



Agenzia
Regionale
per la Salute
ed il Sociale
Puglia



Centro Regionale HTA
PUGLIA

TELEMONITORING OF CHRONIC DISEASES: THE EXPERIENCE OF AZIENDA SANITARIA LOCALE BR, BRINDISI (IT) WITH HEART FAILURE, DIABETES AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

HTA REPORT N.1/2021

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

6

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

8 Bari, July 2021

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15 *This document should be cited as follow:*

16 F Bonifazi, R Lagravinese, F Cangialosi, E Chiarolla, P Notarangelo, R Giuliani, G Chetta, EA Graps.
17 Telemonitoring of chronic diseases: The Experience of Azienda Sanitaria Locale BR, Brindisi (IT). AReSS Puglia,
18 Agenzia Regionale Strategica per la Salute ed il Sociale. Bari, February 2021

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24 **Funding**

25 The production of the present report was made possible by financial contributions from AReSS Puglia. The
26 intellectual content of the report is property of AReSS Puglia.

27 **Limitations**

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

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36 **Declaration of Conflict of Interest**

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

40 **Acknowledgements**

41 **Data provided by:** Antonio Chieti, Vito Lepore (data from AReSS Regional Health System Database named
42 “Banca Dati Assistito”); Francesco Galasso (data on local experience at ASL-BR)

43 **Internal reviewer:** Giovanni Mastrandrea

44 **External reviewer:**

45 **Industry:** Item Oxygen S.r.l. [70022 Altamura (BA) – ITALIA, <https://www.itemoxygen.com/>]

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	Description
ADI	Assistenza 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

127 1. Abstract (en)

128 1.1. Background

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

132 1.2. Objectives

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

138 1.3. Search Methods

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

141 1.4. Selection criteria

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

145 1.5. Main results

146 1.5.1. Published evidence

147 **Heart Failure**

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

153 **Diabetes type I and II**

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

160 **Chronic obstructive pulmonary disease**

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

168 1.5.2. Cost-Minimization Analysis of the TM platform in use at ASL-BR

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

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

176 1.6. Limitations of the Cost-Minimization Analysis

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

180 1.7. Conclusions

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

188 2. Abstract (it)

189 2.1. Background

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

193 1.2 Obiettivi

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

199 1.3 Metodi di ricerca

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

202 1.4 Criteri di selezione

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

206 1.5 Principali risultati

207 1.5.1. Evidenze in letteratura

208 **Insufficienza Cardiaca**

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

214 **Diabete di tipo I e II**

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

221 **Broncopneumopatia cronico ostruttiva**

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

230 [1.5.2. Analisi di minimizzazione dei costi della piattaforma di TM in uso presso ASL-BR](#)

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

238 [1.6. Limitazioni della Analisi di Minimizzazione dei Costi](#)

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

243 [1.7. Conclusioni](#)

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

252 3. Introduction

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

261 In Italy, telemedicine is defined as that “innovative approach to healthcare practice which allows the delivery
262 of service at distance using digital devices, internet, software and telecommunications networks”
263 [Conferenza permanente per i rapporti tra lo Stato, le Regioni e le Provincie Autonome di Trento e Bolzano,
264 2020].

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

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

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

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

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

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

287 4.1. Health problem

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

290 4.1.1. Definition of target condition/disease

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

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

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

321 4.1.2. Symptoms, consequences

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

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

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

340 [4.1.3. Number of patients \(epidemiology\)](#)

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

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

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

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

356 *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	

357 [4.1.4. Burden of disease, resource use](#)

358 It has been observed [Stewart, 2001] observed that the overall population rate of expected life-years lost
 359 due to **heart failure** in men was 6.8 years/1000 and for women 5.1 years/1000. HF imposes a huge economic
 360 burden, estimated globally at \$108 billion per annum [Cook, 2014], with total costs expected to increase by
 361 127% between 2012 and 2030 [Savarese, 2017]. In developed countries 1-2% of all healthcare expenditures
 362 is devoted towards HF [Liao, 2008]. HF is the most common cause of readmission, and HF-related mortality
 363 has a similar or even higher incidence than cancer mortality [Yun, 2017]. The global economic burden of HF
 364 is estimated at \$108 billions per annum, with \$65 billions attributed to direct and \$43 billions to indirect costs.
 365 Europe accounts for 6.83% of total global HF costs [Lesyuk, 2018]. In Italy, the direct cost per patient per year
 366 is approximately €11 864 (National Health Service perspective), of which 84.6% related to hospitalizations,
 367 10.1% to medicines prescriptions and 5.3% to specialist examination/diagnostic procedures [Maggioni,
 368 2016].

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

373 countries [WHO, 2016]. Estimates of healthcare expenditure due to diabetes in the adult population (aged
374 20-79 years) in the European Region in 2017 was 181 billion international dollars [EU SCIENCE HUB, 2020].

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

387 4.1.5. Current management of health condition

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

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

393 4.1.6. Existing quality standards

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

398 4.1.7. Relations to other conditions or treatments

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

402 4.1.8. Change in patient segments

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

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

413 4.2. Description of the health technology

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

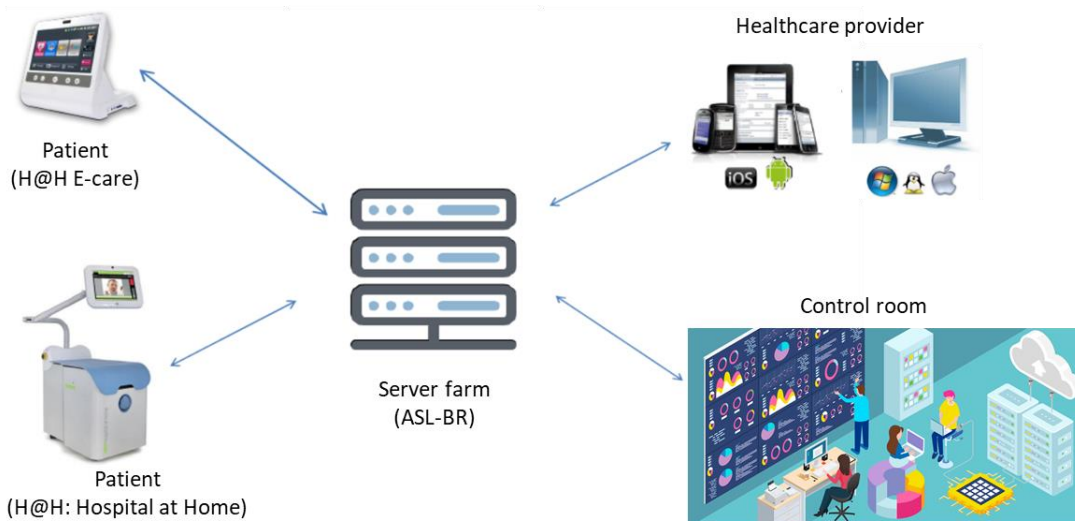
420 ASL-BR has adopted the technical solution, named H@H, designed and implemented by ITEM Oxygen srl, an
421 Italian manufacturer (<https://www.itemoxygen.com/en/>) who was awarded the call for tender issued by ASL-
422 BR. H@H is a web-based TM system providing a telemonitoring solution to support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

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

429 4.3. Technical characteristics

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

438
439 *Figure 1 – H@H structure*



440
441 The **control room** is located in the Community Care Centre of Ceglie Messapica (Presidio Territoriale di
442 Assistenza, PTA).

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

449 It allows:

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

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

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

456 It is provided with:

- 457 • Intracavitary suction pump (-0.8 bar)
- 458 • Oxygen therapy by O2 concentrator (O2 flow: 0 ÷ 4 l/min. @ 94 ÷ 95% or 5 l/min. @ ≥ 90%)
- 459 • 17" touch screen with high quality video call through webcam
- 460 • Integrated stereo audio system and ambient microphone
- 461 • Physiological parameters monitor

462 The **H@H E-care** device², thanks to its web-based technology, allows the simultaneous and remote activation
 463 of the videoconference and/or video consultation and the visualization of the patient's clinical parameters,
 464 trends and abnormality thresholds, thus resulting in a clinical tool “close to the patient” as it allows to
 465 establish a continuous and psychologically reassuring link. *H@H: E-care* is a **medical device** compliant with
 466 the requirements of EC Directive 93/42/CEE (notified body no. 1023).

467 It allows:

- 468 • Video Consultation
- 469 • Clinical Parameter Measurement/Personalized Chart consultation
- 470 • Remote auscultation

471 It is provided with:

- 472 • Supporting voice guidance
- 473 • 10.1 cm touch screen
- 474 • Multiuser support
- 475 • Wired or Wireless connection mode.

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

479 [4.3.1. Interoperability: Integration needs \(EPR, devices, with current applications, technical standards](#)
 480 [etc.\)](#)

481 In addition to interacting with the different types of clients (tablets, smartphones, personal computers, H@H:
 482 Hospital at Home, H@H-care, H@H-Care app), the H@H platform interacts through a web service technology
 483 with the information system of the Puglia Region “*Edotto*”³ from which, in read-only mode, it retrieves
 484 patients’ healthcare civil registry data. If such information is not present in *Edotto*, the authorised operator
 485 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.

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

489 [4.3.2. Technical and users' support](#)

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

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

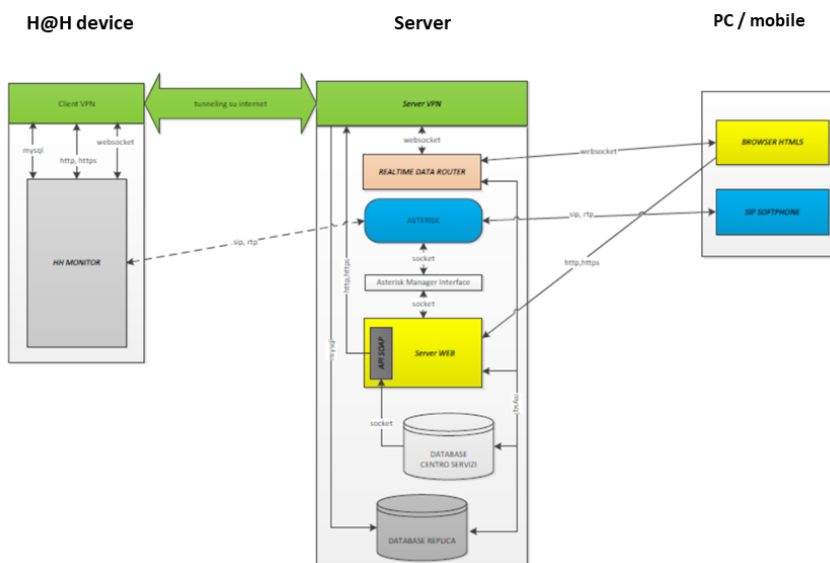
498 GPs and specialists to be involved in the TM service are supported during the first two weeks by control room
 499 operators and ITEM Oxygen telemedicine specialists, to be adequately trained in the use of the system.
 500 Patients enrolled in the TM service are appropriately trained by ITEM Oxygen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

502 [4.3.3. Technical environment](#)

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

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

508 *Figure 2 – System architecture*



509
 510 The web platform is developed using programming tools and libraries for Java and PHP. The DBMS is MySQL.
 511 Clients interact with the platform via the http/https protocol, websockets and via VPN connection.

512 4.3.4. Back-up systems and procedures

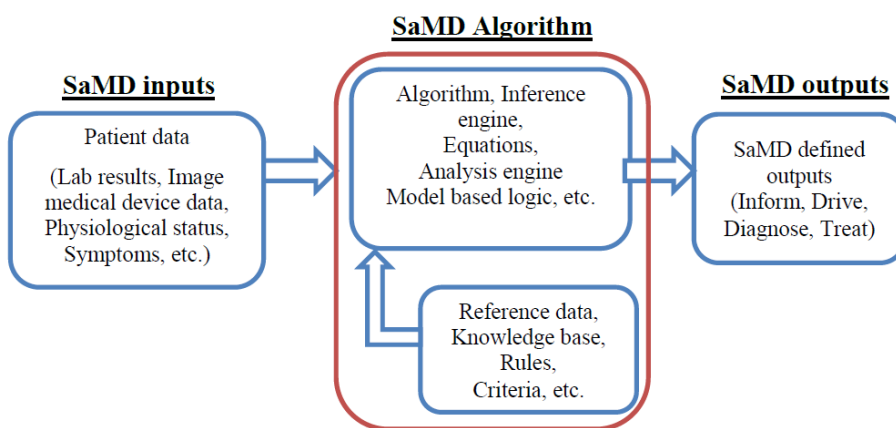
513 The management of the platform (server side) - including security procedures and measures, backups,
514 operational continuity, management of network equipment (firewall, antivirus, etc.) - is the responsibility of
515 the ASL-BR server farm manager.

516 5. Domain: Safety

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

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

527 *Figure 3 – risks and benefits posed by SaMD*



528

529 5.1. Clinical safety (patients and staff)

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

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

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

538 5.2. Technical safety (technical reliability)

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

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

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

546 5.2.1. What do the Service Level Agreements cover?

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

- 548 • High: totally blocking the system

- 549 • Medium: partially blocking the system
- 550 • Low: blocking only some functions

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

552 *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

553

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

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

557 The reporting of problems is managed in the following ways:

- 558 • 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.
- 560 • Telephone:
 - 561 ○ The service is provided by control room operators from Monday to Saturday (8.30-12.30 / 14.00-18.00).
 - 562 ○ If the problem is not resolved by phone, an appointment is scheduled for technical intervention with the ITEM OXYGEN specialist.

566 [5.2.2.How is security of data and the database \(data privacy\) and quality of data managed?](#)

567 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.

570 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.

572 [5.2.3.encryption/cryptography](#)

573 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.

576 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.

579 [5.2.4.data ownership](#)

580 Data are owned and managed by ASL-BR.

581 6. Domain: Clinical effectiveness

582 6.1. Methods

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

585 Table 3. - PICO

Population	Patients with one or more of the following conditions: <ul style="list-style-type: none"> - 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

586 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])

587 Searched on 18 Feb. 2020

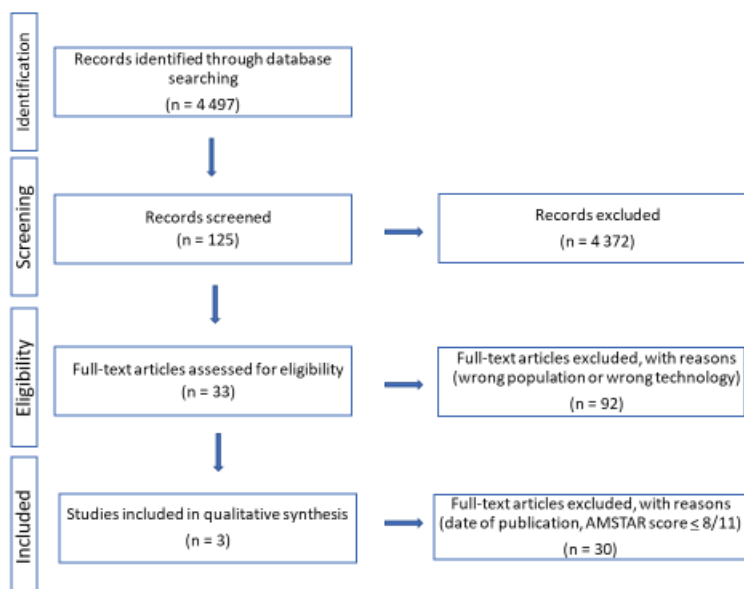
588 The systematic search was conducted on 18 Feb 2020 in the PubMed database, and we retrieved 4 497
 589 articles. The search was then limited to Systematic Reviews published in English, in the last five years and
 590 filtered by “humans”. Overall, 125 hits were identified.

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

595 6.3. Flow chart of study selection

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

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



600

601 6.4. Analysis

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

607 6.5. Results

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

- 610 • **Heart Failure (HF):** Yun JE, Park JE, Park HY, Lee HY, Park DA. Comparative Effectiveness of
611 Telemonitoring Versus Usual Care for Heart Failure: A Systematic Review and Meta-analysis. J Card
612 Fail. 2018;24(1):19-28. doi:10.1016/j.cardfail.2017.09.006
- 613 • **Diabetes mellitus (DM):** Faruque LI, Wiebe N, Ehteshami-Afshar A, et al. Effect of telemedicine on
614 glycated hemoglobin in diabetes: a systematic review and meta-analysis of randomized trials. CMAJ.
615 2017;189(9):E341-E364. doi:10.1503/cmaj.150885
- 616 • **Chronic obstructive pulmonary disease (COPD):** Hong Y, Lee SH. Effectiveness of tele-monitoring by
617 patient severity and intervention type in chronic obstructive pulmonary disease patients: A
618 systematic review and meta-analysis. Int J Nurs Stud. 2019;92:1-15.
619 doi:10.1016/j.ijnurstu.2018.12.006

620 6.5.1. Heart Failure

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

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

634 6.5.2. Diabetes

635 Telemedicine achieved a statistically significant but **modest reductions in HbA1C** in all 3 follow-up periods
636 (difference in mean **at ≤ 3 mo: -0.57%** , 95% confidence interval [CI] -0.74% to -0.40% [39 trials]; **at 4–12**
637 **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]).
638 TM interventions were defined as any electronic form of communication between provider and patient,
639 including telephone, smartphone application, email, text messaging, web portal (websites where patients
640 upload blood glucose levels or other clinical data and share these with their health care providers, with or
641 without provider-to-patient communication) and “smart” device or glucometer (any computerized device
642 specifically developed to collect and transmit patients’ data to health care providers).

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

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

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

660 6.5.3. COPD

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

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

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

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

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

684 *Table 4. - Main results from the selected studies*

Effect of TM compared to usual care	HF	DM	COPD
Mortality	Decreasing all-cause mortality (RR 0.81, 95% CI 0.70–0.94; I2 = 16%) HF-related mortality (RR 0.68, 95% CI 0.50–0.91; I2 = 8%) The all-cause mortality rate significantly lower in studies: published in Europe, involving patients > 65 years, transmitting ≥3 biologic indicators	No good evidence found to support a reduction of mortality	Not available
Healthcare resources use	reduced risk of HF-related hospitalization (RR 0.86, 95% CI 0.74–1.00; I2 = 36%)	Not available	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] 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]
Quality of life	Not available	No good evidence found to support an improvement in QoL	Improved mental health QoL [RR 3.06, CI 2.15–3.98], failed at improving QoL

Effect of TM compared to usual care	HF	DM	COPD
Other improvements	Not available	<p>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%.</p>	Not available
		<p>No good evidence found to support a reduced risk of hypoglycaemia</p>	

685

686 7. Domain: Patient perspectives

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

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

692 8. Domain: Economic aspects

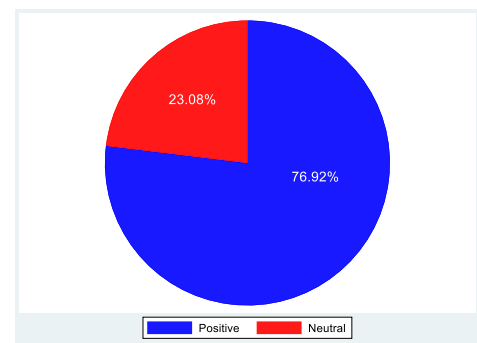
693 The development of this assessment framework is based on a two-step approach; the first step involves a
694 review of the literature and collecting information on the costs of telemedicine solutions and services. The
695 second step compares costs and savings of the Hospital & Home(H@H) pilot with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

696 8.1. Economic evaluation

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

704 The duration of the Remote Patient Monitoring (RPM) service provision varied a great deal: from 3 months
705 to 2.5 years, and the number of participants ranged from 4 to a sample of 538 seniors suffering from various chronic conditions
706 including chronic obstructive pulmonary disease, congestive heart failure, diabetes mellitus and hypertension (HTN). All studies,
707 except the articles by Walsh et al. (2005), are based on randomized trials with a treatment group (which uses TM) compared with a
708 control group (usual care). The results from these 13 articles show that, in essence, telemedicine is generally perceived and judged to
709 be cost effective in 76.92% of the cases addressed by the literature's neutral effects (23.08%). The latter, mainly found in systematic
710 reviews that reach a conclusion on the lack of robust and high-quality studies regarding the evaluation of telemedicine services,
711 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
712 results of the analysis.
713
714
715
716
717
718
719

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



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

725 Paré et al [Paré, 2013a], analysed the consumption of healthcare services by 95 patients in Canada with
726 various chronic diseases over a 21-month period (12 months before, 4 months during home telemonitoring
727 use, and over 5 months after withdrawal of the technology). The economic analysis strategy adopted for this
728 study was the one of cost minimization. This strategy can be used to compare the costs of different
729 interventions, whose clinical results are considered similar, to determine which costs less. It provides a
730 comparative basis which, in addition to calculations of costs and benefits, must be able to indicate whether
731 telehealth appears to be better than the usual care. The total costs for the 95 patients were 364,840 \$
732 for usual care and 216,903 \$ for TM (see Table 5). In summary, the TM program resulted in a significant saving
733 (41% compared with traditional home care).

734 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

735

736 Cost-Minimization Analysis: the case of Hospital@Home

737 8.1.1.Setting of analysis

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

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

755 8.1.2.Treatment Group versus Control Groups

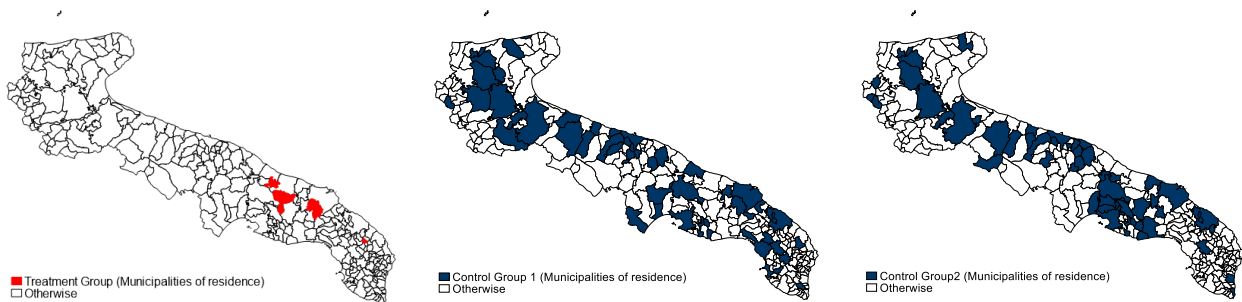
756 From 2015 to April 2020, 207 patients have been enrolled into the study, and TM was used 302 times⁴ (some
757 patients used TM services multiple times). The patients considered in this analysis were those who have used
758 the technology at least once from mid-2015 to the end of 2019. Data on outpatients' visits and
759 pharmaceutical prescriptions costs and hospital information are available in the Regional Health System
760 Database (RHSD) up to 2019 for only 191 of the 207 patients, and RHSD was used to calculate resources
761 consumption.

762 The patients included in the treatment group were all resident in the Ceglie Messapica health district. The
763 patients in the control groups, on the other hand, were stratified over the entire regional territory extracted
764 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.

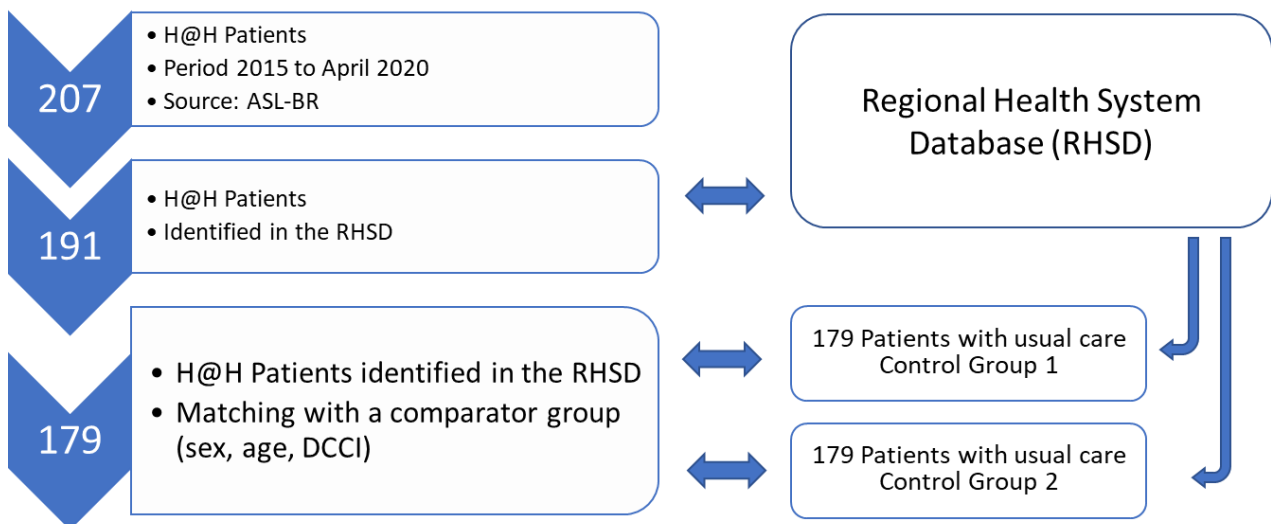
765 each of the two control groups has been feasible for 179 patients only of the initial 207. Therefore, our
766 analysis was carried out on the sample of 179 patients (86,4% of the total patients in the H&H project).

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



769 Figure 6 summarises the adopted procedure.

770 *Figure 6 – Procedure Used to identify Treatment and Controls groups*



771
772 The analysis undertaken in this study aimed to identify and measure the potential impact of TM on healthcare
773 costs compared with the traditional model (usual care).

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

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

784 In particular, the selected variables are:

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

- 790 f) Pharmaceutical costs;
- 791 g) Outpatient clinics cost;
- 792 h) Number of emergency room visits;
- 793 i) Emergency room costs.

794
795 Table 6 shows the demographic characteristics of the three analysed population (treatment group and the
796 two control groups) during the index year; the average age of the treated patients is 72.06 years, and it is
797 slightly lower in the two control groups: 71.27 (group 1) and 72.03 (group 2), respectively. 53.63% of patients
798 in the treatment group are men. The same percentages were recorded in the two control groups. More
799 details are reported in Annex 6.

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

806 *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%)

807
808 To assess the level of homogeneity between the three groups under evaluation and before analysing the
809 costs incurred by the regional health service for TM Vs usual care. The t-test was performed to compare
810 between- and within-group differences of scores for health resource variables.

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

821

	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 (€)					
Intervention	179	964.09	2500.61	-1.19	0.24
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			

823 t=5%

824

	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					
Intervention	179	964.09	2500.61	-0.08	0.94
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		

826 t=5%

827

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

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

Variables	Intervention	Control 1	Control 2
<i>Number of hospitalizations</i>	49	62	51
<i>(of which) Number of urgent hospitalizations</i>	29	29	30
<i>Total length of hospitalization under the ordinary regime (LOSH)</i>	421	537	458
<i>Duration of urgent hospitalization (LOSUr)</i>	225	275	286
<i>Hospital cost (A)</i>	172,572	256,216	176,989
<i>Pharmaceutical Cost (B)</i>	200,910	198,721	306,505
<i>Outpatients clinics services costs (C)</i>	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
<i>Number of visits to the emergency room</i>	67	111	86
<i>Emergency room costs (D)</i>	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

833 The analysis of data in Table 9 allows to identify the average total saving equal to € 114,493.50
 834 [(529,057+542,616)/2 -421,343] and the average saving per patient equal to € 639.63 (114,493.5/179).
 835

836 8.1.3. Unit costs or prices for each resource used

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

840 *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

841 *Table 11. - unit and yearly costs (excluding VAT) for TM devices and services*
 842

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

843 Moreover, additional information on human resources used to run the service during the pilot phase (2015-
844 2019) can be extracted from the documentation provided by ASL-BR:

- 845 • GP accessing the system at least twice a day, 10 times per week (in the morning and in the evening)
- 846 to check patients' status as measured by the H@H device: 144.60 €/patient/week⁶;
- 847 • Number of monthly accesses of a nurse at patient home: 44⁷;
- 848 • Average duration of a single access of a nurse at patient home: 20 minutes⁷.

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

- 850 - Yearly cost of a nurse (estimated from CAT. D3 - INFERMIERE, CCNL: Comparto Sanità, 2016-2018)
851 → 28,000.00 (146 workable hours per month)
- 852 - Personnel in the control room (office worker) is to be engaged for 5 minutes each time a nurse is
853 caring a patient at home (44 per month) → office workers' time: 5*44=220 minute/month per patient;
- 854 - Personnel in the control room (office worker) may receive requests for support from
855 patients/caregivers for an additional time estimated to be about 10% of the monthly time per patient
856 → 10%*220=22 minute/month per patient;
- 857 - Yearly cost of an office worker (estimated from CAT. D, CCNL: Comparto Sanità, 2016-2018) → 25,000
858 €/year (152 workable hours per month)

859 8.1.4. Limitation

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

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

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

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

873 8.2. Business case (institutional level)

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

877 Considering that:

- 878 • the average duration of each treatment is 25 days⁶;

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)

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

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

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

- 884 • € 186.96 medical device unit cost per treatment [2,243.52/12];
- 885 • € 272.96 medical device unit yearly cost per patient [(2,243.52/12)*1.46].

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

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

890 *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

891

892 [8.2.1. Results of the business case](#)

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

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

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

905 9. Domain: Organisational aspects

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

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

914 Eligibility criteria in ADI with TM include:

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

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

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

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

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

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

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

940 Nurses are in charge for visiting patients at home daily.

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

942 10.1. Ethical issues

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

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

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

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

958 10.2. Legal issues

959 In EU Countries, the GDPR⁸ provides the regulatory framework to develop telemedicine applications assuring
960 privacy and data protection. However, several concerns should be addressed as the maintenance, use, and
961 replacement of devices^{Errore. Il segnalibro non è definito.} as well as the cybersecurity system (TM implies the storage,
962 archiving and transmission of data concerning the health of patients, as well as the remote collaboration of
963 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)



Bari, 15 Giugno 2020

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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

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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 autoprodotta/ 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, autoprodotta, 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, Colesterolo metro)
 - 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 sì, esplicitare se i dispositivi portatili hanno subito "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.

Sez 2: Architettura software H&H

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

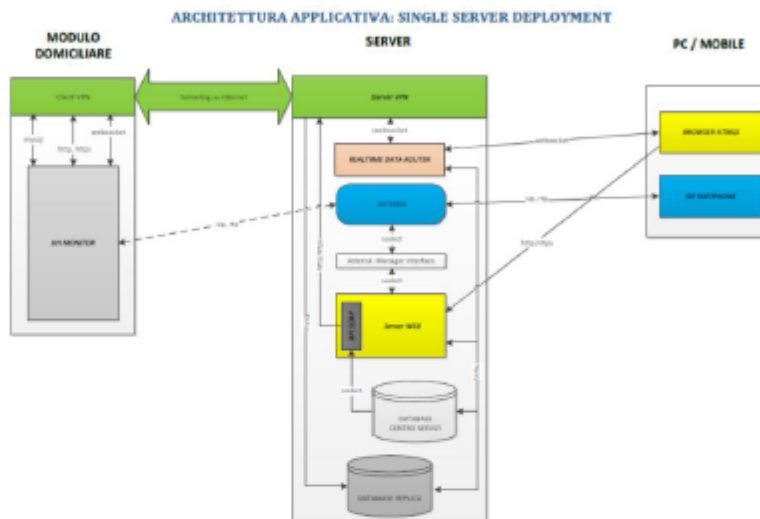


Figura 1 – Architettura applicativa

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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 sì, 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

971 Annex 2 – Included studies

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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
				<p>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)</p>	<p>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</p>	
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		

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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

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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

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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