**CDC**) that "changes in the way that health care is delivered during the COVID-19 pandemic have occurred to reduce staff and patient exposure to sick people, preserve personal protective equipment (PPE), and minimize the impact of patient surges on facilities. Healthcare systems may need to adjust the way they triage, evaluate, and care for patients using methods that do not rely on in-person encounters. Telehealth services help provide necessary care to patients while minimizing the transmission risk of SARS-CoV-2, the virus that causes COVID-19, to healthcare workers and patients" [CDC, 2020].

4.2. Description of the health technology

The description of the health technology is based on the system already in use at ASL-BR, where TM has been added to usual care to support home care for chronically ill patients with HF, DM or COPD living in the area of Ceglie Messapica (a small town near Brindisi), and to facilitate the interactions among healthcare providers (including GPs, specialists, nurses), caregivers and patients. Considering the prevalence data for Puglia region (table 1) and the resident population in Ceglie M. at 1 Jan. 2020 (19,241 inhabitants), the estimated number of chronic patients in the municipality includes 1,058 HF patients, 1,251 DM patients and 808 COPD patients.

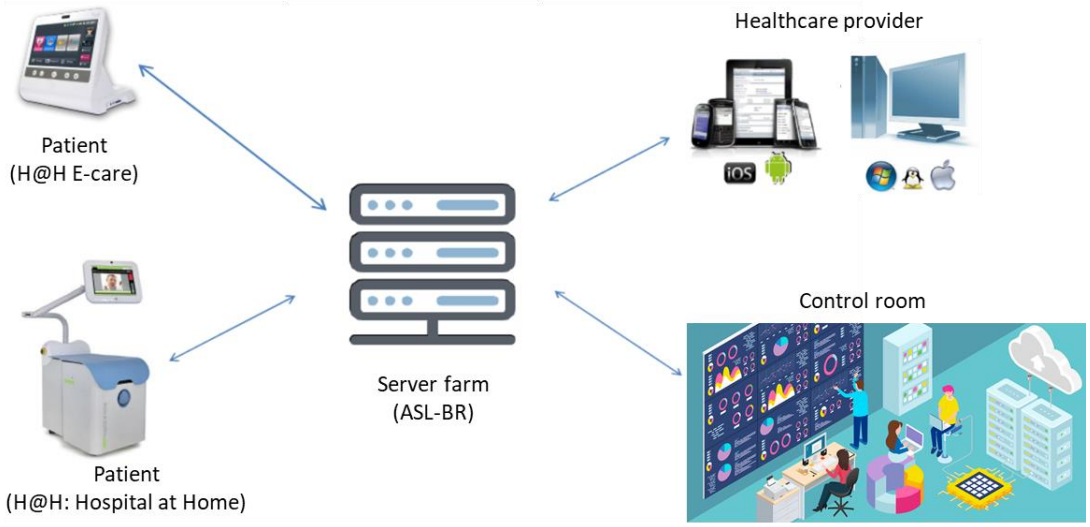
ASL-BR has adopted the technical solution, named H@H, designed and implemented by ITEM Oxygen srl, an Italian manufacturer (https://www.itemoxygen.com/en/) who was awarded the call for tender issued by ASL-BR. H@H is a web-based TM system providing a telemonitoring solution to support patients' clinical management at distance.

The organisational model which has been tested and implemented by ASL-BR aims to facilitate interactions among healthcare providers, caregivers and patients. It is based on a web platform, managed through a control room, which collects patients' vital signs – measured by the medical devices placed in their home or community care centre where patients temporary live – and make them available for healthcare providers (additional details are provided in § 8. Domain: Organisational aspects).

4.3. Technical characteristics

This system is based on a client-server architecture (as shown in *Figure 1 – H@H structure*) with a physical server, hosted at the ASL-BR server farm located in Brindisi, on which the H@H web application is installed and configured to be accessible through internet connections from different types of devices – including tablets, smartphones, personal computers as well as the dedicated medical devices manufactured by ITEM Oxygen itself, namely H@H: Hospital at Home and H@H-care – and from the dedicated app, H@H-Care app. Technical information on the system has been requested (Annex 1) and obtained from the manufacturer. Healthcare professionals can have shared access to patients' electronic health record based on accounts and permissions, facilitating integrated care approaches.

Figure 1 – H@H structure



The **control room** is located in the Community Care Centre of Ceglie Messapica (Presidio Territoriale di Assistenza, PTA).

The ***H@H: Hospital at Home***[1] is a web-based telemedicine device that guarantees, from any device connected to the internet, the continuous monitoring of the patient at home physiological parameters and of the therapy (oxygen therapy and endocavitary aspiration) allowing also the interaction between health workers and patients through video communication. *H@H: Hospital at Home* is a **medical device** for monitoring of physiological parameters and oxygen therapy compliant with the requirements set out in Annex II of EC Directive 93/42/CEE (notified body no. 0425).

It allows:

- Electrocardiogram (ECG) detection (5 and 12 leads)

[1] Information source: manufacturer website https://www.itemoxygen.com/hh-systems/, last access 11 March 2021

- Non-invasive blood pressure (NIBP) detection
- Pulse oximeter oxygen saturation (SpO2) detection
- Temperature Detection (two channels)
- Heart rate (HR) detection
- Respiratory Rate (RR) Detection

It is provided with:

- Intracavitary suction pump (-0.8 bar)
- Oxygen therapy by O2 concentrator (O2 flow: 0 ÷ 4 l/min. @ 94 ÷ 95% or 5 l/min. @ ≥ 90%)
- 17'' touch screen with high quality video call through webcam
- Integrated stereo audio system and ambient microphone
- Physiological parameters monitor

The ***H@H E-care*** device[2], thanks to its web-based technology, allows the simultaneous and remote activation of the videoconference and/or video consultation and the visualization of the patient's clinical parameters, trends and abnormality thresholds, thus resulting in a clinical tool "close to the patient" as it allows to establish a continuous and psychologically reassuring link. *H@H: E-care* is a **medical device** compliant with the requirements of EC Directive 93/42/CEE (notified body no. 1023).

It allows:

- Video Consultation
- Clinical Parameter Measurement/Personalized Chart consultation
- Remote auscultation

It is provided with:

- Supporting voice guidance
- 10.1 cm touch screen
- Multiuser support
- Wired or Wireless connection mode.

H@H E-care can communicate with a large number of measuring devices, including glucometers, sphygmomanometers, thermometers, pulse oximeters, body fat analysers and point of care test (POCT) for haemoglobin, INR, urine.

4.3.1. Interoperability: Integration needs (EPR, devices, with current applications, technical standards etc.)

In addition to interacting with the different types of clients (tablets, smartphones, personal computers, H@H: Hospital at Home, H@H-care, H@H-Care app), the H@H platform interacts through a web service technology with the information system of the Puglia Region "*Edotto*"[3] from which, in read-only mode, it retrieves patients' healthcare civil registry data. If such information is not present in *Edotto*, the authorised operator will manually register the personal data in the H@H database through the web platform.

[2] information source: manufacturer website https://www.itemoxygen.com/hh-systems/, last access 11 March 2021

[3] Edotto is the Health Information System of the Puglia Region, in use since 2012 as an essential tool for the governance of the regional health service. The system, based on the most innovative ICT tools, facilitates the widest interaction between the subjects operating at the various levels of the health organization (Department of Welfare, Regional Health Agency, local health authorities, GPs and paediatricians, pharmacies, etc.) with the aims of satisfying the growing needs for healthcare and monitoring the health services provided in Puglia. It is structured in many modules to manage different health and administrative data flows.

Other kind of interoperability are not currently provided, but the web service technology is ready for future developments and integration with third party systems. Standard reference protocols, such as http, https, VPN, TCP / IP and socket, are used.

4.3.2.Technical and users' support

Technical support to system users (patients and their caregivers, General Practitioners, specialists) includes:

- **I Level support**: interventions and supports provided remotely by control room operators, specifically trained by the H@H system provider (ITEM Oxygen srl) experts, for the resolution of problems related to H@H devices usability.
- **II Level support**: interventions related to HW/SW malfunctions and problems. Control room operators, through a web-ticketing service, forwards the formal request for support to the technicians of the ITEM Oxygen srl. Technicians can operate remotely or, if the identified problem requires onsite visits, at patient's home or at the control room site within 24h to 48h.

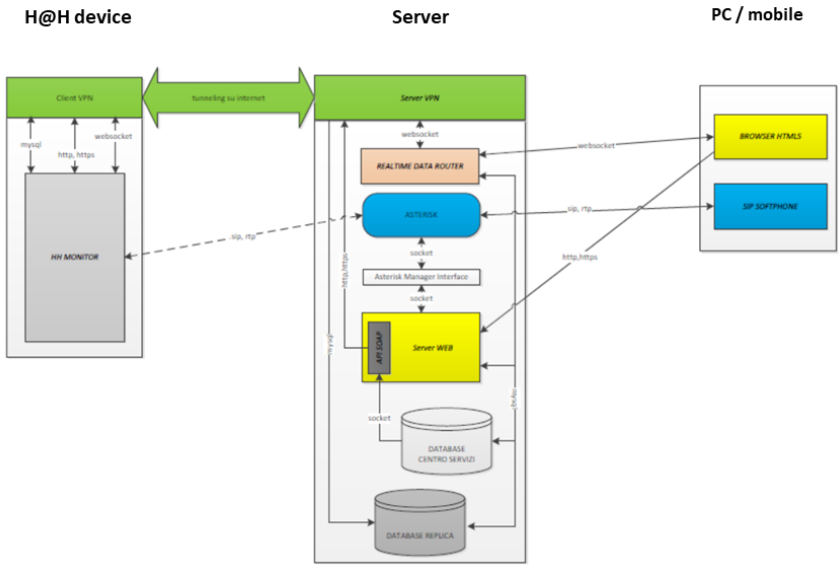
GPs and specialists to be involved in the TM service are supported during the first two weeks by control room operators and ITEM Oxygen telemedicine specialists, to be adequately trained in the use of the system. Patients enrolled in the TM service are appropriately trained by ITEM Oxygen telemedicine specialists in the use of the device when it is installed and configured at their home.

4.3.3.Technical environment

The H@H system is mainly characterized by three macro-components (**Errore. L'autoriferimento non è valido per un segnalibro.**):

- The server on which the web platform, database and web service modules are installed;
- The H@H device at patient's home (H@H, H@H E-care) with its measuring devices;
- The control room and the healthcare providers devices (PC, Tablet, smartphone, etc.).

Figure 2 – System architecture



The web platform is developed using programming tools and libraries for Java and PHP. The DBMS is MySql.

Clients interact with the platform via the http/https protocol, websockets and via VPN connection.

4.3.4. Back-up systems and procedures

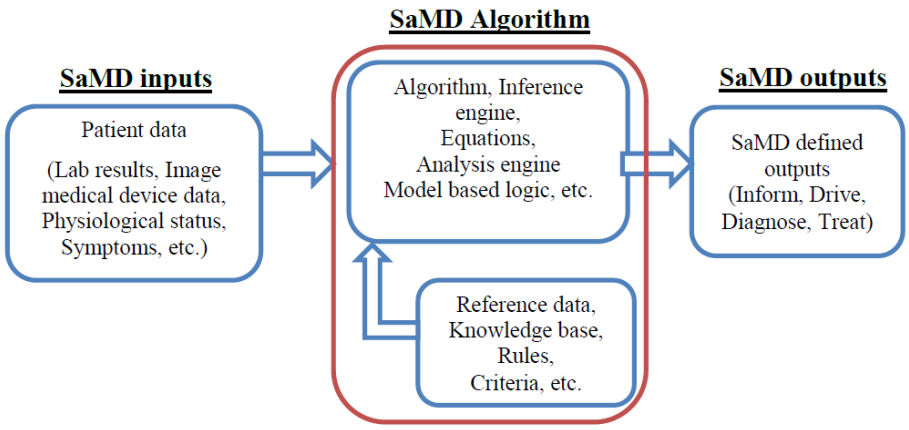
The management of the platform (server side) - including security procedures and measures, backups, operational continuity, management of network equipment (firewall, antivirus, etc.) - is the responsibility of the ASL-BR server farm manager.

5. Domain: Safety

The International Medical Device Regulators Forum (IMDRF) states that the greatest risks and benefits posed by software which acts as a medical device (SaMD) relates to its output and how it impacts on a patient's clinical management or other healthcare related decisions, not from direct contact with the device itself. Apps which utilize poor/weak evidence bases could present a range of clinical harms. For example, chronically ill patients using medication incorrectly due to inaccurate feedback from the mobile medical application (MMA); rehabilitation patients doing inappropriate exercises; or, potentially more seriously, the long-term consequences to health of receiving a false negative diagnosis from an investigational MMA [Moshi, 2018].

The risks and benefits posed by SaMD outputs are largely related to the risk of inaccurate or incorrect output of the SaMD, which may impact the clinical management of a patient [FDA, 2017].

Figure 3 – risks and benefits posed by SaMD



5.1. Clinical safety (patients and staff)

The following sources were searched for data on safety (last access 12 Jan. 2021):

- Ministero della Salute (Italian Ministry of Health) Avvisi di sicurezza sui dispositivi medici at http://www.salute.gov.it/portale/news/p3_2.html#tab-avvisi-di-sicurezza;
- ECRI Medical Device Safety Reports (MDSR) at http://www.mdsr.ecri.org/default.aspx;
- MAUDE - Manufacturer and User Facility Device Experience at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm.

None of the investigated sources provided information and we are not aware of safety issues nor technical recall related to the telemedicine platform in use at ASL-BR.

5.2. Technical safety (technical reliability)

To protect systems from cyber-attacks, it is needed to consider regulatory references and guidelines as well as consolidated good practices. The domain of security does not concern IT protection only, but physical protection as well.

In the specific case of the H@H system, in addition to the protection of the server farm, it is necessary to protect client devices.

Home devices have been customized by ITEM Oxygen, inhibiting changes by unauthorized personnel as well as allowing access only via password authentication.

5.2.1. What do the Service Level Agreements cover?

Technical problems and failures are classified into three categories of severity:

- High: totally blocking the system

- Medium: partially blocking the system
- Low: blocking only some functions

According to the severity of the problem, reporting and intervention timelines may change (see Table 2).

Table 2. - reporting and intervention timelines

LEVEL	METHOD OF REPORTING	ANOMALY REPORTING	PROBLEM RESOLUTION
High	Telephone, e-mail, ticketing,	Immediate	12 h
Medium	Telephone, e-mail, ticketing	By the day	24 h
Low	Telephone, e-mail, ticketing	By 7 days	48 h

Moreover, for each problem, specific quality indicators are measured:

- Time to take charge of the problem (from the moment of reporting/detection)
- Time to resolve the problem encountered by the user

The reporting of problems is managed in the following ways:

- Ticketing: requests for intervention are recorded in the system and ordered according to priority and type in appropriate queues defined by the system manager. In this way, it is always possible to provide statistics relating to the number of open tickets and their status.
- Telephone:
  - The service is provided by control room operators from Monday to Saturday (8.30-12.30 / 14.00-18.00).
  - If the problem is not resolved by phone, an appointment is scheduled for technical intervention with the ITEM OXYGEN specialist.

5.2.2.How is security of data and the database (data privacy) and quality of data managed?

During the detection of patient's vital parameters, the H@H device stores data in its internal local DB. Once a VPN connection with the server is established, the H@H device replicates stored data directly in the server DB, using a web socket protocol.

The quality of vital parameters monitoring is managed directly by the board on the H@H device which, in case of incorrect readings, sends an alert message to the platform.

5.2.3.encryption/cryptography

A VPN encryption is used for the communication between the devices and the server, while https encryption is used between platform and users. The encryption system is OPENVPN DHE-RSA-AES256-SHA (256 Bit); SSL certificates are self-generated.

Patient's date of birth, fiscal code and user password are encrypted within the database. In compliance with the privacy regulation, vital parameters, measured using the H@H device, are not directly linked to the patient's personal data. In addition, sensitive data are encrypted in the database.

5.2.4.data ownership

Data are owned and managed by ASL-BR.

6. Domain: Clinical effectiveness

6.1. Methods

In order to identify – for each of the three conditions (HF, DM, COPD) – the most recent systematic review scoring 8 or more with AMSTAR 1 [Shea, 2007], we designed the PICO in Table 3.

Table 3. - PICO

Population	Patients with one or more of the following conditions: - heart failure - diabetes (Type I and II) - chronic obstructive pulmonary disease
Intervention	Home management of patients by telemedicine
Comparator	Standard outpatient care (usual care)
Outcomes	**Effectiveness**: number and duration of hospitalisations (related DRGs 88, 127, 294); number of emergency room admissions, outpatient visits, mortality. ***HF patients***: blood pressure, changes in heart rate, ischemia, HF-related mortality. ***Diabetes patients***: reductions in HbA1C, glycaemic control. ***COPD patients***: COPD exacerbations
Study design	Systematic Reviews
Publication Period	2016-2020
Language	Italian, English

6.2. Search strategy

Population						Technology
Diabetes: (("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields] OR "diabetes"[All Fields] OR "diabetes insipidus"[MeSH Terms] OR ("diabetes"[All Fields] AND "insipidus"[All Fields]) OR "diabetes insipidus"[All Fields])	OR	Heart failure: ("heart"[MeSH Terms] OR "heart"[All Fields])	OR	COPD: "pulmonary disease, chronic obstructive"[MeSH Terms] OR ("pulmonary"[All Fields] AND "disease"[All Fields] AND "chronic"[All Fields] AND "obstructive"[All Fields]) OR "chronic obstructive pulmonary disease"[All Fields] OR ("chronic"[All Fields] AND "obstructive"[All Fields] AND "pulmonary"[All Fields] AND "disease"[All Fields]))	AND	("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields])

Searched on 18 Feb. 2020

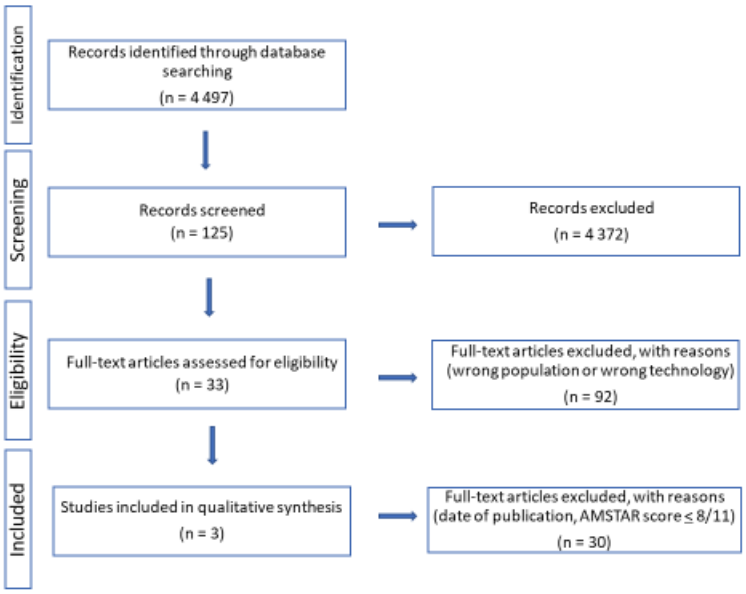
The systematic search was conducted on 18 Feb 2020 in the PubMed database, and we retrieved 4 497 articles. The search was then limited to Systematic Reviews published in English, in the last five years and filtered by “humans”. Overall, 125 hits were identified.

Then, according to the title, we removed all articles dealing with the use of mobile technologies (including smartphone) or referred to other conditions; we obtained 33 articles. Finally, titles and abstracts were independently screened by 2 readers (BF, CE) to exclude obviously irrelevant articles. Discordant classifications between the 2 readers were resolved through discussion.

6.3. Flow chart of study selection

Overall, 4 497 hits were identified. The references were screened by two independent researchers (FB, EC) and in case of disagreement a third researcher (EG) was involved to solve the disputes. The selection process is showed in Figure 4.

Figure 4: Flow chart of study selection (PRISMA Flow Diagram)



6.4. Analysis

After a full-text review, 33 articles were identified to be relevant. The Assessing the Methodological Quality of Systematic Reviews (AMSTAR) [Shea 2007] was used as the tool to assess studies' quality. The assessment was carried out in quadruple (by FB, EG, EC, RL) and is reported in Annex 3. Date of study publication and AMSTAR [Shea 2007] score equal/higher than 8/11 were finally used as criteria to select the systematic reviews to gather evidence from, in each of the research fields (heart failure, diabetes and COPD).

6.5. Results

Evidence related to the effectiveness of telemedicine in the three main long-term target conditions considered in this report was gathered from the three selected systematic reviews:

- **Heart Failure (HF)**: Yun JE, Park JE, Park HY, Lee HY, Park DA. Comparative Effectiveness of Telemonitoring Versus Usual Care for Heart Failure: A Systematic Review and Meta-analysis. J Card Fail. 2018;24(1):19-28. doi:10.1016/j.cardfail.2017.09.006
- **Diabetes mellitus (DM)**: Faruque LI, Wiebe N, Ehteshami-Afshar A, et al. Effect of telemedicine on glycated hemoglobin in diabetes: a systematic review and meta-analysis of randomized trials. CMAJ. 2017;189(9):E341-E364. doi:10.1503/cmaj.150885
- **Chronic obstructive pulmonary disease (COPD)**: Hong Y, Lee SH. Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: A systematic review and meta-analysis. Int J Nurs Stud. 2019;92:1-15. doi:10.1016/j.ijnurstu.2018.12.006

6.5.1. Heart Failure

This systematic review of 37 studies showed that TM intervention is more effective than usual care in **decreasing all-cause mortality** (RR 0.81, 95% CI 0.70–0.94; I^2 = 16%) **and HF-related mortality** (RR 0.68, 95% CI 0.50–0.91; I^2 = 8%) among patients with chronic HF. In addition, a tendency toward **reduced risk of HF-related hospitalization** was observed in the TM group (RR 0.86, 95% CI 0.74–1.00; I^2 = 36%). TM intervention was defined as the transmission of biologic information, such as weight, blood pressure, and heart rate, via information communication technologies.

Subgroup analysis produced results that are consistent with those of all-cause mortality; however, the effect of TM differed according to the modality of intervention. The all-cause mortality rate of the TM group was significantly lower than that of the usual care group among studies published in Europe, studies involving patients older than 65 years, and studies transmitting ≥3 biologic indicators, such as body weight, blood pressure, electrocardiography (ECG). TM also reduced the risk of mortality in studies that monitored medication adherence, administered prescription changes, monitored symptoms, transmitted biologic information on a daily basis, or transmitted biologic information via remote devices.

6.5.2. Diabetes

Telemedicine achieved a statistically significant but **modest reductions in HbA1C** in all 3 follow-up periods (difference in mean **at ≤ 3 mo: −0.57%**, 95% confidence interval [CI] −0.74% to −0.40% [39 trials]; **at 4–12 mo: −0.28%**, 95% CI −0.37% to −0.20% [87 trials]; and **at > 12 mo: −0.26%**, 95% CI −0.46% to −0.06% [5 trials]). TM interventions were defined as any electronic form of communication between provider and patient, including telephone, smartphone application, email, text messaging, web portal (websites where patients upload blood glucose levels or other clinical data and share these with their health care providers, with or without provider-to-patient communication) and "smart" device or glucometer (any computerized device specifically developed to collect and transmit patients' data to health care providers).

Compared with usual care, the addition of telemedicine appeared to significantly improve HbA1C in people with either type 1 or 2 diabetes. Although there was a substantial heterogeneity, the pooled analyses showed that telemedicine lowered HbA1C by 0.57% within 3 months and by 0.28% beyond 4 months. The lower apparent magnitude of benefit with longer follow-up may reflect reduced adherence to the intervention. Nonetheless, the effect on HbA1C appears clinically relevant and is comparable to improvements associated with some oral antidiabetic agents (0.5% - 1.25%), psychosocial interventions (0.6%, 95% CI 1.2% to 0.1%) or quality improvement strategies (0.42%, 95% CI 0.29% to 0.54%) among patients with diabetes. However, the authors of the review **did not find good evidence that telemedicine reduced the risk of hypoglycaemia, quality of life or mortality**, although it is unlikely that benefits for the latter would have been observed given the short duration of the included trials.

The meta-regression analyses suggested that telemedicine interventions that facilitated medication adjustments were more effective in improving glycaemic control than interventions that did not allow such adjustments. Findings suggest that text messaging and Web portals may be especially effective mechanisms for linking providers to patients with diabetes. The authors were also able to show that effects on HbA1C diminished but were sustained over time.

This systematic review showed that telemedicine may be a useful supplement to usual clinical care to control HbA1C, at least in the short term.

6.5.3. COPD

Tele-monitoring **reduced emergency room visits and hospitalizations**, **improved the mental health quality of life**, but did not make a difference in mortality, outpatient visits, or length of stay, though the result was in favour of tele-monitoring. Tele-monitoring was more effective at preventing emergency room visits and hospitalizations in patients with severe respiratory failure with FEV1/FVC < 0.70 and FEV1 < 50% (the same categories of patients as in the ASL-BR protocol) or those who required home oxygen therapy and/or mechanical ventilation. The TM interventions analysed by Hong at al. could be divided into those that provided only tele-monitoring service and those represented integrated tele-monitoring, such as the delivery of self-management education or teleconsultation by phone in addition to telemonitoring of vital sign and

systems. Integrated interventions, including the delivery of coping skills or education online produced more significant improvement.

The meta-analysis results also showed that tele-monitoring significantly decreased emergency room visits in patients with severe chronic obstructive pulmonary disease [RR 0.48, CI 0.31-0.74]. However, there was no difference in the moderate patients [RR 1.28, CI 0.61–2.69]. The same was observed for the hospitalization rate. Tele-monitoring of the severe chronic obstructive pulmonary disease patient group tends to decrease hospitalization rate [RR 0.92, CI 0.31–1.02], while there was no difference in patients with moderate chronic obstructive pulmonary disease [RR 1.24, CI 0.57–2.70].

This systematic review examined the use of tele-monitoring in addition to standard care and found that tele-monitoring failed at improving quality of life in the intervention group compared to the control group. But, when the authors analysed the physical health quality of life and the mental health quality of life separately, the mental health quality of life did improve significantly [RR 3.06, CI 2.15–3.98], while the physical health quality of life still did not improve.

This suggests tele-monitoring makes patients become more aware of their illness and facilitates their natural coping and acceptance of their disease, which may improve the mental component of quality of life.

Table 4. - Main results from the selected studies

<table>
<tr><th>Effect of TM compared to usual care</th><th>HF</th><th>DM</th><th>COPD</th></tr>
<tr><td rowspan="3">Mortality</td><td>Decreasing all-cause mortality (RR 0.81, 95% CI 0.70–0.94; I2 = 16%)</td><td rowspan="3">No good evidence found to support a reduction of mortality</td><td rowspan="3">Not available</td></tr>
<tr><td>HF-related mortality (RR 0.68, 95% CI 0.50–0.91; I2 = 8%)</td></tr>
<tr><td>The all-cause mortality rate significantly lower in studies: published in Europe, involving patients > 65 years, transmitting ≥3 biologic indicators</td></tr>
<tr><td rowspan="2">Healthcare resources use</td><td rowspan="2">reduced risk of HF-related hospitalization (RR 0.86, 95% CI 0.74–1.00; I2 = 36%)</td><td rowspan="2">Not available</td><td>Decreased hospitalization rate of severe patients [RR 0.92, CI 0.31–1.02]; no difference in moderate patients [RR 1.24, CI 0.57–2.70]</td></tr>
<tr><td>Decreased emergency room visits in severe patients [RR 0.48, CI 0.31-0.74]; no difference in moderate patients [RR 1.28, CI 0.61–2.69]</td></tr>
<tr><td>Quality of life</td><td>Not available</td><td>No good evidence found to support an improvement in QoL</td><td>Improved mental health QoL [RR 3.06, CI 2.15–3.98], failed at improving QoL</td></tr>
</table>

Effect of TM compared to usual care	HF	DM	COPD
Other improvements	Not available	Reductions in HbA1C in all 3 follow-up periods (at ≤ 3 mo: −0.57%, 95% confidence interval [CI] −0.74% to −0.40%; at 4–12 mo: −0.28%, 95% CI −0.37% to −0.20%;at > 12 mo: −0.26%, 95% CI −0.46% to −0.06%.	Not available
		No good evidence found to support a reduced risk of hypoglycaemia	

7. Domain: Patient perspectives

To investigate this domain, we planned a survey to be addressed to those patients who received the intervention at ASL-BR. The survey will be based on the use of the Service User Technology Acceptability Questionnaire (SUTAQ) [Dario, 2016]. SUTAQ includes 22 questions regarding patient acceptability of telemedicine and based on the answers six acceptability scales can be estimated [Kidholm, 2017].

This section 6 will be completed once data from the survey are available.

8. Domain: Economic aspects

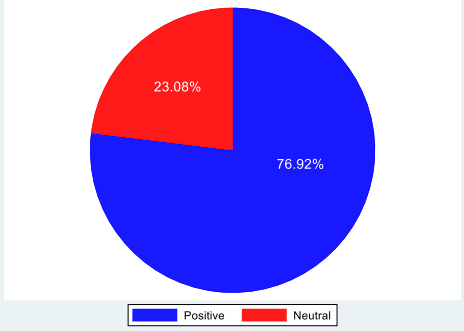
The development of this assessment framework is based on a two-step approach; the first step involves a review of the literature and collecting information on the costs of telemedicine solutions and services. The second step compares costs and savings of the Hospital & Home(H@H) pilot with those of usual care.

8.1. Economic evaluation

The systematic review described in section 5 identified only two reviews discussing the economic domain, and we choose the one [Peretz 2018] which considered more studies from several countries (not only from the US). Peretz et al [Peretz, 2018] focused on the economic costs of telemedicine services and identified 13 studies published from 2004 to 2015 in different Countries: USA, New Zealand, Canada, Holland, Italy and the United Kingdom. The targeted diagnoses included those covered by this report, such as COPD, DM and HF. Of the 13 studies, 9 reported information on the comparison between Telemedicine and Usual Care regarding costs and hospital admissions (see Annex 4).

The duration of the Remote Patient Monitoring (RPM) service provision varied a great deal: from 3 months to 2.5 years, and the number of participants ranged from 4 to a sample of 538 seniors suffering from various chronic conditions including chronic obstructive pulmonary disease, congestive heart failure, diabetes mellitus and hypertension (HTN). All studies, except the articles by Walsh et al. (2005), are based on randomized trials with a treatment group (which uses TM) compared with a control group (usual care). The results from these 13 articles show that, in essence, telemedicine is generally perceived and judged to be cost effective in 76.92% of the cases addressed by the literature's neutral effects (23.08%). The latter, mainly found in systematic reviews that reach a conclusion on the lack of robust and high-quality studies regarding the evaluation of telemedicine services, advocate further research and evaluation and do not purport to be in favour of a positive or negative assessment. **Errore. L'origine riferimento non è stata trovata.** shows the results of the analysis.

Figure 5: Distribution of cost-effective effects from the assessed literature



The review of the literature on the cost effectiveness of telemedicine led to the collection of data related to monetary costs and benefits (in terms of costs, time and logistics savings). In order to identify the telemedicine costs, we then focused our attention on Paré's study [Paré, 2013a], discussed in the systematic review by Peretz et al [Peretz, 2018], which presents many similarities with our report in terms of diseases under analysis and used data.

Paré et al [Paré, 2013a], analysed the consumption of healthcare services by 95 patients in Canada with various chronic diseases over a 21-month period (12 months before, 4 months during home telemonitoring use, and over 5 months after withdrawal of the technology). The economic analysis strategy adopted for this study was the one of cost minimization. This strategy can be used to compare the costs of different interventions, whose clinical results are considered similar, to determine which costs less. It provides a comparative basis which, in addition to calculations of costs and benefits, must be able to indicate whether telehealth appears to be better than the usual care. The total costs for the 95 patients were 364,840 $ for usual care and 216,903 $ for TM (see Table 5). In summary, the TM program resulted in a significant saving (41% compared with traditional home care).

Table 5. - Total costs (Parè et al 2013a). Values expressed in US$

	Average	Standard Deviation	Total
Home Visit by nurses			
Pre-Treatment (12months)	201	428	19,114
Treatment + Adjusted Post (9Months)	344	686	32,713

Emergency room visits			
Pre-Treatment (12months)	151	183	14,316
Treatment + Adjusted Post (9Months)	100	242	9,488
Costs Hospitalizations			
Pre-Treatment (12months)	3,489	5,692	331,410
Treatment + Adjusted Post (9Months)	968	3,051	92,052
Home telemonitoring costs			
Pre-Treatment (12months)			
Treatment + Adjusted Post (9Months)	394	-	37,430
Technology costs			
Pre-Treatment (12months)			
Treatment + Adjusted Post (9Months)	476	-	45,220
TOTAL COSTS			
Pre-Treatment	3,840	5919	**364,840**
Treatment + Adjusted Post	2,283	3380	**216,903**

Cost-Minimization Analysis: the case of Hospital@Home

8.1.1. Setting of analysis

The pilot project Hospital at Home (H@H) in Ceglie Messapica, established to test a TM application, enrolled a real-world population, and it was not based on an observational study or a RCT with a list of predefined outcomes and strict inclusion criteria that allow an easy comparison between a Treatment Group versus a Control Group. In this report we compared the cost of patients treated according to the usual care management with patients using the H@H TM system. The cost analysis was performed from a regional healthcare perspective (i.e., all costs in the healthcare sector were included) thus, without taking into account the costs incurred by patients and their caregivers.

The analysis was performed by comparing patients with chronic obstructive pulmonary disease (COPD), heart failure (HF) and diabetes (DM) in homogeneous groups. The analysis has a quasi-experiment setting and consists of a cost-minimization analysis between a treatment group with TM and two homogenous control groups of patients with the same characteristics in terms of diagnosis, sex, age, and severity degree of pathology. In detail, patients were stratified on the basis of the Drug Delivery Complexity Index (DDCI) [Robusto, 2016], a reliable prognostic index, solely based on drug prescriptions, able to stratify the entire population into homogeneous risk groups, since it can accurately predict one-year and long-term mortality, as well as the risk of unplanned hospitalization and hospital readmission. Regarding the severity level of the patients' conditions, the DDCI at two severity levels was used, with a value of 1 for medium-severe patients (DDCI $\geq$ 3) and a value of 0 for patients of mild severity (DDCI 0-2).

8.1.2. Treatment Group versus Control Groups

From 2015 to April 2020, 207 patients have been enrolled into the study, and TM was used 302 times[4] (some patients used TM services multiple times). The patients considered in this analysis were those who have used the technology at least once from mid-2015 to the end of 2019. Data on outpatients' visits and pharmaceutical prescriptions costs and hospital information are available in the Regional Health System Database (**RHSD**) up to 2019 for only 191 of the 207 patients, and RHSD was used to calculate resources consumption.

The patients included in the treatment group were all resident in the Ceglie Messapica health district. The patients in the control groups, on the other hand, were stratified over the entire regional territory extracted from RHSD. **Matching each patient in the treatment group** with a patient with the same characteristics in

[4] ASL-BR provided a figure with 218 patients. However, among these, records for 11 patients were not complete, so they were excluded from the analysis.

each of the two control groups has been feasible **for 179** patients only of the initial 207. Therefore, our analysis was carried out on the sample of 179 patients (86,4% of the total patients in the H&H project).

In the period 2015-2019, the 179 patients in the intervention group were assisted with a TM H@H device at least once, for a total number of treatments with a TM device equal to 269 (data from ASL-BR).

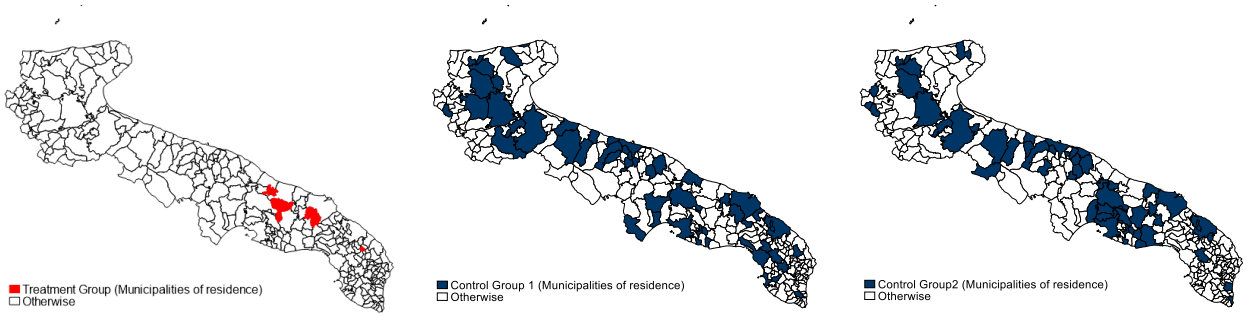
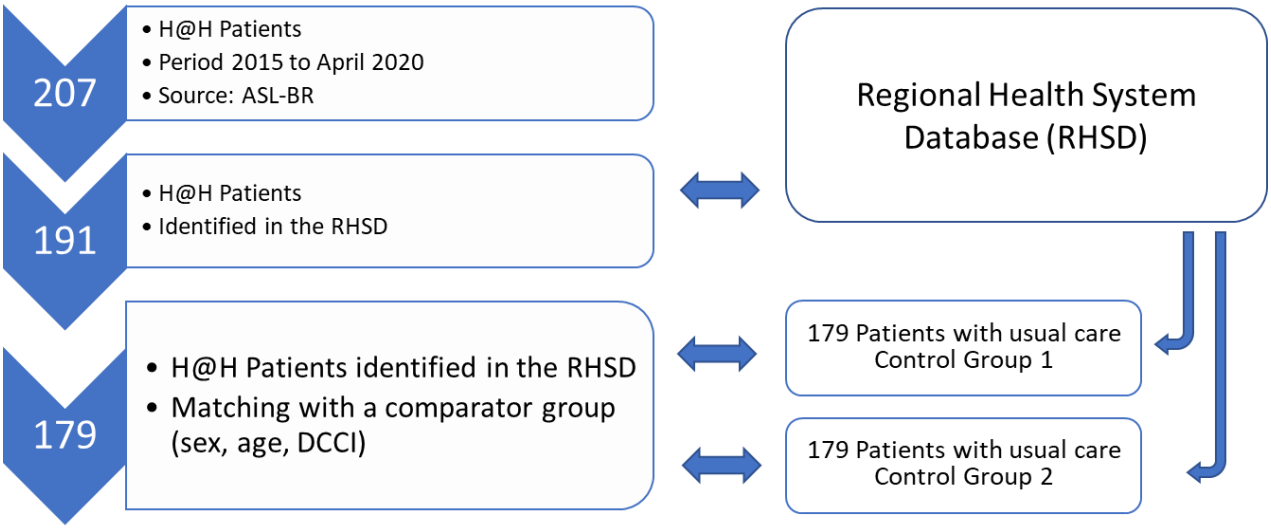


Figure 6 summarises the adopted procedure.

Figure 6 – Procedure Used to identify Treatment and Controls groups



The analysis undertaken in this study aimed to identify and measure the potential impact of TM on healthcare costs compared with the traditional model (usual care).

To measure resources used when a patient in the treatment group has been using TM more than once in several years, only the first year of use has been considered. Consequently, the costs related to a patient from the treatment group in the considered year have been compared with data related to the specific matching person in the control groups in the same considered year, if available in the regional dataset. Otherwise, data of the very first year available for that specific control person has been taken into account.

Only direct costs were included in our analysis. The monitoring period covered the costs of the service between 2015 and 2019. All information on costs (expressed in Eur at constant 2019 values) and hospital admissions is taken from the Regional Health System Database. Data analysis included t-tests in order to control whether the unknown population means of two groups were equal or not. We used STATA 16 software for statistical analysis.

In particular, the selected variables are:

a) Number of Hospital days;
b) Number of urgent hospitalizations;
c) Average length of hospitalization under the ordinary regime (Length Of Stay, **LOSH**);
d) Average duration of urgent hospitalization (Length Of Stay for urgent hospitalization, **LOSUr**);
e) Hospital costs;

f) Pharmaceutical costs;
g) Outpatient clinics cost;
h) Number of emergency room visits;
i) Emergency room costs.

Table 6 shows the demographic characteristics of the three analysed population (treatment group and the two control groups) during the index year; the average age of the treated patients is 72.06 years, and it is slightly lower in the two control groups: 71.27 (group 1) and 72.03 (group 2), respectively. 53.63% of patients in the treatment group are men. The same percentages were recorded in the two control groups. More details are reported in Annex 6.

As it can be seen, 66.48% is the percentage of patients with a higher level of severity (DDCI 1), of which, with regard to pathologies, heart failure as a sole diagnosis appears to be the disease affecting most patients in this subgroup (38.55%), then diabetes (17.88% of patients) and COPD (10.06% of patients). Among the patients with comorbidities, 14.53% of the sample has a concomitant diagnosis of both diabetes and heart failure problems. Finally, only 6.70% of the sample presented a comorbid situation in which all three investigated diseases were present.

Table 6. - Descriptive statistics of the demographic characteristics

		Intervention	Control 1	Control 2
Sex	Male	96 (53.63%)	96 (53.63%)	96 (53.63%)
	Female	83 (46.37%)	83 (46.37%)	83 (46.37%)
Age	Mean	72.06	71.27	72.03
	Under 65	38 (21.23%)	50 (27.93%)	49 (27.37%)
	Over 65	141 (78.77%)	129 (72.07%)	130 (72.63%)
Severity	DDCI 0	60 (33.52%)	60 (33.52%)	60 (33.52%)
	DDCI 1	119 (66.48%)	119 (66.48%)	119 (66.48%)
Disease	DM	32 (17.88%)	32 (17.88%)	32 (17.88%)
	COPD	18 (10.06%)	18 (10.06%)	18 (10.06%)
	HF	69 (38.55%)	69 (38.55%)	69 (38.55%)
	DM+COPD	8 (4.47%)	8 (4.47%)	8 (4.47%)
	DM+HF	26 (14.53%)	26 (14.53%)	26 (14.53%)
	COPD+HF	14 (7.82%)	14 (7.82%)	14 (7.82%)
	DM+COPD+HF	12 (6.70 %)	12 (6.70 %)	12 (6.70 %)

To assess the level of homogeneity between the three groups under evaluation and before analysing the costs incurred by the regional health service for TM Vs usual care. The t-test was performed to compare between- and within-group differences of scores for health resource variables.

As can be seen in Tables 7 and 8, the t-statistic between the groups is never statistically different from zero with regard to ordinary and urgent hospitalizations. These confirm that the 3 groups are homogeneous. However, some significant differences, can be observed from the comparison with a t-statistic, statistically different from zero with a significance level of 95%, when we compare the Outpatients clinics services costs with the Emergency room costs. Indeed, for these variables, the t-test is different from 0 and the p-value is lower than previous variables. This result suggests that although the patients of the 3 populations are homogeneous, the costs for both the Outpatients clinics visits and procedures are significantly different from a statistical point of view from those of the emergency room between intervention and control group, and so difference is not explained by chance. This difference can be attributed to the use of telemedicine. The results are confirmed comparing the treatment group patients with both control group 1 and 2.

Table 7. - Treatment Group versus Control Group 1

	Observations	Mean	SD	*t*	*p-value*
Length of Hospital stay (in days)					
Between Group				-0.94	0.35
intervention	179	0.27	0.71		
Control 1	179	0.35	0.75		
Number of urgent hospitalizations					
Between Group				0.00	1.00
Intervention	179	0.16	0.43		
Control1	179	0.16	0.48		
LOSH (number of days)					
Between Group				-0.76	0.45
Intervention	179	2.35	6.87		
Control 1	179	3	9.12		
LOSUr (number of days)					
Between Group				-0.54	0.59
Intervention	179	1.25	4.43		
Control 1	179	1.53	5.28		
Hospital costs (€)				-1.19	0.24
Intervention	179	964.09	2500.61		
Control 1	179	1431.37	4637.53		
Pharmaceutical costs (€)					
Between Group				0.08	0.94
Intervention	179	1122.40	1581.16		
Control 1	179	1110.17	1269.89		
Outpatients clinics services costs (€)					
Between Group				**-2.42**	**0.02**
intervention	179	252.57	322.09		
Control 1	179	382.33	641.62		
Number of visits to the emergency room					
Between Group				**-2.29**	**0.02**
intervention	179	0.37	0.78		
Control 1	179	0.62	1.19		
Emergency room costs (€)					
Between Group				**-2.44**	**0.02**
intervention	179	14.81			
Control 1	179	31.74			

t=5%

Table 8. - Treatment Group versus Control Group 2

	Observations	Mean	SD	*t*	*p-value*
Length of Hospital stay (in days)					
Between Group				-0.15	0.88
intervention	179	0.27	0.72		
Control 2	179	0.29	0.68		
Number of urgent hospitalizations					
between				-0.12	0.90
Intervention	179	0.16	0.44		
Control2	179	0.17	0.44		
LOSH					
Between Group				-0.29	0.77
Intervention	179	2.35	6.87		
Control 2	179	2.55	6.75		
LOSUr					
Between Group				-0.69	0.49
Intervention	179	1.25	4.43		
Control 2	179	1.59	4.94		
Hospital costs				-0.08	0.94
Intervention	179	964.09	2500.61		
Control 2	179	988.77	3330.60		
Pharmaceutical costs					
Between Group				-1.14	0.26
Intervention	179	1122.4	1581.16		
Control 2	179	1712.3	6770.12		
Outpatients clinics services costs					
Between Group				**-2.19**	**0.03**
intervention	179	14.81	43.76		
Control 2	179	31.57	92.48		
Number of visits to the emergency room					
Between Group				1.03	0.30
intervention	179	0.37	0.78		
Control 2	179	0.48	1.13		
Emergency room costs					
Between Group				**-2.19**	**0.03**
intervention	179	14.81	43.76		
Control 2	179	31.57	92.48		

t=5%

Table 9 summarises data collected for the intervention group and the two control groups in relation to: hospitalizations in ordinary regime and urgent hospitalizations, the average length of hospitalization, the cost of hospitalization, pharmaceutical costs, outpatients clinics services costs, number of emergency room visits and emergency room costs.

Table 9. - Summary of costs for one year and for 179 patients

Variables	Intervention	Control 1	Control 2
Number of hospitalizations	49	62	51
(of which) Number of urgent hospitalizations	29	29	30
Total length of hospitalization under the ordinary regime (LOSH)	421	537	458
Duration of urgent hospitalization (LOSUr)	225	275	286
Hospital cost (A)	172,572	256,216	176,989
Pharmaceutical Cost (B)	200,910	198,721	306,505
Outpatients clinics services costs (C)	45,210	68,438	53,470
Total Costs (A+B+C)	**418,692**	**523,374**	**536,963**
Average total Costs (A+B+C) per patient	**2,339**	**2,924**	**3,000**
Number of visits to the emergency room	67	111	86
Emergency room costs (D)	2,651	5,682	5,652
Total Costs + Emergency Room costs (A+B+C+D)	**421,343**	**529,057**	**542,616**
Average Total Costs + Emergency Room costs (A+B+C+D) per patient	**2,354**	**2,956**	**3,031**

The analysis of data in Table 9 allows to identify the average total saving equal to € 114,493.50 [(529,057+542,616)/2 -421,343] and the average saving per patient equal to € 639.63 (114,493.5/179).

8.1.3. Unit costs or prices for each resource used

Outcomes of the tender awarded by ASL-BR in March 2018 (Table 10) allow to identify both unit and yearly costs (excluding VAT) for the devices and services needed to implement the TM system as designed by ASL-BR (Table 11).

Table 10. - results of the tender awarded by ASL-BR in March 2018

description	Unit cost (€)	Quantity	Source of the information
A. H@H Hospital at home (TM device)	15,835.50	41	Tender procedure, ASL-BR official minutes (14.03.2018)
B. H@H e-care (TM device)	4,189.11	96	
C. Maintenance, device transport to and from patients' home, device sanitisation after use (yearly cost)	126,482.22	2	
D. Overheads, other costs and profit	395,625.50	1	
E. Total value of the contract awarded with the tender procedure in 2018[5]	1,700,000.00		ASL-BR official act No. DL0594/18, 26 March 2018

Table 11. - unit and yearly costs (excluding VAT) for TM devices and services

Description	Formula	Value (€)
F. H@H Hospital at home total cost	F=A*41	649,255.50
G. H@H e-care total cost	G=B*96	402,154.56
H. Total cost for medical devices	H=F+G	1,051,410.06
I. Medical device unit cost (average)	I=(D+H)/(41+96)	10,562.30
J. Medical device yearly unit cost (average) (8 years depreciation)	J=I/8	1,320.29
K. Maintenance, device transport to and from patients' home, device sanitisation after use; yearly cost per device (average)	K=C/(41+96)	923.23
L. Medical device total unit yearly cost (average)	L=J+K	2,243.52

[5] The total value of the contract included the H@H software platform and no. 4 PCs for the control room

Moreover, additional information on human resources used to run the service during the pilot phase (2015-2019) can be extracted from the documentation provided by ASL-BR:

- GP accessing the system at least twice a day, 10 times per week (in the morning and in the evening) to check patients' status as measured by the H@H device: 144.60 €/patient/week[6];
- Number of monthly accesses of a nurse at patient home: 44[7];
- Average duration of a single access of a nurse at patient home: 20 minutes[7].

Finally, to estimate the cost of the human resources involved in the process, we assume that:

- Yearly cost of a nurse (estimated from CAT. D3 - INFERMIERE, CCNL: Comparto Sanità, 2016-2018) → 28,000.00 (146 workable hours per month)
- Personnel in the control room (office worker) is to be engaged for 5 minutes each time a nurse is caring a patient at home (44 per month) → office workers' time: 5*44=220 minute/month per patient;
- Personnel in the control room (office worker) may receive requests for support from patients/caregivers for an additional time estimated to be about 10% of the monthly time per patient → 10%*220=22 minute/month per patient;
- Yearly cost of an office worker (estimated from CAT. D, CCNL: Comparto Sanità, 2016-2018) → 25,000 €/year (152 workable hours per month)

8.1.4. Limitation

The results of the economic evaluation should be interpreted considering its limitations. The study was constrained by the lack of data and we relied on numerous assumptions (see § 0) in the absence of available evidence.

First, the control groups were identified *ex post* and not through an *ad hoc* clinical protocol. This may have somehow influenced the identification of control groups and costs.

Second, no clinical data are available from electronics health records on the therapeutic efficacy of TM compared to usual care. Also, for this purpose, it would be necessary to collect clinical information and outcomes (e.g., FEV1/FVC ratio, HbA1C, blood pressure, SpO2, QALY, Mortality rate, etc ...) and to make them available to carry out a pilot study on Cost Effectiveness Analysis (CEA).

To overcome these limitations, designing and implementing a specific protocol, which clearly identifies all the direct and indirect costs it is highly recommended as well as to conduct multiple-sites, large-sample, homecare TM prospective studies recording all information regarding direct/indirect costs, clinical outcomes and social benefits/harms.

8.2. Business case (institutional level)

In the period 2015-2019, 179 patients in the intervention group were assisted with a TM H@H device at least once, for a total number of treatments with a TM device equal to 269 (data from ASL-BR). Thus, the average number of treatments per year and per patient was 1.46 (=262/179).

Considering that:

- the average duration of each treatment is 25 days[6];

[6] Source: agreement signed on 26 June 2019 between the ASL-BR and the trade unions representing GPs

[7] Source: XVI CARD meeting, 2018, Dr. F. Galasso's oral presentation (ASL-BR scientific coordinator of the TM pilot phase)

- retrieving the device from a patient, sanitising, delivering and making it available for another patient may require some days;

we can estimate that the whole cycle from one patient to another lasts 30 days and we can assume that each device can be used for 12 treatments per year.

Combining these findings with the information on unit costs from § 0, we can assume:

- **€ 186.96** medical device unit cost per treatment [2,243.52/12];
- **€ 272.96** medical device unit yearly cost per patient [(2,243.52/12)*1.46].

NB: the above costs include overheads, other costs, profit and maintenance.

Table 12 reports the estimated costs of the resources used to treat one patient for one year. The involvement of clinical specialists in the process is not clearly codified and, thus, excluded from the cost-minimization analysis.

Table 12. - estimated costs of the resources to treat one patient for one year

Description	Formula	Value (€)
General practitioner (144.60 €/patient/week)	144.6*25/7	516.43
Nurse (44 access/patient/month, 20 min. each)	44*28,000.00/12/146/3	234.40
Control room worker	1.1*44*25,000/12/152/12	55.28
Total cost of the human resources per treatment		806.11
Total yearly cost of the human resources per patient	806.11*1.46	**1,176.92**
Medical device unit yearly cost per patient	2,243.52/12*1.46	272.96
Total yearly cost per patient		**1,449.88**

8.2.1. Results of the business case

A cost-minimization analysis comparing the total cost per patient in one year (€ 1,449.88) with the total saving per patient (€ 639.63), identifies a **loss in this business case**, equal to € 810.25, thus suggesting that the investigated intervention appears to be economically disadvantageous.

The main cost item contributing to this result is the cost for the GPs. To balance costs and benefits, without changing the organisational model, the only items whose cost could be lowered seems to be the cost of the technology (e.g., in a more competitive and mature market, devices and platform costs could decrease) and the costs of personnel (e.g., GPs could be engaged on a different basis instead that on a tariff basis).

Despite the inherent limitations of this evaluative approach, the omission to measure potential effects of the intervention on clinical outcomes such as quality of life, and the absence of marginal and sensitivity analyses, we believe that our results are valid for several reasons. First, the estimates of costs come from reliable sources. Second, our assessment compares costs with and without home telemonitoring. Third, all resources (human and technology) associated with the intervention program were identified and measured/estimated.

9. Domain: Organisational aspects

The TM service implemented by ASL-BR has been designed to support home care and to facilitate the interactions among healthcare providers (including GPs, specialists, nurses), caregivers and patients. The aim of the service is to implement an intermediate level of care in which patients can be properly monitored and assisted at home thus improving continuity of care from hospital to home setting, reducing costs due to prolonged hospital stays and avoiding frequent accesses to emergency rooms.

Patients eligible for the service are those enrolled on integrated homecare (ADI) following a request from their GPs, with a multi-disciplinary baseline assessment resulting in an individual care plan (PAI) listing the schedule of healthcare professionals access to patient throughout the week.

Eligibility criteria in ADI with TM include:

- HF: NYHA class II/III, III or IV
- DM: Complicated DM (any complications)
- BPCO: stage III o IV Gold 2018 guidelines

Patients are enrolled in the TM service based on their clinical status (chronically ill patients with HF, DM or COPD in need of monitoring due to their unstable conditions) and an H@H device is placed in their home so that GPs can easily monitor patients' status by accessing (twice a day, five days per week) the web application which provides access to the database located in the ASL-BR server farm.

Operators in the control room are responsible for alerting (by SMS or phone call) the GP in case of vital signs anomalies. Moreover, the H@H system features include:

- Patients classification according to an algorithm "Early Warning Score, EWS", an higher score identifies patients at higher clinical risk;
- Monitoring of the medical devices embedded in the H@H: Hospital at Home device (Intracavitary suction pump and O2 concentrator);
- Management of patients' electronic health records;
- Multiple access to patients' dashboards.

Considering that each device can have up to 12 uses per year, the ASL-BR plan to enrol up to 1,000/1,200 patients/year, at home or in one of its community care centre, using the control room in Ceglie Messapica and all the 148 devices (A+B in Table 10) already provided by ITEM Oxygen srl, appears to be feasible.

An agreement to organise the involvement of GPs has been signed on 26 June 2019 between the ASL-BR and the trade unions representing GPs. The agreement states the voluntary participation of GPs in the service – who are required to access the system at least twice a day, 10 times per week (in the morning and in the evening) to check patients' status as measured by the H@H device – and the fee to be paid for each access.

Clinical specialists from ASL-BR (cardiologists, pneumologists and endocrinologists) are also involved in the service, with the role to define the healthcare plan with the GP, to visit patients upon request of the GP, to report ECGs.

Nurses are in charge for visiting patients at home daily.

10. Domain: Socio-cultural, ethical and legal aspects

10.1. Ethical issues

Legal and ethical concerns are very common in telemedicine. The review by Nittari et al. evaluates different critical concerns, including privacy. Moreover, the ethical aspects of telemedicine are sufficiently analysed in many studies. All authors agree on the importance of patient information protection, informed consent, as well as human approach focusing on patient [Nittari, 2019].

Moreover, several challenges have been identified [Brall, 2019]: challenges about digital illiteracy, resulting inequities in access to healthcare, truthful information to be shared with end users demanding fully informed consent, dignity and fairness in storage, access, sharing and ownership of data. All involved stakeholders bear responsibilities to shape digital health in an ethical and fair way.

Patients need to attend a period of training to acquire sufficient autonomy in the use of medical devices. The training aims to ensure sufficient autonomy and to use the devices safely. Furthermore, the training seeks to overcome cultural limitations and poor aptitude in the use of medical devices and information and communication technologies.

Patients enrolling in the pilot experience in Ceglie M. received detailed information on the policy adopted by ASL BR for personal data protection in compliance with the GDPR EU Regulation 2016/679 and were invited to sign the consent forms for data processing and for telemedicine.

10.2. Legal issues

In EU Countries, the GDPR[8] provides the regulatory framework to develop telemedicine applications assuring privacy and data protection. However, several concerns should be addressed as the maintenance, use, and replacement of devices[Errore. Il segnalibro non è definito.] as well as the cybersecurity system (TM implies the storage, archiving and transmission of data concerning the health of patients, as well as the remote collaboration of professionals).

[8] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)

Annex 1 – Information requested to the manufacturer

Agenzia Regionale per la Salute ed il Sociale Puglia

Bari, 15 Giugno 2020

Spett. **ITEM OXYGEN** S.r.l.
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*Oggetto: Valutazione HTA su modello organizzativo di presa in carico di pazienti cronici con ausilio di tecnologie per il telemonitoraggio DSS03 (ASL BR) – **questionario al fabbricante***

Spettabile ITEM OXYGEN S.r.l.,

L'Area Valutazione e Ricerca e il Centro Regionale HTA in essa allocato stanno lavorando, su mandato del policy maker, alla produzione di un report HTA sul modello organizzativo di presa in carico di pazienti cronici con ausilio di tecnologie per il tele monitoraggio ed in particolare sull'esperienza pilota in essere da qualche anno presso il Distretto Socio Sanitario di Ceglie 03 (ASL BR) dove la presa in carico delle persone con cronicità (BPCO, Diabete mellito, Scompenso cardiaco) è mediata dalla tecnologia Hospital @ Home di codesta Azienda.

*Nell'ambito dell'attività di valutazione di cui sopra, nei domini specifici inerenti alla **descrizione della tecnologia** oggetto di analisi e della sua **sicurezza** anche informatica, sono emersi degli elementi che necessitano di approfondimento ed in particolare, integrazione di dati tecnici, modalità di funzionamento, peculiarità e specificità dei dispositivi in essere.*

A fine di poter ottenere informazioni di approfondimento, laddove possibili, anche alla luce di documentazione disponibile ma al momento non in nostro possesso, chiediamo di voler compilare il questionario in allegato, composto da due sezioni (sez. 1a e 1b –postazioni carrellate e apparecchiature portatili,, sez.2 – architettura informatica) e di volerlo restituire agli indirizzi mail: hta@aress.regione.puglia.it ed e.graps@aress.regione.puglia.it entro il 30/06/2020.

*Si precisa che, ai fini della valutazione HTA, sono necessarie informazioni di natura tecnica **non protette da copyright** o altre forme di proprietà industriale/intellettuale; pertanto si invita alla condivisione delle sole informazioni divulgabili e non riservate.*

Confidando in un cortese riscontro, porgiamo distinti saluti

Dr.ssa Elisabetta Anna Graps
Direttore Medico
Area Valutazione e Ricerca - CReHTA
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Questionario a Item Oxygen – Tecnologia H&H

Sez 1a: Postazioni Carrellate

1. Esplicitare la descrizione tecnica del sottosistema di **aspirazione a vuoto** (es. se dispositivo proprietario integrato, se parte/acquisizione/assemblaggio esterni - marca, modello etc,) e del sottosistema di **somministrazione ossigeno** (es: tipologia concentratore, se dispositivo autoprodotto/ proprietario o acquisto esterno - marca, modello etc).
2. Inoltre:
    a. Confermare che la variazione di portata Ossigeno e Vacuum è possibile a bordo del carrellato (onsite) manualmente tramite manopola e/o tramite altri dispositivi integrati
    b. come da manuale, la portata flusso è in funzione delle indicazioni del Medico curante (MMG). Fermo restando la presenza di manopola del dispositivo di regolazione (da Manuale sembrerebbe mod. *Mediflow Ultra II* – GCE Mediline), confermare che è presente il riscontro (l/m) per lettura flusso e non presente il manometro.
    c. Esplicitare se, qualora presente, tra i parametri di misurazione monitorati in remoto vi è anche la possibilità di visualizzare il dato numerico della misurazione della portata di flusso per ossigenoterapia nell'ambito della schermata di monitoraggio paziente (fermo restando la presenza della SpO2)
3. Modalità di azionamento sia per Aspiratore, sia per Ossigenoterapia:
    a. *come riportato nelle caratteristiche del "modulo software Centro Servizi" sulla scheda tecnica del modulo Domiciliare H&H , è presente la* modalità di azionamento "remoto" sia per Aspiratore, sia per Ossigenoterapia – Esplicitare modalità di azionamento remota, ovvero *se per "modulo software" si intende esclusivamente un modulo integrato sull'hardware del carrellato e/o anche sui Client del Centro Servizi, e quindi se ciò permette un effettivo azionamento a distanza remota da Centro Servizi, oppure in altra modalità.*
4. Chiarire le priorità di autorizzazione all' azionamento di terapia per "Ambiente Operatore" e per "Ambiente AD (Assistente Domiciliare)" poiché da manuale è riportato che:
    a. (Flussimetro) l'attivazione è ad opera di **Assistente Domiciliare** e altresì da **Operatore H@H** tramite comando a schermo mentre lo spegnimento è (solo ?) a cura dell' **Operatore H@H** tramite comando a schermo.
    b. (Vuoto) l'attivazione e lo spegnimento del vuoto è << ad opera di **Assistente Domiciliare e Operatore H@H** >> tramite comando a schermo
    c. << ***L'Operatore H@H****, oltre ad essere l'unico utente abilitato sul dispositivo domiciliare ad avviare le misure dei parametri fisiologici, è anche* ***l'unico*** *operatore abilitato ad attivare/disattivare i dispositivi terapeutici di cui è dotato il Sistema H@H* >>

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5. Per ciascuno dei seguenti sottocomponenti (es: *Flussimetro O2, Umidificatore, regolatore di flusso Vacuum, innesto rapido, Filtro aspirazione antibatterico, vasetto sicurezza, vaso di raccolta*) - confermare se la configurazione consegnata è comune a tutti i carrellati; esplicitarne modello consegnato (es: Serres, Dz Medicale, GCE Medline, o altro)
6. Inoltre:
    a. Sonde Temp : confermare che le due sonde consegnate trattansi di MedLab (esplicitare eventuali modelli)
    b. Sonda ECG : esplicitare se dispositivo proprietario, autoprodotto, parte integrante del carrellato o esterna (marca/modello, etc)
    c. Sonda SpO2: confermare che trattasi di "MedLab Pearl" (esplicitare)
    d. Misurazione NiBP: esplicitare se dispositivo proprietario integrato o esterno (marca /modello etc)

Sez 1b: Postazioni Paziente - apparecchiature portatili (domiciliare)

1. Definire se il set di portatili consegnati coincide tutto con dispositivi "e-Care" (Cod. **HX-461**) oppure "Care HUB" (Cod **HH-800**) oppure fornitura mista
2. definire se nel proposto modello organizzativo i suddetti sistemi sono esclusivamente in uso al paziente finale o anche da intendersi dedicati per operatori MMG del paziente o di II Opinion (Specialistica)
3. fermo restando le ampie compatibilità di connettività *gateway* delle suddette postazioni portatili con finalità misurazione tramite USB/Bluetooth di periferiche
    a. confermare, per ciascun portatile i dispositivi consegnati (es: termometro, glucometro, Manometro NiBP, Saturimetro, Bilancia, ECG 12d, Pulsossimetro, Colesterolometro)
    b. confermare che costituiscono parte integrante del dispositivo principale, oppure accessorio esterno (in tal caso, marca, modello, etc)
4. confermare che i suddetti portatili domiciliari trattansi di dispositivi prodotti da *Seers Technology* (o altro produttore) (*)
    a. Se si, esplicitare se i dispositivi portatili hanno subìto "personalizzazione" tecnologica (modifica successiva "ad hoc") per gli usi specifici della funzione chiamata a svolgere nello specifico del Progetto in ASL (es. software/firmware per *lingua* di interfaccia, ampliamento *connessioni* a periferiche , modifica dell' *interfaccia*, *porte* etc,)

(*) Utile, per sintesi, il manuale d'uso del/i portatile/i.

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Sez 2: Architettura software H&H

Si richiede la descrizione tecnica dell'architettura applicativa (**Errore. L'origine rif** dalla documentazione fornita e la risposta ai punti sotto-elencati citando, laddove possibile, anche le normative di riferimento.

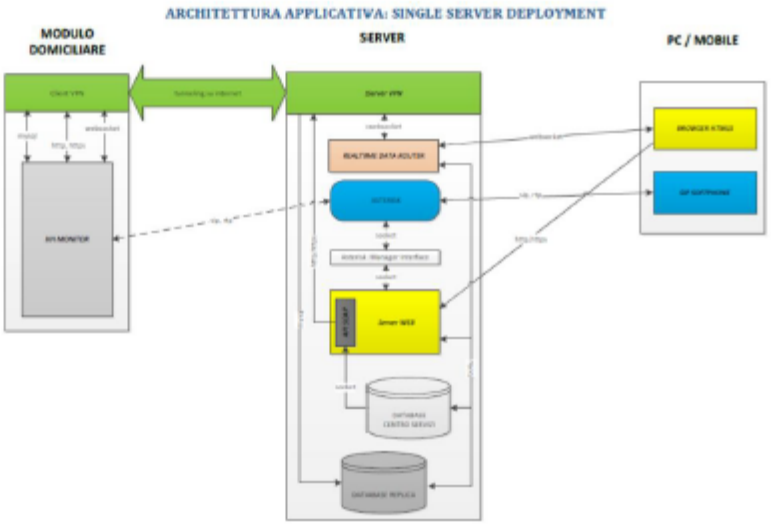

Figura 1 – Architettura applicativa

1. Descrizione tecnica della piattaforma e del suo funzionamento;
2. Requisiti infrastrutturali: Es. Sim dati, specifiche tecniche, meccanismi di sicurezza, etc…
3. Descrizione dell'interoperabilità della piattaforma:

    a. Integrazione con Edotto (DOCUMENTO EDOTTO-ARES.pdf: "*Entrando nella sezione "Gestione Pazienti", dato come input il codice fiscale, viene popolata tutta la scheda (Anagrafica) in automatico grazie al collegamento con il sistema EDOTTO. In caso di assenza del codice fiscale all'interno del database EDOTTO , si procederà con l'inserimento dei dati in maniera manuale*") -> Edotto viene interrogato in sola lettura tramite web-service e, nel caso manchi il codice fiscale, si procede all'inserimento manuale dei dati in quale database?

    b. Oltre che con Edotto, la piattaforma interagisce o è predisposta all'integrazione con componenti terze? Se si, quali ed in che modo.

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c. La comunicazione con il server presso la server Farm di Brindisi avviene tramite VPN sia per il modulo domiciliare sia per i pc/mobile? (Es. connessione dedicata? Protocolli utilizzati? Etc..)

4. Descrizione degli eventuali servizi di supporto tecnico, modalità e tipologia
5. Descrizione degli standard di riferimento impiegati
6. Descrizione dei servizi di supporto all'utente
7. Sistema di Back-up e procedure: descrizione del meccanismo di back-up, delle policy di back-up, continuità operativa e disaster recovery con le relative stime dei tempi di ripristino in caso di evento disastroso.
    a. Queste informazioni andrebbero estese anche con le specifiche della server farm di Brindisi dove è ospitato il server e se vi sono policy di sicurezza/backup anche sui client.
    b. Dall'architettura, inoltre, si evince un database di replica in merito al quale servirebbe spiegare la modalità con cui viene implementata/gestita la replica.
    c. Dallo schema dell'architettura sembra esserci anche un database sul client se così fosse descrivere, anche con un caso d'uso, ciò che avviene tecnicamente (Es. meccanismi di sincronizzazione, salvataggi locali, politiche di cancellazione, salvataggio credenziali, etc…)
8. Descrizione Service Level Agreements
9. Descrivere, anche con dei casi d'uso se esistenti, l'eventuale condizionamento dell'esperienza tecnologica e le relative conseguenze sull'impiego della tecnologia. (Es. Usabilità ed accessibilità)
10. Riportare, se esistono, tecnologie/componenti sicure comparabili ad H@H. (Es. DBMS, moduli hardware/software, librerie di codice, tools, etc…)
11. Descrizione degli strumenti di crittografia utilizzati e relativa modalità di impiego:
    a. Nel documento di architettura (DOCUMENTO DI PROGETTAZIONE ARCHITETTURA SISTEMA SOFTWARE.pdf) viene fatto riferimento all'utilizzo dei protocolli VPN, HTTPS, sono utilizzati altri protocolli in formato sicuro?
    b. Quale sistema di crittografia viene utilizzato?
    c. I certificati sono rilasciati da autorità o auto-generati?
    d. Cosa viene crittografato? (Es. password nel database, tabelle parziali, intero db, etc…)
12. Descrizione della gestione sicura dei dati:
    a. Gestione dei dati nel rispetto della privacy;
    b. Come viene gestita la qualità del dato (Es. incongruenze, ridondanze, etc…)
    c. Modalità di salvataggio (Es. sincrono, remoto, etc…) e proprietà dei dati

Annex 2 – Included studies

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Annex 3 - AMSTAR

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
Farnia, 2018	To list the criteria used in published evaluations of noninvasive HF telemonitoring projects, describe how they are used in the evaluation studies, and organize them into a consistent scheme	4 databases; 15 Aug. 2015	128 original reports	Reviewed articles led to 52 evaluation criteria classified into 6 dimensions: clinical, economic, user perspective, educational, organizational, and technical. The clinical and economic impacts were evaluated in more than 70% of studies, whereas the educational, organizational, and technical impacts were studied in fewer than 15%. User perspective was the most frequently covered dimension in the development phase of telemonitoring projects, whereas clinical and economic impacts were the focus of later phases	Telemonitoring evaluation frameworks should cover all 6 dimensions appropriately distributed along the telemonitoring project lifecycle. Our next goal is to build such a comprehensive evaluation framework for telemonitoring and test it on an ongoing noninvasive HF telemonitoring project	4/11

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
Hong, 2019	To analyze the effect of tele-monitoring on chronic obstructive pulmonary disease patients and perform subgroup analysis by patient severity and intervention type	3 databases; May 2017	27 RCTs	The included studies were divided by intervention [15 studies used tele-monitoring only, 4 studies used integrated tele-monitoring (pure control), and 8 studies used integrated tele-monitoring (not pure control)] and by patient severity [16 studies included severely ill patients, 8 studies included moderately ill patients, and 3 studies did not discuss the severity of the patients' illness]. Meta-analysis showed that tele-monitoring reduced the emergency room visits (risk ratio 0.63, 95% confidence interval 0.55-0.72) and hospitalizations (risk ratio 0.88, 95% confidence interval 0.80–0.97). The subgroup analysis of patient severity showed that tele-monitoring more effectively reduced emergency room visits in	Tele-monitoring reduced rates of emergency room visits and hospitalizations and improved the mental health quality of life score. Integrated tele-monitoring including the delivery of coping skills or education by online methods including pulmonary rehabilitation is recommended to produce significant improvement. This application of integrated tele-monitoring (the delivery of education, exercise etc. in addition to tele-monitoring) is more useful for patients with (very) severe chronic obstructive pulmonary disease than those with moderate disease. Tele-monitoring might be a useful application of information and communication technologies, if the intervention includes the appropriate	8/11

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
				patients with severe vs. moderate disease (risk ratio 0.48, 95% confidence interval 0.31–0.74; risk ratio 1.28, 95% confidence interval 0.61–2.69, retrospectively) and hospitalizations (risk ratio 0.92, 95% confidence interval 0.82–1.02; risk ratio 1.24, 95% confidence interval 0.57–2.70, retrospectively). The mental health quality of life score (mean difference 3.06, 95% confidence interval 2.15–3.98) showed more improved quality of life than the physical health quality of life score (mean difference -0.11, 95% confidence interval -0.83–0.61)	intervention components for eligible patients. Further studies such as large size randomized controlled trials with sub-group by patient severity and intervention type is needed to confirm these finding	
Lee, 2018	To create an evidence base for the effectiveness of telehealth on glycemic control in type 2 diabetes, we conducted the first systematic review of	5 databases; April 2016	4 systematic review and/or meta-analysis of RCTs	Evidence from pooling four systematic reviews found that telehealth interventions produced a small but significant improvement in HbA1c levels compared with	Current evidence suggests that telehealth is effective in controlling HbA1c levels in people living with type 2 diabetes. However there	10/11

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
	systematic reviews and meta-analyses of randomised controlled trials (RCTs) to assess the evidence of the effects of telehealth interventions on glycemic control in patients living with type 2 diabetes			usual care (MD: -0.55, 95% CI: -0.73 to − 0.36). The greatest effect was seen in telephone-delivered interventions, followed by Internet blood glucose monitoring system interventions and lastly interventions involving automatic transmission of SMBG using a mobile phone or a telehealth unit	is need for better quality primary studies as well as systematic reviews of RCTs in order to confidently conclude on the impact of telehealth on glycemic control in type 2 diabetes	
Pekmezaris, 2018	To examine the impact of intervention duration on important patient outcomes, compare HTM versus usual care on emergency department (ED) and inpatient use as well as mortality, and examine the extent to which home care moderates the effect of HTM	6 databases; Nov. 2016	26 RCTs	We found that home telemonitoring decreased the odds of all-cause mortality and heart failure–related mortality at 180 days but not at 365 days. Home telemonitoring did not significantly affect the odds of all-cause hospitalization at 90 or 180 days, or of heart failure–related hospitalization at 180 days. At 180 days, home telemonitoring significantly increased the odds of all-cause emergency department	It is critical that future studies deliberately test all essential intervention elements, such as intervention duration and the moderating effect of home care. Researchers, clinicians, and policy makers must not assume that, with HTM, decreased mortality is necessarily associated with decreased utilization.With HTM, early recognition of exacerbation can be promptly resolved at home, whereas	5/11

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
				visits. Home care provision did not moderate the effects of home telemonitoring on all-cause hospitalization	a patient who may have delayed or more serious symptom recognition can be managed successfully in the ED. Either way, the result is decreased mortality	
Yun, 2018	To comparatively evaluate the clinical effectiveness of TM versus usual care among patients with HF, including health care outcomes defined by specific characteristics such as the type of information transmission and the specific details of the study populations and interventions.	3 databases; May 2016	37 RCTs	Thirty-seven randomized controlled trials (9582 patients) of TM met the inclusion criteria: 24 studies on all-cause mortality, 17 studies on all-cause hospitalization, 12 studies on HF-related hospitalization, and 5 studies on HF-related mortality. The risks of all-cause mortality (risk ratio [RR] 0.81, 95% confidence interval [CI] 0.70–0.94) and HF-related mortality (RR 0.68, 95% CI 0.50–0.91) were significantly lower in the TM group than in the usual care group. TM showed a significant benefit when ≥3	TM intervention reduces the mortality risk in patients with HF, and intensive monitoring with more frequent transmissions of patient data increases its effectiveness	8/11

Reference	Objective	Searches	Included studies	Results (data presented)	Conclusions	AMSTAR
				biologic data are transmitted or when transmission occurred daily. TM also reduced mortality risk in studies that monitored patients' symptoms, medication adherence, or prescription changes		

Annex 4 – Summary of the studies reported in Peretz et al 2018

Author	Year	Country	Patient count	Intervention period (months)	Targeted Diagnosis	Outcome	Sentiment Analysis
Kenealy et al.	2015	New Zealand	98	4.5	COPD, HF or DM	Costs did not differ significantly between the groups.	Neutral
Boyne et al.	2013	Netherlands	197	12	HF	There were no significant differences in annual costs per patient between groups.	Neutral
Henderson et al	2013	UK	538	3	COPD, HF or DM	There were no significant differences in annual costs per patient between groups.	Neutral
Paré et al	2013	Canada	60	5.9	COPD	TM reduced the number of hospitalization days and, to a smaller extent, the number of emergency room visits. TM saved $1613 per patient per year compared to traditional homecare, representing a net gain of 14%.	Positive
Paré et al	2013	Canada	95	4	COPD, HF or DM	Significant benefits to the TM program in terms of large reductions in number of hospitalizations, length of average hospital stay, and, to a lesser extent, number of emergency room visits. the telehomecare program resulted in significant savings (41% less than usual care)	Positive

Author	Year	Country	Patient count	Intervention period (months)	Targeted Diagnosis	Outcome	Sentiment Analysis
Hicks et al	2009	USA	47	6	Post surgery; long cancer	Telehealth technology had a very positive impact on the provider–client relationship and improved care. The study also suggests that home care monitoring reduces hospitalizations and decreases personnel expenses.	Positive
Vitacca et al	2009	Italy	118	12	COPD	TM group experienced significantly fewer hospitalisations (-36%), urgent GP calls (-65%) and acute exacerbations (-71%). the average overall cost for each patient was 33% less than that for usual care	Positive
Finkelstein et al	2006	USA	20	30	COPD HF	The average visit costs were $48.27 for face-to-face home visits, $22.11 for average virtual visits (video group), and $32.06 and $38.62 for average monitoring group visits for congestive heart failure and chronic obstructive pulmonary disease subjects, respectively.	Positive
Paré et al	2006	Canada	19	6	COPD	TM over a 6-month period generated $355 in savings per patient, or a net gain of 15% compared to traditional home care.	Positive

Annex 5 – Bibliography

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DGR Deliberazione della Giunta Regionale 30 ottobre 2018, n. 1935. Modello di gestione del paziente cronico "Puglia Care". Governo della domanda e presa in carico dei pazienti cronici – Determinazioni. Bollettino Ufficiale della Regione Puglia n. 151 del 26-11-2018

DGR Deliberazione della Giunta Regionale 16 luglio 2020, n. 1088. DGR n. 1231/2016 Indirizzi operativi per la promozione e la diffusione della telemedicina nel servizio sanitario. Istituzione della Centrale Operativa Regionale per la Telemedicina delle cronicità e delle reti cliniche

Edotto is the Health Information System of the Puglia Region, in use since 2012 as an essential tool for the governance of the regional health service. The system, based on the most innovative ICT tools, facilitates the widest interaction between the subjects operating at the various levels of the health organization (Department of Welfare, Regional Health Agency, local health authorities, GPs and paediatricians, pharmacies, etc.) with the aims of satisfying the growing needs for healthcare and monitoring the health services provided in Puglia. It is structured in many modules to manage different health and administrative data flows

EU SCIENCE HUB. 15.10.2020. Cost of Non-Communicable Diseases in the EU https://ec.europa.eu/jrc/en/health-knowledge-gateway/societal-impacts/costs last access 25.03.2021

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Annex 6 Descriptive Statistics for the cost-minimisation study

Descriptive Statistics: Intervention Group

Variable	Obs	Mean	Std. Dev.	Min	Max
Sex (=1 male)	179.00	1.46	0.50	0.00	1.00
Age under65 (=1 under 65)	179.00	0.21	0.41	0.00	1.00
Severity (=1 higher severity)	179.00	0.66	0.47	0.00	1.00
DM (=1 Diabetes only)	179.00	0.18	0.38	0.00	1.00
COPD (=1 COPD only)	179.00	0.10	0.30	0.00	1.00
HF (=1 Hearth Failure only)	179.00	0.39	0.49	0.00	1.00
DM+COPD (=1 with DM and COPD)	179.00	0.04	0.21	0.00	1.00
DMHF (=1 with DM+HF)	179.00	0.15	0.35	0.00	1.00
COPDHF (=1 with COPD+HF)	179.00	0.08	0.27	0.00	1.00
DMCOPDHF (=1 with DM+COPD+HF)	179.00	0.07	0.25	0.00	1.00

Descriptive Statistics: Control Group 1

Variable	Obs	Mean	Std. Dev.	Min	Max
Sex (=1 male)	179.00	1.46	0.50	0.00	1.00
Age under65 (=1 under 65)	179.00	0.28	0.45	0.00	1.00
Severity (=1 higher severity)	179.00	0.66	0.47	0.00	1.00
DM (=1 Diabetes only)	179.00	0.18	0.38	0.00	1.00
COPD (=1 COPD only)	179.00	0.10	0.30	0.00	1.00
HF (=1 Hearth Failure only)	179.00	0.39	0.49	0.00	1.00
DM+COPD (=1 with DM and COPD)	179.00	0.04	0.21	0.00	1.00
DMHF (=1 with DM+HF)	179.00	0.15	0.35	0.00	1.00
COPDHF (=1 with COPD+HF)	179.00	0.08	0.27	0.00	1.00
DMCOPDHF (=1 with DM+COPD+HF)	179.00	0.07	0.25	0.00	1.00

Descriptive Statistics: Control Group 2

Variable	Obs	Mean	Std. Dev.	Min	Max
Sex (=1 male)	179.00	1.46	0.50	1.00	2.00
Age under65 (=1 under 65)	179.00	0.27	0.45	0.00	1.00
Severity (=1 higher severity)	179.00	0.66	0.47	0.00	1.00
DM (=1 Diabetes only)	179.00	0.18	0.38	0.00	1.00
COPD (=1 COPD only)	179.00	0.10	0.30	0.00	1.00
HF (=1 Hearth Failure only)	179.00	0.39	0.49	0.00	1.00
DM+COPD (=1 with DM and COPD)	179.00	0.19	0.39	0.00	1.00
DMHF (=1 with DM+HF)	179.00	0.15	0.35	0.00	1.00
COPDHF (=1 with COPD+HF)	179.00	0.08	0.27	0.00	1.00
DMCOPDHF (=1 with DM+COPD+HF)	179.00	0.07	0.25	0.00	1.00

Costs per patient: Intervention group

Variable	Obs	Mean	Std. Dev.	Min	Max
Hospital Costs (A)	179	964	2501	0	18684
Pharmaceutical Costs (B)	179	1122	1581	0	16727
Outpatients costs (C)	179	253	322	0	1821
Emergency room costs (D)	179	15	44	0	370

Costs per patient: Control group 1

Variable	Obs	Mean	Std. Dev.	Min	Max
Hospital Costs (A)	179	1431	4638	0	42863
Pharmaceutical Costs (B)	179	1110	1270	0	6925
Outpatients costs (C)	179	382	642	0	5456
Emergency room costs (D)	179	32	82	0	687

Variable	Obs	Mean	Std. Dev.	Min	Max
Hospital Costs (A)	179	989	3331	0	32829
Pharmaceutical Costs (B)	179	1712	6770	0	56597
Outpatients costs (C)	179	299	418	0	2725
Emergency room costs (D)	179	32	92	0	376